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Molecular polymer – polymer compositions. Synthetic aspects

A D Pomogailo

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Abstract. The main ways of improving the compatibility of polymer – polymer compositions containing polyolefins as one component are considered. Considerable attention is given to the preparation of polyolefins in the presence of an ingredient bound to the catalyst in the catalytic (including consecutive) polymerisation of olefins. The so-called reactor blends and the synthesis and structure of diblock and conducting composites are described. The important role of compatibilisation of polymers of different nature with the use of a third component is pointed out. The formation mechanism of molecular compositions, the structure and properties of the intermediate layer and the main fields of application of synthetic polyolefin – polymer compositions are discussed. The bibliography includes 335 references.

I. Introduction

In recent decades, the assortment of composite materials produced from industrially important polymer blends or alloys has much expanded. Blending of two or more thermoplastics, an intricate physicochemical process which proceeds under the action of mechanical forces and high temperatures, is an efficient method for the preparation of novel materials with desired properties. Most pairs of polymers are incompatible; however, targeted modification of their morphology allows preparation of polymer blends with reasonable operating characteristics.

Molecular design of multicomponent polymeric systems is a rather complicated problem. That is why communications concerning various physicochemical, structural and other aspects of this problem have been reported only recently.^{1–13} One of the reasons preventing direct blending of polyolefins (PO) with engineering plastics is the non-polar character of the PO. In this

connection design of multicomponent thermoplastic composite materials requires that considerable attention be given to the structural and chemical modification of ingredients (compounds). To achieve compatibility means to minimise the interfacial stress and to improve the interfacial adhesion. This allows the preparation of materials with good deformation – strength characteristics, high impact viscosity, thermal stability, are readily reprocessed, *etc.*, without essential modification of their structure. In particular, improvement of the operating characteristics (*e.g.*, mechanical strength, crack resistance, light stability, colorability and printing sensitivity, reduction of electrifiability and sweating, *etc.*) of PO and, first of all, low-density polyethylene (LDPE) and polypropylene (PP) requires that they be modified with various additives including those of high-molecular-mass. Modification of the PO components of polymer – polymer compositions (PPC) is performed in both the formation (copolymerisation) stage by post-modification (graft polymerisation, modification of the surface, *etc.*) and immediately during the preparation of PPC (the so-called reactor blends or *in situ* preparation of PPC). Such modified PO act as compatibilisers (interfacial agents) and improve the compatibility of ingredients.

Yet another reason for increased interest in PPC is the fact that these types of polymer blends are often formed as processing waste and cheap, degraded polymeric products can be re-used.^{14–16} For both economic and environmental safety reasons, the volume of utilised polymer blends and thermoplastic alloys has been substantially increased since the early 1980s. Currently, requirements imposed on the environmental safety of processing and consumption of polymeric products are continuously increasing. This gives an impetus to researchers to place the problems of recycling of such materials as PO (60% of the total volume of polymeric waste), polystyrene (PS), poly(vinyl chloride) (PVC), poly(methyl methacrylate) (PMMA), poly(ethylene terephthalate) (PETP), poly(tetrafluoroethylene) (PTFE), polyurethane (PU), polyamide (PA), rubber, cross-linked polyethers, cellulose-containing and multilayered materials as a focus of their efforts. After development of efficient methods for separation, reprocessing and/or modification, these materials would be a cheap and important source of polymeric raw materials, since the countries with well-developed economies produce 20 vol.%, or 8 mass %, of

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of nearly 200 million tons of solid household waste per year. However, different compositions of such complex raw materials are responsible for the formation of some incompatible ingredients in the recycling. This causes a deterioration in the physical properties of the end products and the materials become brittle. Moreover, some environmentally hazardous components of polymer blends favour the destruction of other blend components (in particular, PVC causes destruction of PETP and other polymers). Recycling and, especially, sorting expenditures aimed at separating raw materials into individual, compatible types of polymers lead to a substantial increase in the cost : property ratio compared to that for the processes based on the use of primary polymer blends. Different types of plastics, *e.g.*, thermoplastics, thermosetting plastics, multilayered blend-based composite materials, *etc.*, require a different approach.

A pair of polymers is considered compatible if its components have similar polarities, have similar functional groups or can interact under blending conditions to form donor–acceptor, hydrogen and other types of bonds, as well as if they are structurally similar and have similar solubilities. However, meeting these conditions is sometimes insufficient, so the number of compatible polymers is small. This especially concerns such non-polar polymers as PO. For instance, LDPE and high-density polyethylene (HDPE) are poorly compatible; co-crystallisation of linear low-density polyethylene (LLDPE) and LDPE results in the formation of separate crystal aggregates on the micrometre level;¹⁷ and PE and PP are immiscible on the molecular level. Moreover, even such a pair as isotactic and syndiotactic PP is also incompatible on the molecular level.

Therefore, when analysing polymer compatibility, one should take into account not only thermodynamic, but also chemical aspects, namely, the interaction between macromolecules. There are two approaches to the design of compatible polymer–polymer systems.⁴ These are (i) linking of macromolecules by chemical bonds (the synthesis of block copolymers, interpenetrating polymer networks, cross-linking of blend components) and (ii) modification of the chemical structure of polymers to obtain negative free energy of mixing (if polymer macromolecules contain functional groups that can strongly interact, some of the components are either modified, thus changing the chemical structure of the monomer units, or copolymerised). Thermodynamic incompatibility of polymer blend components prevents the formation of a common crystal lattice (*i.e.*, no mixed crystals are formed). Nevertheless, an intermediate, interfacial layer between the ingredients of a PPC can exist in this case due to the formation of common supramolecular structures, specific packing of the polymer chains and the absence of well-defined interfaces between the elements of supramolecular order even for crystalline polymers. This to a great extent determines the strength and nature of adhesive forces in the system, which strongly affects the surface area of true interface (phase contact), microrheological processes and contact reactions at the interface. Specific features of the adhesive interactions also depend on the preparation conditions of PPC: *e.g.*, mechanical mixing of components leads to the formation of intermediate layers only as a result of physical interparticle interaction.

A way to design novel materials with improved properties involves the preparation of microheterogeneous compositions with controllable structural inhomogeneity. This class of materials comprises compositions containing PO as one of the ingredients. The results of economic and environmental analysis¹⁶ of the ‘life cycle’ of polymers, which includes their synthesis, processing and modification, usage, waste separation, recycling, re-use and final utilisation of waste allowed one to rank (i) PO first among the widely used plastics and (ii) PP first among all PO. This choice is also determined by the variety of PO-based polymer blends, alloys and composites (including the *in situ* prepared compositions).

This review concerns main approaches to the PO-containing PPC. Particular emphasis is placed on the synthetic aspects of the

problem. Often, though not always, the use of such systems allows compatibility of components on the molecular level. The definition of such compositions as ‘molecular compositions’ (see the title of this review) should be considered to some extent conventionally since the preparation of PPC involves blending of components not only on the molecular level, but also on the level of microphase aggregates consisting of a large number of like macromolecules. In addition, sometimes it is impossible to clearly distinguish between different procedures for the preparation of PPC because many of them can be formed following different mechanisms. This also makes formal classification of PPC difficult.

II. Modern approaches to the description of the properties of polymer–polymer compositions

To gain an insight into specific features of PPC-containing systems, we have to briefly outline the methods for analysis of their thermodynamic and physicomechanical properties.

It does not always happen that the use of simple physical polymer mixtures consisting of components with complementary properties leads to desired results. The reason is thermodynamic incompatibility of most polymer pairs, which is largely because of a small entropy of mixing. Therefore, all polymer compositions to some extent undergo separation into different phases that are characterised by weak adhesion, which deteriorates the properties of the compositions. Usually, ‘compatibility’ of polymers refers to their mutual solubility. In the case of polymer blends, the term ‘miscibility’ is most often used. A necessary, but not sufficient, condition for thermodynamic compatibility of polymers is negative free energy of mixing, G_m :

$$\Delta G_m = \Delta H_m - T\Delta S_m.$$

Due to the high molecular mass of polymers, the entropy of mixing of two macromolecules, ΔS_m , changes only slightly. Hence, compatibility of a pair of polymers requires that the enthalpy of mixing, ΔH_m , be negative, zero or very slightly positive. In addition, specific interactions between miscible polymers must occur (see above).

Methods for studying and improving the thermodynamic compatibility of polymers have been reviewed by Tager and Blinov.¹⁸ According to their concept, the best miscibility is characteristic of those polymers whose molecules contain functional groups with opposite functionalities, capable of forming hydrogen, donor–acceptor, ionic, π -bonds and other types of bonds, rather than of structurally (or compositionally) similar polymers. The following simple equation for calculating the free energy of mixing of polymers was proposed by Tager:¹⁹

$$-\Delta g_x = \Delta G_{III} - (\omega_I \Delta G_I + \omega_{II} \Delta G_{II}),$$

where Δg_x is the mean free energy of mixing of polymers with each other per gramme of the blend; ΔG_I , ΔG_{II} and ΔG_{III} are the Gibbs energies of mixing of polymers I, II and their blend dissolved in the same solvent, respectively; and ω_I and ω_{II} are the mass fractions of polymers I and II in the PPC. Compatibility of polymers is strongly affected by not only the molecular nature and molecular masses of the components, but also their molecular mass distribution.²⁰ However, often, ‘compatibility’ of polymers means the achievement of good mechanical properties rather than compatibility on the thermodynamic level. Keeping this in mind, it should be noted that practically even compatible polymers can appear to be immiscible due to problems arising during the preparation of PPC.

There are three main methods for polymer blending. They include mechanical mixing, film casting from common (the same) solvent and *in situ* blending, *i.e.*, polymerisation of a monomer in the presence of the other (most often, preliminarily swollen) polymer. Each of these methods has specific advantages and drawbacks. For instance, the simplest method, mechanical mixing, cannot always be realised due to limited thermal stability of a

particular ingredient in specified temperature and homogenisation time ranges. Other polymers, being compatible at room temperature, can be incompatible at higher temperatures. Sometimes, casting from common (the same) solvent is precluded by solubility problems and by immiscibility of particular polymers in the presence of specific solvents. Often, the only way of overcoming these obstacles is to use *in situ* polymerisation. However, this is also not a universal procedure since during the polymerisation one monomer can become a solvent for the other polymer and this can induce phase separation of the components. For instance, polymerisation of vinyl chloride in the presence of chlorinated PE can result in monophase or two-phase products depending on the initial reagent ratio.²¹ Nevertheless, *in situ* polymerisation is considered as a potentially promising industrial method for the preparation of polymer blends. Numerous PPC prepared in this manner have been patented. This method allows the preparation of thermodynamically stable PPC; however, they can become unstable on heating, which means that such PPC have lower critical solution temperatures (LCST) and, hence, should be prepared at temperatures below LCST.

Considerable attention has been given to the problems of design of PPC from ingredients with complementary properties. Unfortunately, no general equations for the description of the dependence of a particular property of a PPC on its chemical composition have been proposed so far. For instance, the problem of calculations of the modulus of elasticity, E_{PPC} , for a polymer blend from the known moduli of elasticity of particular components or phases is still to be solved.^{22,23} The moduli of two-phase blends are often estimated using the Coran–Patel approach²⁴ based on the assumption that the magnitudes of the moduli of elasticity of a two-phase polymer blend (Young's modulus or shear modulus) must lie between the effective upper (E_u) and low (E_l) moduli calculated from the models of parallel and series linking of the components. The moduli E_u and E_l are calculated as follows:

$$E_u = \varphi_1 E_1 + \varphi_2 E_2,$$

$$E_l = \left(\frac{\varphi_1}{E_1} + \frac{\varphi_2}{E_2} \right)^{-1},$$

where E_1 and E_2 are the moduli of elasticity of the starting components 1 and 2 and φ_1 and φ_2 are their volume fractions ($\varphi_1 + \varphi_2 = 1$). The modulus of the two-phase blend, E , can be written in the form

$$E = f E_u + (1-f) E_l,$$

where $0 < f < 1$. The maximum and minimum value of the modulus of elasticity corresponds to $f = 1$ and $f = 0$, respectively.

Considering PPC as specific filled systems, one can use an approach known as the mean field approximation for spherulites in the matrix:²⁵

$$\frac{E_c}{E_m} = \frac{(1-\varphi)E'_m + (v^* + \varphi)E_r}{(1+v^*\varphi)E'_m + v^*(1-\varphi)E_r},$$

where E_c , E_m , E_r are the moduli of the composite, matrix and an elastic inclusion with the volume fraction φ , E'_m is the real part of the elastic modulus of the matrix, $v^* = 2(4 - \nu_m)/(7 - 5\nu_m)$ and ν_m is the Poisson coefficient of the matrix. This expression imposes no limitations on both the volume fractions of ingredients and the ratio of the modulus of elasticity of the matrix to that of the inclusion. If the moduli of elasticity of the matrix (E_m) and inclusion are substantially different, it is appropriate to use the simplified Guth relationship which takes into account the pair interaction between rigid particles:²⁶

$$E_{PPC} = E_m(1 + 2.5\varphi + 14.1\varphi^2).$$

At $\varphi < 0.4$, the results of calculations using this formula coincide with experimental data.

There are many equations derived based on different models of matrix compositions (*e.g.*, the Smallwood and Takayanagi equations, *etc.*); however, they are rarely used. All of them use the volume fraction of a component, φ , as the only structural parameter, though the experimental data show that the physico-mechanical properties of PPC are also affected by salient features of their morphology. For instance, the properties of ultrahigh-molecular-mass PE (UMMPE) depend not only on the volume fraction of crystallites, but also the ratio of the fractions of crystallites with compacted and aligned chains and on the type of mutual arrangement of these crystallites.²⁷

Therefore, PPC should be described using such molecular models that take into account additional morphological parameters. For instance, if a model implies an interaction between components 1 and 2,²⁸ we get

$$E_{PPC} = E_1 + E_2(1 - \varphi_1) + \Delta E.$$

The sign preceding ΔE points to the presence (a 'plus' sign) or the absence (a 'minus' sign) of an interaction. For instance, the modulus of elasticity of a PP–HDPE composition can be larger than those of the individual components at a particular component ratio and at rapid cooling of melt. In other words, the addition of the first ingredient improves the properties of the second (this is also called positive synergism of the polymeric constituents).

Recently, the elastic properties of partially crystalline material were studied theoretically based on the scaling concept and very good agreement with experimental data was achieved (see, *e.g.*, Ref. 29).

If the glass transition temperature, T_g , of the first component of a PPC approaches that of the second ingredient of the PPC, these polymers are partially compatible.³⁰ The degree of compatibility, D , is defined as the ratio of the difference between the T_g values of the blend components to the difference between the T_g values of pure polymers:³¹

$$D = \frac{T_{g1}^b - T_{g2}^b}{T_{g1}^p - T_{g2}^p}, \quad 0 < D < 1,$$

where T_g^b and T_g^p is the glass transition temperature of the blend component and of the pure polymer, respectively. The glass transition temperature of the PPC of compatible polymers is intermediate between the T_g values of the blend components and is determined using the Fox equation (the so-called blend rule)³²

$$\frac{1}{T_g} = \frac{\varphi_1}{T_{g1}} + \frac{\varphi_2}{T_{g2}}.$$

Large deviations from the Fox equation are often considered as an indication of strong interpolymer interaction.³³

According to the Hoffmann equation,³⁴ the melting temperature of a non-isothermally crystallised PPC (T_m) increases linearly as the crystallisation temperature of the ingredients (T_c) increases

$$T_m = \frac{1}{\delta} T_c + \left(1 - \frac{1}{\delta}\right) T_m^\circ,$$

where δ is the crystallite morphological factor and T_m° is the equilibrium melting temperature. For instance, a PPC consisting of poly(but-1-ene) (PB) and hydrogenated oligo(cyclopentadiene) (HOCP) has a $1/\delta$ value of ~ 0.34 , while the ternary PP–PB–HOCP blend (50:30:20)[†] is characterised by $T_m^\circ = 456$ K.³⁵

Szabo *et al.*³⁶ showed that the interpolymer interaction between such blend components as poly(isobutylene) (PIB) and linear LDPE obtained by copolymerisation of ethylene with

[†] Hereafter, the concentrations of blend components are given in per cent by mass.

α -olefins (LLDPE) can be estimated using the modified Flory–Huggins equation³⁷

$$\frac{1}{\phi_1} \left(\frac{1}{T_m} - \frac{1}{T_m^0} \right) = - \frac{RV_2}{\Delta H_2 V_1} \chi_{12} (1 - \phi_2)^2,$$

where ϕ_1 and ϕ_2 are the volume fractions of the polymers 1 and 2, V_1 and V_2 are the molar volumes of repeating units of the polymers 1 and 2, respectively, ΔH_2 is the enthalpy of melting of PE, and χ_{12} is the Flory–Huggins interaction parameter. The ΔH_2 is 4.1 kJ mol^{−1} and the parameter χ_{12} is −0.022 at 393 K. This proves that even relatively weak dispersion forces can make two polymers compatible.

Interesting information for estimation of the interaction between the PPC components can be obtained from the results of measurements of the surface (γ) and interfacial tension.

$$\gamma = \gamma_d + \gamma_p,$$

where γ_d and γ_p are the components of the surface tension of the polymer, which are due to the dispersion and dipole interaction, respectively. These characteristics of intermolecular interaction are immediately related to the cohesive energy of the system under study. The surface tension and its components depend on the nature of PPC ingredients and decrease upon their modification (Table 1).³⁸ In addition, the higher the temperature the smaller the γ values (Table 2). The surface tension at the interface between two immiscible polymers in a PPC (γ_{12}) can be calculated using the following equation:⁴⁰

$$\gamma_{12} = \gamma_1 + \gamma_2 - \frac{4\gamma_{d1}\gamma_{d2}}{\gamma_{d1} + \gamma_{d2}} - \frac{4\gamma_{p1}\gamma_{p2}}{\gamma_{p1} + \gamma_{p2}},$$

where subscripts 1 and 2 correspond to the first and second components, respectively.

Table 1. Surface tension and its components (dyn cm^{−1}) for PP and PA-6.³⁸

Polymer	γ_d	γ_p	γ
PP	28.3	12.5	40.8
PA-6	32.1	20.9	53.0
PP ^a	26.3	9.5	35.8
PA-6 ^a	30.1	10.7	40.8

^a Modified by grafting maleic anhydride (MA, 1%).

Table 2. Surface tension γ (dyn cm^{−1}) for some polymers at different temperatures.³⁹

T/K	LDPE	HDPE	PVA ^a	PMMA
293	35.3	35.3	36.5	41.1
413	27.3	28.8	28.6	32.0
453	24.6	26.5	25.9	28.9

^a PVA stands for poly(vinyl acetate).

Next, we present the surface tension (γ_{12}) values at the interface between the first polymer and the second polymer in the PPC at 423 K.⁴¹

First polymer	LDPE	HDPE	PE	LDPE
Second polymer	PVA	PVA	PVA (25%)	PP
$\gamma_{12}/\text{dyn cm}^{-1}$	9.8	11.0	1.3	1.3

The surface tension at the interface can also be approximated using the Wendt–Owens equation⁴²

$$\gamma = (\gamma_1^{1/2} - \gamma_2^{1/2})^2.$$

Thus, there are some modern methods that often allow a quite reasonable description of the properties of real PPC. However, many aspects of this problem remain unclear as yet.

III. *In situ* preparation of polymer–polymer compositions in the catalytic polymerisation of olefins

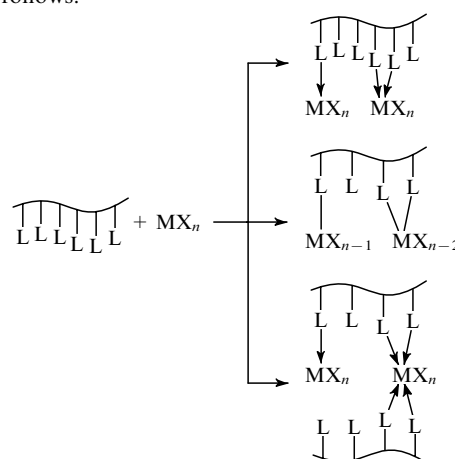
The method for the preparation of molecular PPC (hereafter, we will denote them ‘the *in situ* prepared PPC’) in the catalytic polymerisation or copolymerisation of α -olefins (ethylene, propylene, butene), diene monomers (butadiene, isoprene) and monomers of the acetylene type (acetylene, phenylacetylene, 3-bromopropyne, *etc.*) on metal complex catalysts involves the following stages.⁴³ First, this is a chemical or physical immobilisation of the catalyst components on the ‘polar’ ingredient of the PPC to be prepared. Usually, the catalyst components represent macromolecular metal complexes based on PMMA, PVC, PTFE, poly(vinylidene chloride) (PVDC), polyformaldehyde (PFA), PVA, poly(vinyl alcohol) (PVAle), poly(4-vinylpyridine) (P4VP), cellulose and other polymers. The second stage consists of a liquid-phase or gas-phase polymerisation or copolymerisation of corresponding monomer resulting in the desired PPC.

In the text below we consider the main approaches to the synthesis of catalyst components (of the Ziegler–Natta type), some features of the polymerisations catalysed by these, in essence, polymer-immobilised⁴⁴ catalysts and, finally, selected experimental data on the structure of particular systems.

1. Synthesis of catalyst components

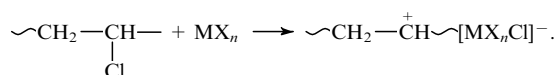
Polymers containing functional groups (L) are macroligands that can bind the components of catalytic systems, *viz.*, a transition metal compound MX_n [TiCl_4 , VCl_4 , VOCl_3 , VCl_3 , TiCl_3 , $\text{Ti}(\text{O}i\text{Bu})_4$, CoCl_2 , MoCl_5 , *etc.*], an organometallic (organoaluminium, organolithium, organomagnesium, organozinc) compound, *etc.*

A general scheme of metal complex immobilisation taking into account the formation of chemical bonds can be represented as follows:

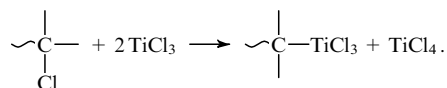


The penetration depth of the active catalyst into the near-surface layer of the component of a PPC can vary depending on the reaction conditions. This can be accompanied by both monodentate and polydentate coordination of MX_n by the intramolecular or intermolecular mechanism.⁴⁴ The optimum immobilisation procedures can involve either the use of a suspension of the PPC component or gas-phase coordination of the complexes. Many transition metal halides are relatively strong Lewis acids capable of forming ionic complexes. It is this type of

bonding that is used for the coordination of MX_n to PVC, PVDC, PTFE and poly- α -bromostyrene.



Yet another approach, applicable to crystalline compounds MX_n (e.g., TiCl_3 , VCl_3), is based on the formation of carboxylic acid salts. For instance, TiCl_3 is coordinated by chlorinated polymers (PVC, chlorinated PP, natural rubber) by the following mechanism:⁴⁵

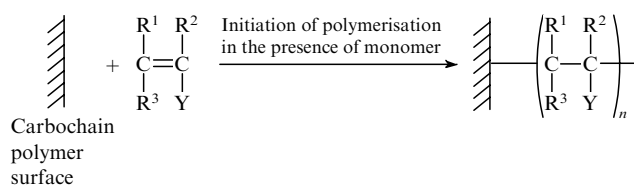


Joint grinding of TiCl_3 and PVC leads to complete disappearance of the crystalline phase. Nearly complete oxidation of Ti^{3+} into Ti^{4+} is evidence for essential transformations in the TiCl_3 –PVC system.

Special methods for immobilisation of compounds MCl_3 (with retention of their submicrostructure) on polymers have been developed. The most efficient procedure involves solid-phase mechanochemical synthesis in the presence of polymeric constituents of PPC (most often, PO). Experimentally, this is achieved by activation of the reacting components in the vibrating, ball or differential agate mills (usually, in an inert atmosphere).^{46, 47}

The surface of polymers is also modified using cationic polymerisation,⁴⁸ which results in macromolecular analogues of stable carbonium salts.

To immobilise metal complexes on the surface of PO (the grafted layer is 10 to 30 Å thick), the surface of the polymer is functionalised by performing graft polymerisation of polar monomers.⁴⁶ In particular, the surface of PE, PP or ethylene/propylene copolymer can be modified by grafting, e.g., acrylic acid, 4-vinylpyridine, acrylonitrile, allyl alcohol, vinylpyrrolidone, etc.



$\text{R}^1 = \text{H, Me; R}^2 = \text{H, Me, C}_6\text{H}_5; \text{Y} = \text{OH, NHR, CH}_2\text{NH}_2, \text{SR, CH}_2\text{OH, CH}_2\text{SR}^2, \text{CO}_2\text{H, OCOMe; R}^3 = \text{H, Me, C}_2\text{H}_5, \text{CH}_2\text{CH}=\text{CH}_2, \text{C}_6\text{H}_5.$

In the text below we will show that graft polymerisation products can also be used individually as the third components (compatibilisers) to improve the compatibility of components of binary PPC.

Table 3 lists some characteristics of catalyst components MX_n that are used for the *in situ* preparation of PPC.

Polymer–polymer compositions can also be prepared *in situ* by anionic-coordination or ionic polymerisation using an alternative approach which involves immobilisation of organometallic compound on the polar component. In this connection, it is of interest to consider the modification of the surface of PETP or PA-66 via 1,2-polyaddition of compounds LiR to carbonyl groups.⁴⁹ Organomagnesium compounds are immobilised on graft-functionalised polymers.⁵⁰ Addition reactions of AlR_3 or AlR_2H to the multiple bonds of polymers, resulting in the formation of reactive organometallic centres have been reported. In particular, addition products of dialkylaluminium hydrides to random styrene (25%)/butadiene copolymers have been studied in detail.^{51, 52}

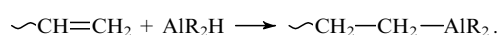


Table 3. Characteristics of catalyst components used for *in situ* preparation of PPC.⁴⁶

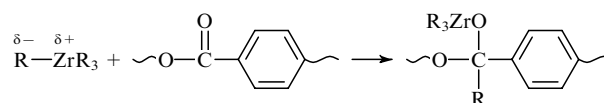
Polymer	Component MX_n	Immobilisation conditions of MX_n on the polymer surface			Immobilised metal content /mg g ⁻¹
		solvent	$T/^\circ\text{C}$	time /h	
PVC	VCl_4	CCl_4	20–40	2.0	0.8
	TiCl_4	heptane	50–70	2.0	1.1
PVDC	VCl_4	CCl_4	30–35	2.0	1.5
PMMA	VCl_4	CCl_4	20–25	1.5	0.5
	TiCl_4	heptane	60	2.0	0.8
PFA	VCl_4	CCl_4	20–25	1.5	1.0
Cellulose	VCl_4	CCl_4	20–25	1.5	1.2
PTFE	VCl_4	CCl_4	20–25	1.5	0.6
HDPE	VCl_3	see ^a	20–40	0.5	10.0
	TiCl_3	"	20–40	1.0	10.0
PP	VCl_3	"	20–40	1.0	10.0
	TiCl_3	"	20–40	1.0	10.0
PE–g-P4VP	TiCl_3	"	20–40	0.5	10.0
	VCl_3	"	20–40	0.5	10.0
PE–g-PAA ^b	$\text{Ti}(\text{OBu})_4$	heptane	60	1.0	0.5
PE–g-PAAc ^c	$\text{Ti}(\text{OBu})_4$	"	60	1.0	1.0
	$\text{Ni}(\text{acac})_2$	toluene	40	1.0	8.0
	VCl_4	CCl_4	25	1.0	7.5
	CoCl_2	methanol	40	1.0	8.0
PE–g-PVP ^d	VCl_4	CCl_4	25	1.0	6.0

^a Immobilisation is performed by grinding a mixture of components in a ball mill in the absence of solvent. ^b PAA stands for poly(allyl alcohol).

^c PAAc stands for poly(acrylic acid). ^d PVP stands for polyvinylpyrrolidone.

Organoaluminium compounds can undergo insertion into the multiple bonds of functional groups of the polymeric constituents of PPC.⁴⁴ Most likely, immobilisation of alumoxanes proceeds by the same mechanism. Both components of the metal complex system can be immobilised on the same polymer.

The coordination mechanism of polymers to transition metal compounds (one-component catalysts of olefin polymerisation) is much simpler. In particular, immobilisation of ZrR_4 (R — benzyl, π -allyl) and $\text{Cr}(\pi\text{-allyl})_3$ on the surface of polymer fibres proceeds via 1,2-polyaddition to the carbonyl groups of PETP or the reaction with amido groups of PA-66.⁴⁹



Probably, organometallic zirconocene derivatives known as the most efficient catalysts of olefin polymerisation, are immobilised on polymers following the same mechanism.

Currently, a new method for immobilisation of two different reactive centres on the same polymeric constituent of PPC has been developed. It allows bifunctional catalysis, i.e., simultaneous polymerisation of monomers of different chemical nature or conversion of one monomer into products of different structure. This method will be considered below.

2. *In situ* preparation of polymer–polymer compositions: general kinetic rules

The composition of PPC prepared *in situ* in the presence of catalyst components can be controlled by varying the polymerisation conditions and, first of all, duration of polymerisation and the amount of monomer consumed.

The rate of ethylene polymerisation (a PE-based, *in situ* prepared PPC) is to a great extent dependent on the nature of the polar component and the type of its bonding to the catalyst

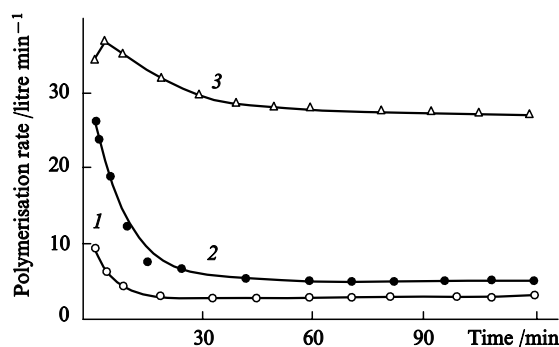


Figure 1. Catalytic activity of $\text{VCl}_4 \cdot \text{L} - \text{AlBu}_2\text{Cl}$ systems in the polymerisation of ethylene for different types of immobilisation. Ligand (L): (1) vinyl acetate; (2) PVA; (3) PVAlc.

components. Generally, immobilisation of MX_n or $\text{AlR}_x\text{Cl}_{3-x}$ by covalent bonds is considered optimum. The component playing the role of macroligand stabilises the process,⁵³ which manifests itself as a steady-state polymerisation (except for the initial stage). It should be noted that polymerisation at 313 K in the presence of the traditionally used system $\text{VCl}_4 - \text{AlR}_2\text{Cl}$ is essentially a non-steady-state process. Here, the maximum activity is achieved immediately after blending the components; however, the rate of ethylene polymerisation reduces by a factor of 45 after 30 min.⁵⁴ In contrast to this, catalytic activity of the systems based on macrocomplexes reduces by 3 to 8 times after the same time interval. Systems in which VCl_4 is covalently bound to, e.g., PVAlc, exhibit higher catalytic activity compared to macrocomplexes with PVA (Fig. 1). Catalyst components formed in the reactions of TiCl_4 or VCl_4 with PVC or PVDC also demonstrate a stabilising effect.

Kinetic studies revealed⁵⁵ that the rate constants for the chain propagation and chain termination (by monomer or organo-aluminium compound) stages and the activation energies for the PE chain propagation in the presence of both the macrocomplex-based systems under consideration and traditionally used Ziegler–Natta catalysts have similar values. However, the formation of the reactive centres proceeds by different mechanisms, which is responsible for the stabilising effect of the polymeric catalysts.

The molecular mass of PE formed depends on the nature of the catalyst component and on the polymerisation conditions. Standard procedures for controlling the molecular mass of PE include addition of hydrogen. The *in situ* prepared PPC are isolated and treated using the same procedures as those used in the low-pressure polymerisation of olefins. This type of PPC can also be prepared under conditions of the gas-phase polymerisation of ethylene (in this case, the catalyst component is dispersed in the suspension layer).⁵⁶ Using components with specific molecular shape also allows preparation of granulated PPC.

Binary polyolefin compositions (e.g., PE–PP) can be synthesised using the catalyst components obtained by co-grinding of PO and MCl_3 (e.g., the size of TiCl_3 submicrocrystals co-ground with PE is ~ 1 nm).⁵⁷ The stereosequence of PP formed on such catalysts is determined by conventional factors. This method also allows the *in situ* preparation of such PPC as PE–PB, PE–polycyclohexene, PE–PS, etc. The PE–polybutadiene (PBd) and PE–polyisoprene (PI) compositions are prepared by polymerisation of the diene monomer on the PE–g-P4VP– $\text{CoCl}_2 - \text{AlEt}_2\text{Cl}$ system.⁵⁷ In these catalysts each Co atom produces the polydiene chain, the molecular mass of PI lies between 370 000 and 1 300 000 and the content of 1,4-*cis*-PI exceeds 80%.

In situ preparation of conducting compositions PE–polyacetylene (PAC) involves immobilisation of the catalytic system $\text{Ti}(\text{O}i\text{Bu})_4 - \text{AlR}_3$ on the surface of modified PE films followed by gas-phase or liquid-phase polymerisation of acetylene⁵⁸ and

results in the formation of *trans*-PAC similarly to the process in homogeneous systems.

Thus, the use of catalyst components allows the preparation of PPC based on polyolefins and various polymers in the anionic-coordination polymerisation. Let us consider the structure of particular PPC in more detail.

3. HDPE–PMMA Compositions

Main characteristics of the properties of the *in situ* prepared polymer–polymer compositions HDPE–PMMA and polymer blends of HDPE and PMMA (with similar molecular mass characteristics) are listed in Table 4.

Table 4. Density (ρ), yield stress (σ), elongation at break (ε) and glass transition temperature of polymer–polymer compositions HDPE–PMMA.⁶⁰

Parameter	Starting components ^a	PMMA content in composition ^b /volume fraction			
		0.04	0.07	0.14	0.29
ρ /kg m ⁻³	1.190	0.959	0.968	0.983	1.019
	0.948	0.962	0.965	0.965	1.017
σ /MPa	5000	3200	3155	3500	—
	2500	2700	1200	1150	—
ε (%)	2–3	250	210	180	—
	370	80	70	45	—
T_g /K	225	217	221	221	221
	221	203	—	221	221

^a The data for PMMA are listed in the numerator and the data for HDPE are given in the denominator. ^b The data for molecular (*in situ* prepared) compositions are presented in the numerator and the data for polymer blends are listed in the denominator.

An increase in the volume fraction of PMMA (φ) in the synthetic PPC is accompanied by a decrease in the relative elongation at break (ε) and an increase in the yield stress (σ). Compared to the *in situ* prepared PPC of similar chemical composition, polymer blends are characterised by smaller ε and σ values (by 3 to 4 times for ε and 1.5 to 2 times for σ). The glass transition temperatures of the components are virtually independent of the procedure for the preparation of PPC, which suggests low thermodynamic compatibility. Both components of such PPC are linear polymers whose chemical composition and structure can be studied by selective extraction. This method is often used for analysing polymer blends and, in particular, interpenetrating polymer networks (IPN).⁵⁹ Polymer blends prepared without the formation of a complex with VCl_4 in the ethylene polymerisation using the $\text{VCl}_4 - \text{AlEt}_2\text{Cl}$ system exhibit a ready and complete separation into the starting components. In the case of *in situ* prepared PPC the content of non-extractable PMMA ($\varphi = 0.007 - 0.14$) varies between 4.4 mass % and 6.7 mass %.⁶⁰ Most likely, this is evidence that a fraction of PMMA molecules is chemically grafted onto PE. This assumption is confirmed by the results of various physicochemical studies. For instance, new bands with maxima at 1740 and 1300 cm⁻¹, corresponding to stretching vibrations of carbonyl and ester groups, appear in the IR spectra of non-extractable products along with the main absorption bands typical of the PE backbone.

The assumption that the integrated intensity of X-ray diffraction reflections is proportional to the content of the crystalline component in a polymer blend consisting of amorphous and crystalline phases holds for any blend including polymer blends based on crystalline PE and amorphous PMMA. Hence it follows that if the structure of the PE constituent of a PPC is independent of the chemical composition of the PPC, the height of the most intense peak of PE, corresponding to the (110) reflection, can serve

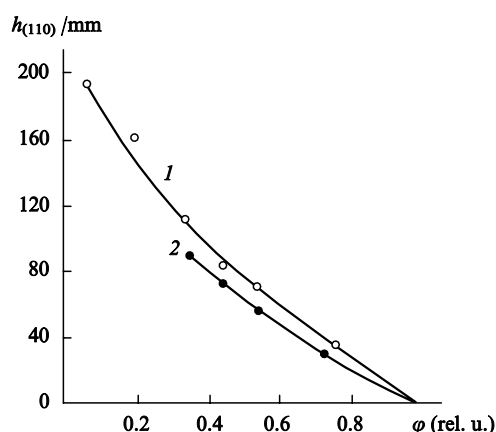


Figure 2. Empirical correlation between the height of the (110) peak of HDPE and the chemical composition of polymer blends of HDPE and PMMA (1) and molecular polymer–polymer compositions HDPE–PMMA (2).⁶⁰

as a quantitative characteristic of the chemical composition of the PPC. For mechanically mixed polymer blends, this correlation corresponds to curve 1 in Fig. 2, whereas for *in situ* prepared PPC the plot is shifted to the left. This looks like an apparent reduction of the volume fraction of PE and does not correspond to the true chemical composition of the *in situ* prepared PPC determined independently (from the density, material balance of polymerisation, *etc.*). This contradiction can be readily eliminated assuming that some structural domains of PE formed do not contribute to the (110) peak intensity.

Indeed, in contrast to polymer blends, the X-ray diffraction patterns of the *in situ* prepared PPC display a clearly seen peak labelled by an arrow in Fig. 3. This peak corresponds to a new

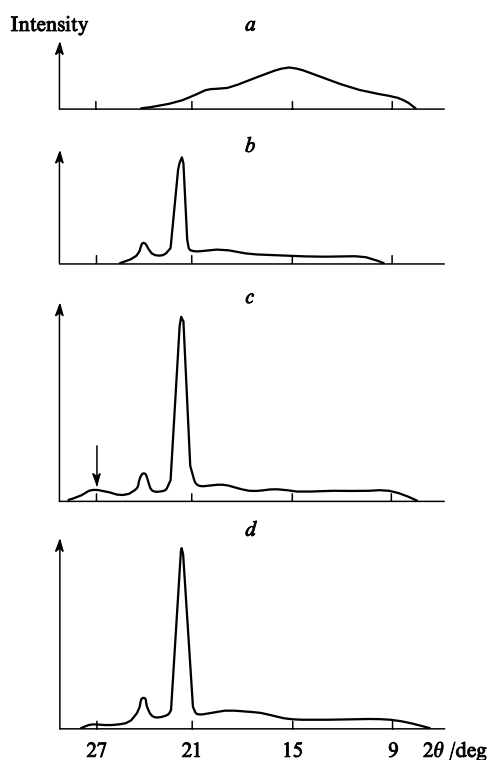


Figure 3. X-Ray diffraction patterns of PMMA (a), HDPE (b), *in situ* prepared composition HDPE–PMMA (c) and a blend of HDPE and PMMA (d) ($\phi = 0.19$).⁶⁵

interplanar distance ($\sim 3 \text{ \AA}$) in the structure of PPC and is indicative of the interaction between PE and PMMA on the molecular level and of a local distortion of the phase boundaries. The latter is due to the fact that chain propagation (the growth) of the PE macromolecules is accompanied not only by crystallisation, but also by interpenetration of the first component into the bulk of the second component (due to diffusion of macromolecules or their segments). As the distance from the surface of PMMA increases, this interaction, which determines the thickness of the intermediate layer, weakens. If the intermediate layer is sufficiently thick, it can form an individual phase. In addition, a salient feature of this system is the propagation of the PE chains accompanied by mixing of the components, which also improves their compatibility and the physicochemical properties of *in situ* prepared PPC (the so-called operating compatibility) compared to the properties of conventional polymer blends (see Table 4). This type of PPC, prepared by copolymerisation of propylene and CO on phosphinepalladium complexes resulting in a propylene–CO alternating copolymer and followed by blending with PMMA, is thought to be miscible.⁶¹ Experiments⁶² on multicomponent PPC containing LDPE and small amounts of hydrophilic polymers [PVA or poly(vinyl acetal), 2% to 6%] showed that, as a rule, in the presence of surfactants the macromolecular coils of the additives undergo insertion into the LDPE domains in both the amorphous phase and intermediate layer.

4. HDPE–PVC Compositions

PVC-Based materials exhibit some valuable properties. At the same time, they are characterised by low thermal stability and thermal plasticity in processing and by low impact toughness at negative temperatures. Sometimes, these drawbacks can be eliminated by modifying PVC with thermoplastic polymers or copolymers, and the resulting PPC combine the advantages of the starting components. This is also favoured by miscibility of PVC and a broad spectrum of polymers containing appropriate functional groups. Such composite materials can be used for the preparation of, *e.g.*, polymer films for enclosing greenhouses.⁶³

As applied to the HDPE–PVC systems, this method for *in situ* preparation of PPC involves immobilisation of VCl_4 , VOCl_3 or TiCl_4 on the surface of PVC latex or suspension PVC ($M_n = 5.5 \times 10^4$, the specific surface area is $6 \text{ m}^2 \text{ g}^{-1}$ and the particle diameter lies between 50 and 100 μm) via the formation of a macromolecular carbonium salt following the above-mentioned mechanism.^{49, 64–66} Similarly to the case of the HDPE–PMMA systems, the chemical composition of PPC is controlled by varying the consumption of ethylene for polymerisation. Using selective extraction with boiling THF in a Soxhlet apparatus for 24 h, the fraction of graft PVC was estimated (Table 5). The larger the volume fraction of PE in synthetic PPC, the larger the amount of non-extractable PVC due to an increase in the number of polymer

Table 5. Percentage of PVC grafted onto PE in the suspension polymerisation of ethylene using the $\text{PVC} \cdot \text{VCl}_4 - \text{AlEt}_2\text{Cl}$ system.

PVC content in composition		Percentage of grafted PVC ^a (mass %)
mass %	volume fraction	
17	0.12	3.3
25	0.19	3.0
32	0.25	2.3
46	0.38	2.4
60	0.52	1.8
80	0.76	1.0
56 ^b	0.25	5.6

^a The content of PVC that could not be extracted with boiling THF in a Soxhlet apparatus for 24 h. ^b The polymer–polymer composition prepared by gas-phase polymerisation of ethylene.

chains or their segments that enter the reaction. The IR spectra of such graft polymers exhibit new bands at 615, 640, 833, 968 and 1260 cm^{-1} corresponding to PVC in addition to the absorption bands of PE. We will consider possible mechanisms of grafting in the next sections of the review.

Similarly to the HDPE–PMMA compositions, it was found that some of the structural domains of PE in the HDPE–PVC systems are X-ray silent. The plot of the empirical dependence of the height of the (110) peak on the chemical composition of the HDPE–PVC system is shifted to the left relative to the plot of analogous dependence for mechanically mixed polymer blends. The proportion of structural domains that do not contribute to the intensity of the (110) peak of PE is $\sim 20\%$ (estimated from the decrease in φ value taking into account the non-extractable fraction of PVC and also from the results of optical measurements). This value is in reasonable agreement with the decrease in the proportion of the ‘X-ray responsive’ PE. Unlike polymer blends, a salient feature of the structure of *in situ* prepared PPC is the appearance of a new interplanar distance ($\sim 4 \text{ \AA}$). Therefore, grafting of the PE chains or their segments onto PVC macromolecules occurs in the loose, intermediate near-surface layer.

The mechanics of two-component systems treats this type of PPC as compositions with a framework or interpenetrating structure and adhesive interaction between the components over a wide range of component ratios. According to the cubic model which ignores any polymer–polymer interactions,⁶⁷ the yield stress of PE (σ_0) and PPC (σ) must be related by a simple formula:

$$\frac{\sigma}{\sigma_0} = 1 - \varphi^{2/3}.$$

Indeed, the experimental and theoretical data for polymer blends are in reasonable agreement (Fig. 4a), which points to the absence of interactions between the HDPE matrix and PVC particles. No agreement between experiment and theory is observed for the *in situ* prepared PPC. This serves as additional evidence of the polymer–polymer interactions which favour a 60% (on the average) increase in the yield stress, σ , of such compositions. Polymer compositions containing a heat-treated component (*e.g.*, crystalline HDPE) become sensitive to the sample preparation conditions. In particular, the points corresponding to the samples prepared at low and high melt cooling rates are grouped near different theoretical curves (see Fig. 4b).

Table 6 lists the numerical values of the main physicochemical characteristics of different polymer–polymer compositions HDPE–PVC. As can be seen, the *in situ* prepared PPC are characterised by greater ultimate strength at elongation, relative

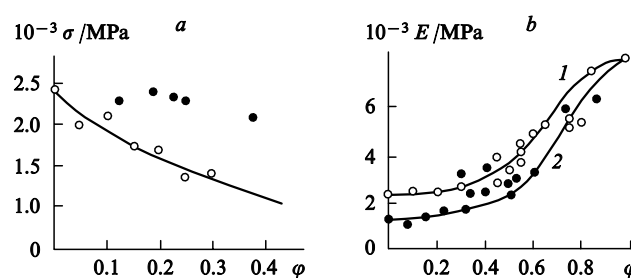


Figure 4. Theoretical (solid curves) and experimental dependences of the yield stress (a) and Young's modulus (b) for polymer blends of HDPE and PVC (open circles) and corresponding *in situ* prepared PPC HDPE–PVC (solid circles) on the volume fraction of PVC.⁶⁵ Stress rate 0.03 s^{-1} ; the cooling rate is 1 (1) and $20\text{--}30 \text{ K min}^{-1}$ (2).

elongation and tear resistance. The impact toughness of the film samples obtained was estimated from the impact cold resistance to a standard load (a 0.5 kg ball) fallen from a height of 0.5 m.⁶⁸ Polymer blends of analogous chemical composition exhibit poorer physicochemical characteristics in the whole range of HDPE/PVC ratios.

Yet another important feature of the *in situ* prepared polymer–polymer compositions HDPE–PVC, *viz.*, their ability to undergo high-frequency welding, should be pointed out. This is apparently due to the improved compatibility of the components and higher homogeneity of the PPC. As the PVC content increases from 23 mass % to 55 mass %, the duration of the welding process is reduced from 70 down to 18 s; however, the impact toughness of the PPC reduces at high PVC content. If the content of PVC is lower than 20%, high-frequency welding of molecular composites becomes impossible. Polymer blends do not undergo high-frequency welding in the whole range of component ratios, which is evidence of high inhomogeneity of their structure.

Comparison of strain–stress diagrams of conventional polymer blends and synthetic PPC showed that the latter behave as ductile materials and are not subject to brittle fracture both at room temperature and at 203 K. This allows the use of the *in situ* prepared PPC at low temperatures. The optimum content of PVC in such compositions is nearly 45 mass %.

It should be noted that the formation of a grafted layer from the polymer formed was also observed during the cationic polymerisation of styrene or isobutylene in a suspension of PVC with immobilised Et_2AlCl (in a heptane–1,2-dichloroethane

Table 6. Numerical values of physicochemical characteristics of polymer–polymer compositions HDPE–PVC.⁶⁶

Property	Starting components		PVC content in the <i>in situ</i> prepared PPC (mass %)					PVC content in mechanical mixtures (mass %)				
	HDPE	PVC	17	23	30	44	55	17	23	30	44.5	55
Ultimate strength at elongation /MPa	30.1	42.0	24	23.8	21.3	20.4	16.8	24.2	14.4	5.0	—	—
Relative elongation (%)	40	23	80	30	20	62.5	13	8.5	5	—	—	—
Rigidity /N	0.7	1.0	0.7	0.6	0.7	0.7	0.7	0.6	0.75	0.7	0.75	0.6
Tear resistance / kN m^{-1}	52	30	19	30	17	25	31	3.0	3.5	3.5	—	—
Impact cold resistance / $^{\circ}\text{C}$	—	0	−80	−80	−80	−80	−60	see ^a	see ^a	see ^a	see ^a	see ^a
High-frequency welding ^b time /s	—	9	see ^c	70	56	30	18	see ^d	see ^d	see ^d	see ^d	see ^d
weld strength (%)	—	28		98	98	65	55					
weld cold resistance / $^{\circ}\text{C}$	—	0		−70	−70	−70	−30					

^a Room-temperature cracking. ^b High-frequency currents. ^c No welding. ^d No welding; surface combustion occurs.

mixture at 253 K).⁴⁸ Depending on the polymerisation conditions, the degree of heterophase grafting varied from 2 vol.% to 13 vol.% for PS and from 7 vol.% to 15 vol.% for PIB (with *n*-pentane as selective extracting agent). In the latter case, the 250 μm PVC particles were coated with a separable PIB layer 50 μm thick. Probably, flaking of the grafted layer from PVC is due to large differences in the surface energy (immiscibility) and mechanical properties of PIB and PVC. The concentration of chlorine in the exterior of the grafted layer is much lower than in the interior and sharply decreases as the thickness of the grafted layer increases.

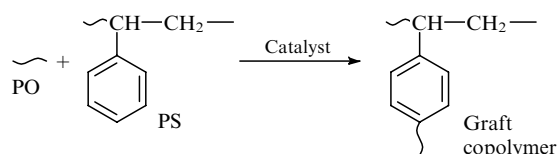
Thus, synthetic methods make it possible to prepare PPC with improved physicomechanical and operating characteristics. Simple blending of the corresponding components does not allow improvement of these characteristics.

IV. Synthesis of polar ingredients in the presence of polyolefins

An alternative approach to the *in situ* preparation of PPC implies the synthesis of the second (hereafter, 'polar') component in the presence of a PO. In the reaction bulk, the PO has little effect on either the radical and ionic polymerisation or on the polycondensation of the component precursors.

Polyolefins can be modified by mechanochemical treatment with the monomer in the presence of Lewis acids.⁶⁹ For instance, the preparation of a layered material based on PE fibre (glass fibre) involves stacking of aligned fibres that were preliminarily soaked with methyl methacrylate (MMA) in a sheet die followed by bulk polymerisation of MMA at room temperature^{70,71} with the amine–peroxide system as initiator.⁷² The polymerisation is conducted until thickening of the material; shrinkage control is achieved by adding excess monomer. The final preparation stage of the composition involves heating to 328 K (this temperature corresponds to complete conversion of MMA).

Compatibility of particular pairs of polymers (*e.g.*, PO and PS) can be improved by performing *in situ* cationic polymerisation of styrene in the presence of corresponding polyolefins with Lewis acids (*e.g.*, AlCl_3) as catalysts.⁷³ The reaction mechanism is similar to the benzene ring alkylation according to Friedel–Crafts.



The degree of grafting depends on the nature of the Lewis acid and reaches a maximum value (15.7%) for AlCl_3 .

The procedure for preparation of polymer–polymer blends based on crystalline polymers (HDPE, PP, PA-12) after their deformation *via* delocalised crazing by drawing in liquid monomers (styrene, MMA, *etc.*) involves drawing a polymer film (*e.g.*, PP) in MMA containing the necessary amount of both initiator and cross-linking agent.^{74–76} As the desired degree of drawing is achieved, *in situ* polymerisation of the monomer in the PP matrix is carried out. Deformation is accompanied by continuous filling of the newly formed, porous polymer structure with the polymerised blend. Generally, delocalised crazing allows substantial enhancement of the swelling of the polymer (swelling of PP or PE in conventional monomers is at most 10 vol.%–15 vol.%, since the low-molecular-mass component can penetrate only the amorphous domains of the polymer structure while crystallites remain intact). From the standpoint of the preparation procedure such PPC can be classified as IPN. Experiments with the HDPE–PMMA system showed that complete separation of the blend components by successive selective extraction with chloroform at 333 K for 6 h (to dissolve PMMA) and with *n*-decane at

393 K for 2 h (to remove HDPE) is also impossible, while the homopolymers are completely dissolved under these conditions. The content of the insoluble (non-extractable) product is 25 mass %–30 mass %. This is due to either or both chemical grafting of the polymer chains and their interpenetration on the molecular level.

Thus, despite thermodynamic incompatibility of their components, the *in situ* prepared polymer–polymer compositions are to some extent compatible and the degree of compatibility is higher than in the case of simple mixing of polymer melts. Nevertheless, such PPC represent two-phase systems, which is confirmed by the data of calorimetric studies, according to which the glass transition temperatures of the components remain unchanged.

It is of considerable interest to consider the formation of the PU phase in PE in more detail. Thermoplastic PU is widely used in blends with other polymers including PO.⁷⁷ For instance, the formation of *in situ* compositions containing 85% PE and 15% PU from diisocyanates (diphenylmethane-4,4'-diisocyanate or dicyclohexylmethane-4,4'-diisocyanate) and diols (polyetherdiol or 1,4-butanediol) in PE melts (413 K) in the presence of catalyst was reported.⁷⁸ During the process the molecular mass of the dispersed phase changes in nearly the same manner as in the case of bulk polymerisation of virgin PU under analogous conditions (Fig. 5). Since the solubility of the isocyanate monomer in PE melts is rather high, while the solubility of the diol is low, the stoichiometry ratio between them violates, which imposes some limitations on the degree of polymerisation by *in situ* blending.[‡] A number of procedures which facilitate the formation and favour strengthening of the interfacial layers was developed. As a rule this is achieved by introducing various additives (compatibilisers) which improve adhesive interactions between the starting components and the *in situ* formed phases.

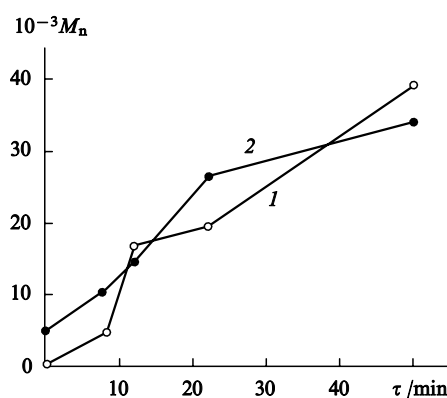


Figure 5. Formation kinetics of PU (curing at 413 K) in the dispersed phase (1) and in the bulk (2) under comparable conditions.⁷⁸

For instance, consecutive anionic polymerisation of styrene and 4-vinylpyridine in the presence of BuLi at 195 K resulted in block copolymers which induce phase separation.⁸⁰ Block copolymers of styrene and 2-vinylpyridine were synthesised using consecutive polymerisation of the monomers with potassium cumene as initiator.⁸¹ Atactic ethylene/propylene diblock copolymers were prepared by hydrogenation of poly(butadiene-*b*-2-methyl-1,3-pentadiene), polybutadiene and poly(2-methyl-1,3-pentadiene).^{82,83} The preparation of a partially deuterated ethylene/propylene diblock copolymer based on perdeuterated butadiene used as co-monomer was also reported.

[‡] Semi-interpenetrating polymer networks based on cross-linked PU and linear poly(butyl methacrylate) are prepared by introducing the latter component in the monomeric form followed by performing radical polymerisation simultaneously with cross-linking.⁷⁹

V. On some synthetic methods for preparation of polyolefin – polyolefin compositions

Multicomponent, PO-based polymer blends represent the most abundant group of PPC; most often, they serve as materials for recycling. This group of polymer compositions comprises blends of normal PE and high-molecular-mass or ultrahigh-molecular-mass HDPE, blends of different types of PE (LDPE, medium density PE and HDPE), *etc.*^{84,85} These materials exhibit some valuable properties, such as improved impact toughness, resistance to external factors including cold resistance, have good optical and rheological characteristics, high crystallisation rate, *etc.*^{86,87} These parameters of the PPC are nonlinear functions of their chemical composition, which is due to the influence of the interfacial layer and to the changes in the structure and properties of the constituent phases in the blends caused by the interaction with other components. One of the main goals of research into such PPC is the development of methods for improvement of processability of PO.

1. Systems based on different types of polyethylene

Design of novel materials with improved properties involves the preparation of microheterogeneous composites as an integral part. Microheterogeneous composites represent (i) PPC based on different types of PE (high density and low density PE) and (ii) highly oriented systems containing LDPE and HDPE.⁸⁸ Low density PE, with its long-chain branchings, and linear HDPE (LHDPE) are of similar chemical nature. Therefore, one could expect that they will form homogeneous blends which, nevertheless, represent microheterogeneous systems. An increase in the concentration of HDPE in the blend leads to a decrease in the crystallite size and to an improvement of the structural homogeneity of PPC. If the content of HDPE exceeds 30%, phase separation occurs, HDPE forms a dispersed phase and interfacial interaction between the polymeric constituents is observed. Further increase in the concentration of HDPE causes the formation of ordered HDPE domains that are structurally similar to the HDPE crystallites. Polymer – polymer compositions containing 80% HDPE have superiority in mechanical properties compared to the starting components. This is thought to be a result of the highest possible structural homogeneity of the polymer compositions due to the maximum compatibility of the components. Neutron scattering studies showed that the melts of HDPE and LDPE are compatible in the whole range of their concentrations.⁸⁹ A key factor that governs the extent of co-crystallisation of HDPE and LDPE is the similarity of crystallisation rates of each component. The amount of co-crystallite formed increases as the isothermal crystallisation temperature reduces under quenching conditions.⁹⁰ The co-crystallisation is also influenced by the branching composition of the constituent macromolecules, as was shown taking a blend of linear PE (1% to 20%) and branched PE as an example.⁹¹ These systems can also exhibit partial compatibility like, *e.g.*, a blend of LLDPE (1-octene comonomer), HDPE and LDPE.⁹²

As the content of LDPE in its blends with the ethylene – propylene – 1,4-hexadiene terpolymer increases, the T_g value is shifted towards higher temperatures (*i.e.*, towards the region of β -relaxation of PE, which is due to an increase in the mobility of small independent structural fragments of the macromolecules).⁹³ This confirms that the blend components are miscible on the molecular level. In addition, LDPE and ethylene/propylene copolymers are characterised by close values of the density of cohesive energy in the amorphous phase; these polymers also seem to be compatible on the molecular level. The addition of small amounts of LDPE (merely 2.5%) to LLDPE (1-hexene co-monomer with a density of 0.900 g cm⁻³) leads to the formation of well-defined spherulites and to a substantial decrease in their size.⁹⁴ Hence, LDPE is a nucleating agent for the crystallisation of LLDPE and the addition of LDPE shifts the α -relaxational processes towards higher temperatures or longer times. The table presented below

lists the melting temperatures (T_m), densities (ρ), crystallite volume fractions (x) and spherulite radii (r) for individual LLDPE and for the LLDPE component of the LLDPE – LDPE composition containing 2.5% LDPE.⁹⁴

Sample	T_m /K	ρ /g cm ⁻³	x (%)	r /μm
LLDPE	370.3	0.9031	33.2	6.5
LLDPE – LDPE	372.5	0.9048	34.3	0.7

Linear LDPE has superiority in mechanical properties (*e.g.*, elongation at break) compared to LDPE. LLDPE-based blends exhibit intermediate properties (*e.g.*, torque⁹⁵) between those of the starting polymers. Studies on both film and melt behavior of such blends revealed no severe problems originating from polymer incompatibility. On the other hand, non-polar and low-polar crystalline polymers are poorly miscible with one another and with non-crystalline polymers. In this respect, a classical example is provided by blends of PE and PIB.⁹⁶

Polymer – polymer compositions prepared from solutions of polyolefins are also used, though much more rarely. For instance, linear PE ($M_w = 53\,000$, $M_n = 16\,000$) and branched PE ($M_w = 76\,800$, $M_n = 11\,300$) are mixed in predetermined ratios from 1% solution in xylene and then precipitated with methanol.⁹¹ Studies on the properties of such PPC allows the development of methods for compatibilisation of these polymers for their blending, processing and further use of the material.

Crystallisation of blends of HDPE and LLDPE has been the subject of intensive research (see, *e.g.*, Refs 97 and 98). The morphology and mechanical properties of films prepared from blends of UMMPE with a viscosity-average molecular mass of 6×10^6 and low-molecular-mass PE (4×10^4) by gelation⁸ or crystallisation from solutions are determined by the degree of entanglement of the macromolecules of both polymers. Here, LDPE has no time to form crystals since it crystallises at a much lower rate than HDPE. The modulus of elongation of such PPC is as high as 50 GPa, which is a quite appropriate value for conventional usage. These PPC exhibit lower viscosity, which favours substantial improvement of the performance of the equipment used for fabrication of blend-based films.

Structural peculiarities of the blend-based PPC under consideration determine^{99–101} the tensile strength of the PE blends,¹⁰² their operating characteristics¹⁰³ and dielectric and other properties. For instance, isothermal crystallisation of blends of the linear and branched PE at 397 K results in compact branched structures. Carrying out the process at 288 K leads to the formation of open, lamellar spherulite structures; quenching favours the appearance of a continuous spherulite texture.⁹¹ The dielectric properties of PPC depend, first of all, on their morphology, heat treatment conditions and the content of linear PE. This also concerns the PPC based on industrially used LDPE and LLDPE.¹⁰⁴ At the same time, HDPE and LLDPE are compatible in the whole range of their concentrations provided that quenching occurs at low melt cooling rate.¹⁰⁵ In the presence of HDPE the blend morphology is governed by the distribution of lamellae (crystallites), which is due to higher mobility of the HDPE molecules. The macromolecules of LLDPE form mixed crystals (co-crystallise) with the HDPE molecules. The lattice parameters of the crystalline phase increase as the number of side chain branchings increases. Vol'fon¹⁶ constructed a 'map' of the morphology behaviour of the LDPE – LLDPE blends with the predominant 'shish-kebab'-like morphology, containing 0.5% to 5.0% LDPE and quenched at different temperatures in the range from 393 to 463 K. Polymer – polymer compositions with low content of LDPE are characterised by a higher degree of crystallinity of LLDPE, higher melting temperature and rigidity.⁹⁴ The ultimate strength decreases while the yield stress increases as the content of LDPE increases (Fig. 6).

§ For gelation, polymer solutions in decalin, prepared at 408 K, are poured in an aluminium pan and the solvent is evaporated.

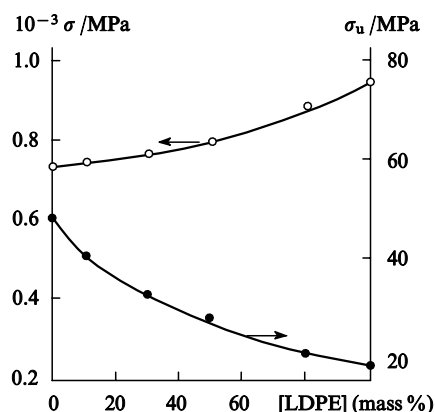


Figure 6. Yield stress (σ) and ultimate strength (σ_u) of compositions LLDPE–LDPE as functions of the component ratio at 296 K.⁹⁴

Information on ‘ternary’ PE-based PPC is scarce. Donatelli⁹⁹ studied ternary films prepared from low, medium and high density PE and showed that two polymers can be compatible within rather narrow limits of the content of branched units while they separate into individual crystalline phases at higher concentration of branchings.

2. Polyethylene–polypropylene systems and other compositions

Low-temperature impact brittleness of PP originates from the relatively high glass transition temperature of this compound (~ 263 K). An increase in the cold resistance of PP-based materials is a topical problem. Blends of PP and HDPE have been studied in most detail. At particular chemical compositions, these PPC are characterised by high breaking strength, modulus of elasticity and impact toughness and low brittleness temperature. The structural-dynamical parameters of the amorphous domains, the supramolecular structure and physicomachanical properties of such systems consisting of polymeric constituents with different molecular-mass characteristics have been studied. The properties of PPC prepared from isotactic PP and PE also depend on which catalyst was used for the polymerisation of ethylene, namely, a heterogeneous (Ziegler–Natta type) or a one-centre homogeneous metallocene catalyst.¹⁰⁶ Isotactic PP and HDPE are thermodynamically incompatible and form different types of crystal lattices. Since the melting temperatures of these polymers are different, they form individual structures.¹⁰⁷

In situ preparation of PPC from HDPE and PP by polymerisation at low pressure involves immobilisation of the catalyst components on either PP or PE. (This procedure was used in the polymerisation of, *e.g.*, propylene with the product of co-grinding of HDPE and TiCl_3 as the catalyst component.⁴⁶) The newly formed PPC can have virtually any chemical composition and exhibits improved strain–stress properties and cold resistance as compared to conventional polymer blends. It should be noted that the polymerisation method allows one to control the properties of the PP polymerisate, its stereosequence and molecular-mass parameters. Not only PE, but also other polymers and copolymers can be used for the preparation of the catalyst component. In particular, blends of PE and synthetic ethylene–propylene rubber (SKEP), PP and polybutene, PP and poly(4-methylpentene), *etc.*, were prepared. The structure of this type of PPC is shown in Fig. 7. Co-grinding of the catalyst (MCl_3) and HDPE leads to coating each catalyst submicroparticle with the polymer layer (‘skin’). Probably, sub-microcrystals (*e.g.*, TiCl_3) are inserted into the amorphous phase of PE. Nucleation of the PP phase with the globular structure gradually transforming into a lamellar one occurs in the bulk of the catalyst component particle. Microheterogeneous mixing of the growing PP phase with the PE phase is thought to result in the formation of IPN.

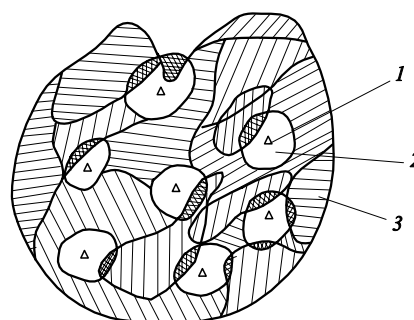


Figure 7. Structure of a submicroparticle of composition HDPE–PP. (1) Catalyst microparticle; (2) HDPE ‘skin’; (3) PP phase.

Binary compositions containing PP (70%) and HDPE (30%) are prepared by *in situ* polymerisation on binuclear metal complex catalysts immobilised on the SiO_2 surface.¹⁰⁸ The mechanical characteristics of this material (Young’s modulus, tensile strength) are 1.5 to 2 times higher than the corresponding characteristics of ‘pure’ PP. This is due to the very complex and unusual morphology of the material.

Considerable attention has been given to the studies of polymer blends based on PP and some other polymers such as elastomers, different crystalline and amorphous thermoplastics [PETP, polycarbonates, PS and acrylonitrile–butadiene–styrene (ABS) terpolymers]. Gupta *et al.*¹⁰⁹ analysed the rheological properties of binary and ternary blends of PP with ABS and LDPE. Ethylene/propylene block copolymers exhibit improved impact toughness and low brittleness temperature (down to 256 K).

At the same time, the strain–stress properties of such blends prepared from, *e.g.*, isotactic PP and LDPE^{110,111} are to a great extent dependent on the blending temperature and duration of blending of the components. The diffraction patterns of the HDPE–PP blends with different chemical compositions represent superpositions of the diffraction patterns of the starting components, which indicates that no co-crystallisation occurs. The average crystallite size in the blends is nearly the same as those in the non-blended components (150 and 170 Å, respectively).¹¹² However, the specific volume of the blend exceeds the value obtained using the additivity scheme. This points to the formation of a loose structure resulting from an increase in the content of the amorphous phase. This conclusion was also confirmed by the results of radiothermoluminescence studies, according to which the glass transition temperatures of the components in blends of LDPE and PP decrease (Fig. 8). Such a negative synergistic effect of the blend components can be rationalised by different rates and

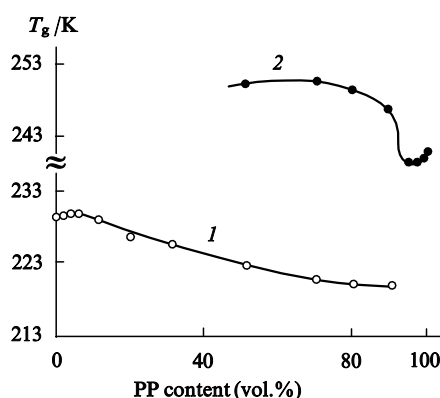


Figure 8. Glass transition temperature of the LDPE (1) and PP (2) phase as a function of the component ratio of LDPE–PP blend.¹¹²

temperatures of their crystallisation, by their thermodynamic incompatibility and by the absence of co-crystallisation in the blend. The rate of crystallisation of isotactic PP blended with LLDPE insignificantly decreases as the content of LLDPE increases.¹¹³ Dissolution of chain segments leads to the formation of an extended amorphous interfacial layer which precludes crystallisation of PP. The LDPE phase can be considered as a poor solvent for the PP phase (and *vice versa*).³

High density PE is incompatible with isotactic PP under steady-state conditions. However, compositions prepared from these polymers (PP:HDPE = 60:40) by injection moulding form a phase with regularly separated structure and an identity period of 0.15 μm . The regular structure cannot be formed by simple melt mixing but only by the spinodal decomposition (at zero shear rate).¹¹⁴ In the compositions consisting of isotactic PP and HDPE (0.1%–3%), phase separation occurs on gradual cooling from 473 down to 443 K.¹¹⁵ The average spherulite diameter is less than 10 μm for HDPE and greater than 100 μm for PP.²⁴ The proportion of ordered polymer chains in the amorphous phase of PP increases upon the addition of HDPE (10 mass % to 20 mass %) even for isotropic blends of these polymers prepared by melt mixing.¹¹⁶ The modulus of elasticity of the blends exhibits a synergistic effect due to the strengthening of the intercrystalline links in both the PP phase and in the interfacial layer.

It is interesting that, unlike the PPC based on syndiotactic PP and random ethylene/propylene copolymer[†] (a 80:20 blend, 4.9 mass % ethylene units), isotactic and syndiotactic PP synthesised on zirconocene catalysts are incompatible even upon heating up to 513 K (a 50:50 blend).¹¹⁸

The mechanical properties of PP–PE compositions can be substantially improved by using UMMPE instead of conventional PE.¹¹⁹ Such blends were prepared by coprecipitation of polymers from 1% xylene solutions at 398 K with excess methanol. Improved compatibility of PP and UMMPE can be most likely rationalised by the interpenetration of polymer chains in the amorphous phase due to the low degree of crystallinity of UMMPE.

A study on the morphology of blends of amorphous-crystalline block copolymers with amorphous homopolymers carried out taking the system consisting of ethylene/propylene diblock copolymer and atactic PP as an example showed that blending of the block copolymer responsible for the formation of the lamellar structure of microdomains and atactic PP leads to changes in the morphology of the microdomain structures and to microphase separation.^{120, 121} If the atactic PP chains are shorter than the block length, morphological transformations from lamellar structure into a bicontinuous cylindrical one, then into a discrete cylindrical and, finally, into a spherical structure occur. If the PP chain is longer than the block length, microphase separation occurs and a morphological change from lamellar to bicontinuous cylindrical structure is observed. In melts, these morphological transformations are accompanied by changes in the blend crystallisation kinetics.

In the blend of isotactic PP and SKEP the morphology of the ethylene domains depends only slightly on the viscosity ratio of the blend components and exhibits a strong dependence on the content of ethylene.¹²² The microstructure and chemical composition of SKEP (the dispersed phase) affect the rheology, morphology and properties of such compositions prepared by injection moulding.¹²³ The microstructure of a composition of isotactic PP and SKEP (60:40) essentially depends on which (a titanium- or vanadium-containing) catalyst it was prepared. Blends of isotactic PP and random SKEP, synthesised on vana-

dium-containing catalysts exhibit substantially improved impact toughness at low temperatures. The structure of the SKEP component affects both the crystallisation kinetics and the internal structure of spherulites of isotactic PP (the thickness of the crystalline lamellae and amorphous layer).

Among other PO–PO compositions, we will dwell on blends of isotactic PP and PIB. Problems of co-crystallisation and compatibility of blend components were considered by Cham *et al.*¹²⁴ Blends of PP and PIB are compatible in the amorphous phase and can even undergo co-crystallisation. Figure 9 presents the glass transition temperature and the Flory–Huggins interfacial interaction parameter of the PE–PIB compositions as functions of their chemical composition.¹²⁵ The maximum shift of T_g is 8.6 K for PE and 5.9 K for PIB (at 90% PE). This means that the solubility of PIB in PE is higher than that of PE in PIB. According to calculations, the solubility of PIB in the PE phase of the PE–PIB (10:90) composition is $\sim 17\%$ by mass, whereas the content of the PE phase in the PIB phase of the PE–PIB (90:10) composition is only 6 mass %. Low values of the Flory–Huggins interaction parameters χ_{12} and χ_{21} (see Fig. 9b) point to some degree of compatibility of the blend components despite the absence of specific interactions between their macromolecules. For unknown reasons, the χ_{12} value differs from χ_{21} .[†]

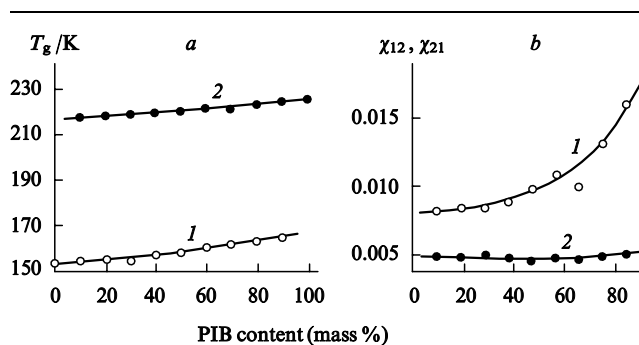


Figure 9. Glass transition temperatures (a) and Flory–Huggins parameters (b) of compositions PE–PIB as a function of the component ratio: (1) PE phase; (2) PIB phase.

Interesting results were obtained in studies of PIB–PS polymer networks containing from 10% to 70% PS.¹²⁷ Such blends were prepared by radical polymerisation of styrene preliminarily swollen in the PIB matrix. Electron microscopy studies did not reveal the formation of PS particles; however, cloudiness and rougher surfaces of the samples observed with increasing the content of PS are evidence of phase separation. Mechanical properties of PS are strongly dependent on its molecular mass. A decrease in the molecular mass probably favours compatibility of PS and PIB and an increase in the degree of grafting of the PS chains onto PIB, which manifests itself as increased ultimate strength, elongation at break and the fracture energy of the samples (at close PS content).

Information on polymer blends based on higher PO is scarce and fragmentary.

3. Preparation of polyolefin–polyolefin compositions by consecutive polymerisation

In the preceding section of this review we considered the formation of PPC in the course of the synthesis of one of the components. However, the *in situ* approach is also efficient if two or more polyolefin components are formed during the synthesis. This type of PPC is prepared by consecutive polymerisation of monomers on metal complex catalysts, which can be done

[†] For comparison, mention may be made that a study on the texture of a blend of syndiotactic and atactic PS revealed that the density of cross-link points strongly depends on temperature and exhibits relatively weak dependence on the initial chemical composition of noncrystallisable materials and on the degree of crystallinity of lamellar stacks.¹¹⁷

[†] This was also observed for polymer–polymer compositions PS–PMMA (the Flory–Huggins parameter for this system is 0.035 ± 0.010).¹²⁶

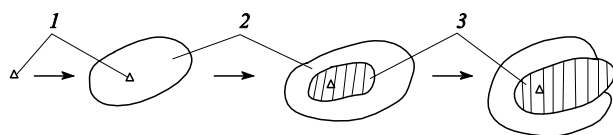


Figure 10. Formation of nascent morphology in the preparation of polyolefin compositions under conditions of polymerisation compatibility.

(1) Catalyst subparticle; (2) polymer prepared in the first stage of polymerisation (phase 1); (3) polymer prepared in the second stage of polymerisation (phase 2).¹²⁸

immediately in the polymerisation reactor using the Ziegler–Natta catalysts. The dispersity of the polyolefin compositions obtained is determined by both the size of the catalytic species (most often, TiCl_3) and peculiarities of the polymer morphology. Salient features of such PPC, differing from polymer blends of identical chemical compositions, are high molecular masses of the components and the presence of corresponding random and block copolymers localised within the interfacial layers.¹²⁸

A scheme illustrating the preparation of this type of PPC is presented in Fig. 10. The growing PP chains linked into crystalline fibrillae form a specific ‘skin’ around the TiCl_3 microcrystal. For instance, after completion of the polymerisation of propylene and removal of excess PP down to the specified post-polymerisation content, the reactor is filled with ethylene and then copolymerisation of ethylene with propylene on ‘living’ PP chains is carried out, followed by the homopolymerisation of ethylene. In this case, nucleation of the polymeric phase of PE occurs in the bulk of the globular PP particles formed in the first stage. The growing PE phase causes deformation of the ‘skin’ of the first submicroparticle and penetrates the PP layer. High-molecular-mass PE dispersed in the PP matrix represents particles of submicron size and is strongly amorphised. Hence, compatibilisation *via* polymerisation involves fine mixing of the components, which is accompanied by the formation of interpenetrating phases. The properties of the resultant product are determined by balance between its rigidity and strength (impact toughness). Semicrystallinity of the phase of isotactic PP has a crucial effect on the mechanical properties of these materials. The chemical composition of the elastomeric component and its content in particular PPC is also of great importance. Polymer–polymer compositions prepared using this approach consist of crystallisable polymers and are called polyallomers.¹²⁹ Studies on the morphology of polyolefins synthesised by consecutive polymerisation of propylene and ethylene in the presence of the $\text{TiCl}_3\text{–AlEt}_2\text{Cl}$ catalytic system showed^{130, 131} that the PE phase formed in the second stage causes deformation of the preliminarily formed PP layer followed by its disturbance and penetrates to the particle surface. A similar phenomenon was also observed for the polymerisation of propylene in the second stage of the process. Here, the PP phase penetrates the PE or SKEP layer formed in the first stage.¹³² The same is true for polymerisation of the butene–ethylene pair. Consecutive polymerisation also allows preparation of homogeneous ternary polyallomers containing, *e.g.*, the PP, PE and PB phases.¹³³

VI. Improvement of compatibility of polymeric components by introduction of compatibilisers

The most widely used strategies of improvement of the compatibility of immiscible polymeric components involve such approaches that initiate strong specific interactions (ion–ion and ion–dipole interactions, hydrogen bonds, *etc.*), formation of IPN, cross-linking, *etc.* Compatibility of the blend components is improved due to strengthening of the interfacial layers. Compatibilisation of different classes of polymers is achieved by introducing polymeric additives (specific ‘concentrates’ of the interface

phases) that favour manifestation of the above-mentioned compatibilising factors. These additives favour the formation of different types of bonds between the blend components and improvement of microheterogeneity of the systems in the stage of dispersion blending. Compatibilisers represent reactive copolymers containing chain segments that are compatible or miscible with both components of the PPC. These additives are of considerable interest as an alternative to conventional or graft copolymers. They can both be synthesised in the polymerisation stage and provide a means for *in situ* modification of the systems under study. This approach allows controlling the surface tension at the interface and the interfacial adhesion, thus providing more homogeneous distribution of the dispersed phase. The third component also acts as plasticiser.

It has been known for long¹³⁴ that block copolymers (in regard to polymer blends, they are often considered as ‘oil-in-oil’-type emulsifying agents¹³⁵) can emulsify polymer dispersions. This prevents phase separation. For instance, the addition of an AB diblock copolymer to a binary blend of polymers A and B causes a marked compatibilisation effect.¹³⁶ Moreover, a diblock copolymer AC can be used as a link between immiscible polymers A and B provided that polymer C is miscible with polymer B.¹³⁷ Yet another version of this approach involves blending of two incompatible polymers A and B using a diblock copolymer CD provided that both A and B are miscible with both C and D.^{138, 139} Blending of the diblock copolymer with the homopolymers having identical monomer units is a thermal process. However, if blending of a diblock copolymer consisting of blocks with different chemical nature with two immiscible polymers is accompanied by exothermic interaction between the blending pairs of polymers, this interaction can become an additional factor of compatibility of the immiscible components.

The most widely used compatibilisers represent additives containing anhydride (most often, maleic anhydride, or MA),^{140–145} carboxylic,^{146, 147} epoxy^{148, 149} and oxazoline¹⁵⁰ functional groups which react with the amino or carboxy groups of various thermoplastic polymers. Binary or ternary blends are also compatibilised using commercial products. Most often, these are PE-g-poly(maleic anhydride), ethylene–butyl acrylate–MA terpolymers (91 : 8 : 1) or poly(ethylene-co-vinyl acetate) (91 : 9) modified by grafting of MA (1%). Here, we restricted ourselves to the typical examples.

1. Compatibilisation of polyolefin blends

Weak interfacial interaction deteriorates the properties of composite materials based on PO blends. Compatibilisation of PO–PO block copolymers allows improvement of the miscibility of blend components and affects the properties of the interfacial layer in heterogeneous PO blends. If the molecular mass of a block copolymer is sufficiently large, it can act as an anchor at both sides of the interface. In particular, compatibility of a blend of isotactic PP and PE is often improved by using SKEP as the interfacial modifier.^{151–153} The cohesive energies of LDPE and ethylene/propylene copolymers in the amorphous phase are similar;⁹³ therefore, they are miscible on the molecular level. The addition (even in small amounts) of a random ethylene/propylene copolymer to the blend of HDPE and PP improves the impact toughness of the PPC;¹⁵⁴ that is, a portion of SKEP is dissolved in the amorphous domains of PE and PP, thus forming the interface layer. Multicomponent blends of LDPE, HDPE, isotactic PP, PB and poly(methylpentene) and recycled PO–PO blends can also be compatibilised by melt blending with ethylene/propylene block copolymers used as additives. An even more pronounced compatibilising effect is achieved by using synthetic ethylene–propylene–diene terpolymers (SKEPT) as additives to these polymeric compositions.¹⁵⁵ Grafting of compatibilisers onto a particular blend component (PE or PP) is also widely used. This approach allows improvement of blend processing conditions and an increase in the performance of the equipment used.

The mechanical properties of the PPC based on different types of PE (LDPE, HDPE, LLDPE and hydrogenated polybutadiene) and melt-mixed PS exhibit a strong dependence on the content (usually 2% to 10%) and molecular mass (60 000 to 270 000) of copolymer G [G stands for poly(hydrogenated butadiene-*b*-styrene)] used as an additive (see Fig. 11).^{156, 157} The hydrogenated triblock styrene-ethylene-butadiene-styrene terpolymer characterised by the total molecular mass of 35 000, the molecular mass of the central block of 7500 and the PS content of 29% is an efficient interfacial modifier for the HDPE-PS systems.^{158–160} Stability of polyolefin blends is often improved using ternary blends. For instance, the ternary blend of PP, polybutene and hydrogenated oligocyclopentadiene (50:30:20)³⁵ has one glass transition temperature, 289 K (*cf.* a value of 286 K obtained from calculations using the Fox equation), which confirms compatibility of the blend components.

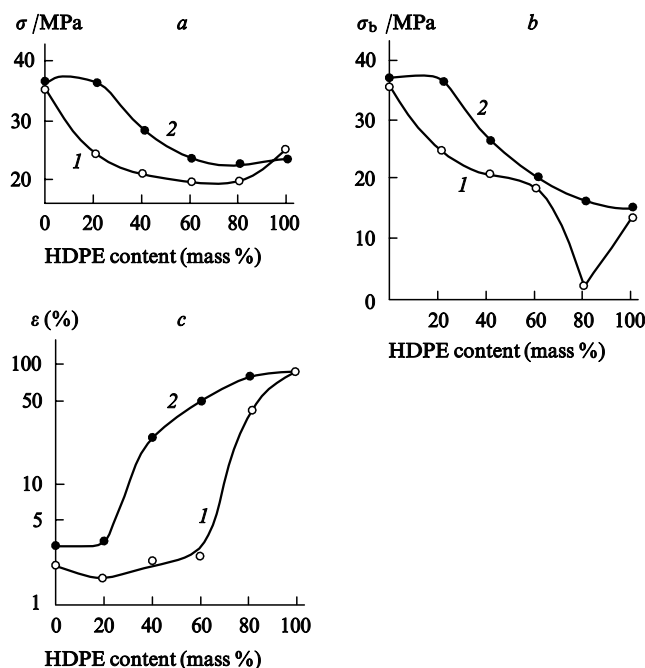


Figure 11. Yield stress (a), tensile strength (b) and relative elongation at break (c) plotted as functions of the component ratio of composition HDPE-PS without (1) and with addition of 10% copolymer G (2).

Graft, triblock and star copolymers have high emulsifying ability and are even more efficient compatibilisers. These types of blends based on PP, HDPE and SKEPT (as a rule, with ethylidene-2-norbornene as the third monomer) are of commercial value and have therefore been the subject of intensive research.^{161–163}

If some fraction of the elastomeric constituent (SKEPT) of the blend of PP, SKEPT and PE is replaced by PE, this system can exhibit a higher or lower impact toughness depending on the blending conditions of the components, their rheological properties and viscosities.¹⁶⁴ Sometimes, the interfacial adhesion is improved by carrying out the reactions of dynamic selective cross-linking (see below).¹⁶⁵

2. Compatibility of polyolefin-polyamide systems

Polyamides (PA-6, PA-66, PA-12, *etc.*) exhibit high mechanical strength, rigidity and good processability and are therefore widely used in the automotive industry and for production of textile fibres. They have high melting temperatures and oil resistance. However, PA are characterised by ready deformation at low temperatures, cracking and high moisture absorption, which imposes limitations on possible applications of these materials.

Polyamides are often used in the form of blends with low-module polymers, such as PO and, in particular, LDPE, which exhibits excellent elastic properties at low temperatures and low moisture absorption. Using such blends reduces the cost of materials. The high commercial value of the systems based on PA-6 and LDPE has attracted considerable attention.¹⁶⁶ Interest in the compatibility problem of PO and PA is also due to the fact that the polyolefins and polyamides represent two main groups of materials for recycling.^{167, 168}

The components of the two-phase system LDPE-PA-6 are incompatible; therefore, this blend is characterised by weak interfacial adhesion and high dispersity of the LDPE domains. The properties of such PPC are determined by the size and shape of the dispersed phase; it should be noted that these parameters depend on the elasticity of the components.^{10, 169} The addition of interfacial modifiers, *viz.*, block or graft copolymers (their content is 0.5% to 1%) leads to a decrease in both the degree of crystallinity of LDPE and the crystal lattice parameters and to improvement of the mechanical properties (especially, yield stress, Young's modulus, impact toughness, relative deformation). The components of this system were compatibilised by the introduction of the block copolymer of styrene, ethylene and butylene to the modified extrudate.¹⁷⁰ Based on the analysis of the shape of thermomechanical curves of the blends, it was suggested that PA-6 was nearly molecularly dispersed in the LDPE matrix in the presence of 5% of the ternary block copolymer.

In the case of melt mixing of blend components the introduction of a third component can facilitate the blending and improve the mutual solubility of the components, thus providing predominant interaction of functional groups with a particular component. The most detailed studies on the problems of graft functionalisation of PO with MA or acrylic acid were carried out taking compositions of PO and PA as examples.^{171–173} *In situ* grafting in the extruder at 473 K in the presence of dicumyl peroxide (DP) (PP:MA:DP = 94:6:0.3) was followed by granulation. Free-radical melt grafting of MA, glycidyl methacrylate and diethyl maleate (DEM) onto PO was also studied in detail.^{174, 175} *In situ* preparation of PPC based on PA-6 and LDPE that was graft functionalised with MA or DEM led to interesting results.¹⁷⁶ The addition of PP-MA compatibilisers improved the interfacial adhesion and the impact toughness of the compositions of PP and PA-6.^{177, 178} Probably, the interfacial adhesion becomes stronger due to the formation of hydrogen bonds between the end amino groups of PA and grafted MA; this leads to nearly complete homogeneity of polymer blends.¹⁴¹ It is appropriate to use functionalised PO, *e.g.*, carboxy derivatives for compatibilisation of polyamide matrices and the dispersed PO phase.^{179, 180} As a rule, grafting of carboxy or anhydride groups onto the PO chains is performed during melt mixing. Reactions of the amino or amido groups of the PA phase with functional groups of the PO phase result in the formation of *in situ* prepared copolymers characterised by weakened interfacial tension and improved interfacial adhesion of their components.¹⁸¹

Improvement of fracture toughness is often achieved by energy dissipation within the interfacial layer of immiscible components of PPC. The introduction of a block copolymer additive should result in a decrease in both the interfacial tension and phase dispersity; in many instances this depends on the number of 'stitches' between the two phases.¹⁸² Nearly perfect compatibility was observed, *e.g.*, upon addition of small amounts of the PP/MA copolymer to blends of PE and PA-6.¹⁸³ Park *et al.*¹⁸⁴ studied the morphology, thermal and rheological properties of the composition of PP, PA-6 and PP/MA (5%) including the dependence of its viscosity on the chemical composition at low shear rate (Fig. 12). The results obtained point to the negative deviations from the additivity rule for the simple system PP-PA-6 and to positive deviations for the blends of PP, PA-6 and PP/MA. These results were used for assessing the texture of the PPC and evaluating the chemical interaction between the starting polymers. Currently, the composition of SKEP, PA-6 and the melt-prepared

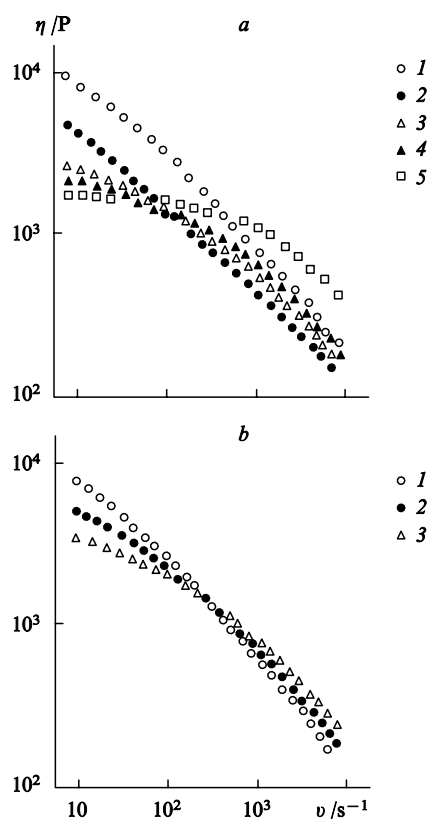
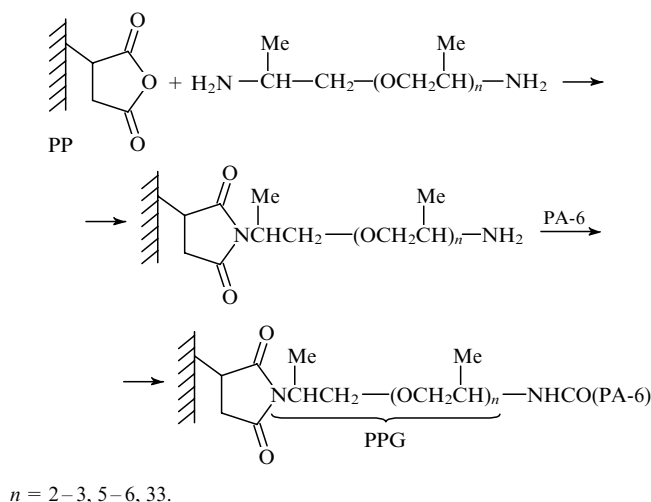


Figure 12. Shear viscosity (η) of compositions PP–PA-6 (a) and PP–PA-6–(PP/MA) (b) plotted vs. shear rate. (a) PP (1), PP–PA-6 = 75:25 (2), PP–PA-6 = 50:50 (3), PP–PA-6 = 25:75 (4) and PA-6 (5); (b) PP–PA-6–(PP/MA) = 75:25:5 (1), PP–PA-6–(PP/MA) = 50:50:5 (2) and PP–PA-6–(PP/MA) = 25:75:5 (3).

graft copolymer of carboxy- or anhydride-modified SKEP and PA-6 has been the subject of intensive research.

Sometimes, more complex interfacial modifiers are used. For instance, *in situ* modification of the blend of PP and MA (the degree of grafting was 0.3 mass % or 0.8 mass %) with poly(propylene glycol)-bis-(2-propylamine) with $M_w = 230, 400$ and 2000 was reported.^{185, 186} This was done based on the fact that polymers containing ether groups [e.g., poly(ethylene glycol) or poly(propylene glycol) (PEG or PPG)] are compatible with PA due to the formation of hydrogen bonds¹⁸⁷ and resulted in the PP–MA–co-PPG composition which exhibits good compatibility with PA-6 due to hydrophobic-hydrophilic interactions between the ether

groups of PPG and amido groups of PA-6. Some characteristics of mechanical properties of the PP–PA-6 compositions prepared in different manner are listed in Table 7. It should be noted that all the compatibilised compositions have lower melt flow indices than the simple polymer blend. Increasing the degree of grafting of MA and the chain length of PPG leads to improvement of the strength properties of the compositions. Schematically, the formation of such a PPC can be represented as follows:



The limiting factor in the design of compatible systems with optimum characteristics is the concentration of reactive groups.

Compatibilisation of immiscible polymers using isocyanate groups which react not only with the amino or carboxy groups, but also with hydroxy groups has been rarely reported. For instance, blending of LDPE and PA-6 involves the modification of LDPE by grafting the product of the interaction of 2-hydroxy-methyl methacrylate and isophoronediiisocyanate (the reaction is carried out in xylene at 393 K in the presence of 1% DP in N_2 atmosphere) followed by mixing the modified LDPE and PA-6 in N_2 atmosphere at 518 K for 4 h.¹⁸⁸ In the course of blending the NCO groups interact with the terminal amino groups. Chemical bonding between the butyl acrylate or MA groups and terminal amino groups is formed in the compositions based on PA-6 and PE–MA, in the ethylene–butyl acrylate–MA (91:8:1) terpolymer and in the ethylene/vinyl acetate (91:9) copolymer modified by grafting MA (1%).⁴¹

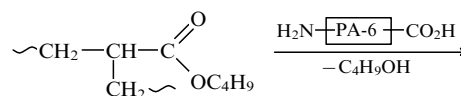
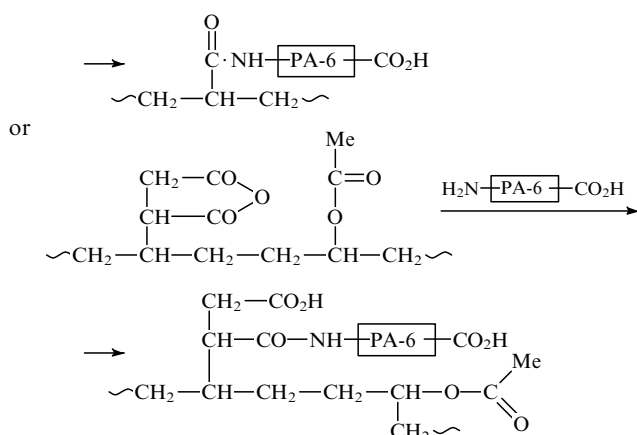


Table 7. Mechanical properties and melt flow indices of PPC modified in a different manner.⁹⁴

PPC	Component ratio (by mass)	Unnotched impact toughness /MPa	Strength properties /MPa		Melt flow index ^a
			tensile strength	fracture toughness	
PA-6–PP	30:70	11.9	25.0	2.2	19.6
PA-6–PP–PP-g-MA (0.3%)	30:70:5	13.8	30.2	2.5	9.3
PA-6–PP–PP–PP-g-MA–co-PPG (400) ^b	30:70:5	15.3	31.3	3.3	10.0
PA-6–PP–PP–PP-g-MA–co-PPG (2000) ^b	30:70:5	19.4	32.3	3.8	6.7
PA-6–PP–PP–PP-g-MA (0.8%)	30:70:5	25.6	34.1	7.7	6.7
PA-6–PP–PP–PP-g-MA–co-PPG (400) ^b	30:70:5	21.4	34.4	8.0	9.6
PA-6–PP–PP–PP-g-MA–co-PPG (2000) ^b	30:70:5	38.6	35.6	11.5	6.4

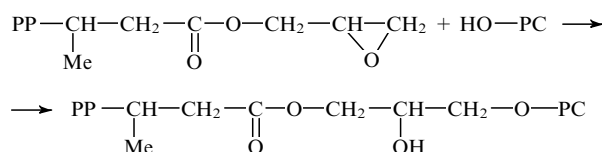
^a Dimensionality: grammes of polymer flown over a period of 10 min at 513 K and a standard load of 21.2 N. ^b Figures in parentheses denote the molecular mass of PPG.



3. Third component in the compatibilisation reactions of polyolefins with other polymers

Compatibility of PVC and chlorinated PE with ethylene/vinyl acetate copolymers (EVAC) is often used to improve the mechanical properties of PPC.⁷⁸ Such a modification can also be performed in the polymerisation stage. For instance, blends of styrene and acrylonitrile or styrene and MMA are selectively grafted onto chlorinated PE using TiCl_3 .⁷⁹ The addition of PE-g-PS (merely 2.5 mass %) to the PE-PS films substantially improves their strain-stress properties.⁸⁰

The LDPE-EVAC-PETP system has considerable advantage over the LDPE-PETP composition, namely, the presence of polar functional groups in the copolymer provides the possibility of controlling the contact reactions, *i.e.*, the chemical interaction at the interface.¹⁸⁹ It is solely the polar interaction of the PP-MA additive (4 mass % MA) and the carbonyl groups of the blend of PP and the liquid-crystalline polymer that is responsible for improvement of the mechanical properties of this system.¹⁹⁰ A number of reaction compatible blends of PO [with PE-g-poly(glycidyl methacrylate) or PE-glycidyl acrylate (GA) as compatibiliser] and polycarbonate (PC), PETP and other polymers was reported.^{142, 191, 192} The composition of PP and PC can be compatibilised using the PP-GA graft copolymer (2.5%–20%), which favours weakening of the interfacial interaction, improves the mechanical properties of the composition, increases the crystallisation temperature of PP and changes the blend morphology. In the molten state (in both the internal blending chamber and twin screw extruder) the epoxy groups of the third component react with the terminal groups of PC by the mechanism shown below



Interestingly, the coupling reaction between the polymeric constituents makes extraction of the entire PC phase from the ternary blend impossible, as in the case of compositions of PE and PMMA, PE and PVC, LLDPE and PA-6, *etc.*

This method allows compatibilisation of LLDPE modified by grafting MA¹⁹³ and PValc (the component ratio is 70:30). Another example is provided by the analogously modified composition of PP and liquid-crystalline polymer, which exhibits improved strength, deformation characteristics and the modulus of elasticity.¹⁹⁴

Numerous methods for the introduction of reactive polymeric reagents capable of *in situ* compatibilising of PO and PS have been reported.^{149, 195} One of them involves generation of reactive radicals on the surface of PO or PS to form the grafted

layer^{196, 197} (detailed consideration of this approach is presented below).

The morphology and properties of PPC based on PP and ethylene/dimethylaminoethyl methacrylate copolymers containing up to 27 mass % dimethylaminoethyl methacrylate units by mass have been studied in detail.¹⁹⁸ The components of this PPC are incompatible and form two-phase structures. As the content of the copolymer increases, the compositions become brittle and the interfacial adhesion between the constituent phases weakens substantially.

The third component, *e.g.*, PS-b-poly(ethylene-co-butene)-b-PS (PSBECB) is often used as plasticiser, especially for improvement of the impact toughness of brittle polymers.¹⁹⁹ This compatibiliser represents a microheterogeneous thermoplastic elastomer in which the PS end blocks (as a rule, 10–35 mass %) are linked into rigid domains that form a lattice in the flexible matrix of the ethylene/butene copolymer (EBC). It is used if one component of a PPC is compatible with the EBC blocks while the other component is compatible with the PS blocks. This additive allows the preparation of polymer blends containing not only PP, HDPE, LHDPE, but also the ABS plastics and other components.^{200, 201}

In studies of ternary systems containing, *e.g.*, PA, a modified additive, PSBECB-MA, is used.²⁰² It is thought that the EBC blocks are compatible with PP and the interfacial adhesion between PA and PSBECB is provided by the formation of imides in the reaction of the terminal amino groups with anhydride. In this case, the formation of domains with rigid polyamide core and flexible elastomer 'skin', which favours improvement of the strength and viscosity without changing the polymer rigidity, cannot also be ruled out.²⁰³ Finally, the PSBECB constituent of ternary blends containing impact-resistant PS reduces the degree of crystallinity of PP.²⁰⁴ The modulus of elasticity and yield stress of PP-PSBECB blends decrease as the content of the block copolymer increases.²⁰⁵ Good compatibility of PSBECB and PP can be due to the random nature of the copolymer in the EBC block. The effect of repulsion²⁰⁶ between different polymer chain segments in EBC (though the repulsion between the ethylene and butene segments must be very weak) can improve the compatibility of the PE-PP pair. It was shown that PSBECB is a good compatibiliser for polymer blends based not only on isotactic PP, but also syndiotactic PP.²⁰⁷ In both cases, the additive, PSBECB, favours a decrease in the modulus of elasticity, yield plateau and an increase in the yield stress. The use of the compatibiliser consisting of PSBECB and MA allows reduction of the tear resistance for the block copolymer and isotactic PP.

Summing up, we considered the most widely used strategies of using polymeric compatibilisers for improvement of compatibility of polymer blend components. It should be mentioned that polymeric supports for metal complex catalysts, obtained by the grafting of corresponding, *in situ* polymerisable monomers onto PO (see the grafting scheme presented in Section III.1) contain the interfacial modifier which improves compatibility of the components of PPC.

VII. Polyolefin-based polymer blends prepared by reactive blending

Many polymeric compositions considered above are prepared by reactive blending in extruder reactors. Since this process is accompanied by numerous chemical reactions between the components or specially introduced compatibilisers, it would be reasonable to call the blends obtained 'reactor blends' or 'extrusion blends'. However, in this review we will use the term 'reactor blends' in a somewhat narrower sense.

As a rule, functionalisation of polymers by graft polymerisation represents an individual stage of the process and is followed by their blending. Currently, extruder reactors are widely used as continuous reactors combining the stages of dispersion of blend components and chemical reactions between

them.^{180, 208–210} In particular, chemical modification of thermoplastics in a twin screw extruder is thought to be a promising procedure for production of novel materials.

Extrusion combines the *in situ* functionalisation of blend components and the formation of block or graft copolymers at the interface. Inter-chain copolymers prepared by extrusion are often used *in statu nascendi* for compatibilisation of thermodynamically incompatible blend components; this particularly concerns the PE–PA-6 blends modified using the third component.²¹¹ In these cases, at low concentrations of the interfacial modifier and initiator the additives favouring improvement of the relative elongation at break and the impact toughness perform three functions. First, they act as reactive interfacial modifiers that improve compatibility of the components in the molten state. Second, they are grafted onto PO by the radical mechanism. Third, their functional groups react with the terminal groups of the components (*e.g.*, PA), thus forming covalent or hydrogen bonds. Most often, reactive blending is performed in the presence of peroxide (0.5% to 2.0%) with MA, bifunctional or multifunctional monomers as interfacial modifiers. The additives having long hydrocarbon chains (*e.g.*, alkylmaleic monoamide or alkylmaleic monoether) are more efficient compatibilisers than the short-chain additives. Non-monomeric additives are used more rarely. For instance, the addition of stearic acid (5%) to the blend of LDPE and PA-6 (75 : 25) allows control of the phase morphology.²¹²

The effect of *in situ* reactive blending in an extruder reactor was also observed in studies of blends of LLDPE modified by grafting of maleic acid or MA with PA-6 or PA-11.^{213–215}

In situ mechanochemical preparation of self-compatible polymer blends by solid-phase extrusion grinding of immiscible polyolefin constituents represents a variant of the approach in question.^{16, 216, 217} The process is accompanied by scission of polymer chains and, hence, generation of free radicals capable of entering the reactions with another polymer chain or undergoing recombination with other macroradicals (this was experimentally proved taking the PE–PP system as an example), thus forming a block copolymer or a graft copolymer. The latter acts as an *in situ* generated compatibiliser. This procedure is particularly convenient when performing recycling since the process proceeds at a low temperature, so both the mechanical and oxidative degradation are reduced to a minimum.

Nearly three decades ago a new product, *viz.*, a thermoplastic blend based on SKEP finely dispersed in the PP matrix appeared in the world market. Such polyolefin blends are prepared by dynamic vulcanisation and called thermoplastic elastomers or thermoplastic vulcanisates.²¹⁸ They represent multicomponent polymer blends which possess the mechanical properties of elastomers at room temperature and the rheological properties of thermoplastic polymers at elevated temperatures. A salient feature of the procedure for their preparation is the combination of blending and vulcanisation (with SKEPT as the third component). This leads to the formation of PPC with specific morphology, namely, two-phase systems in which the particles of the cross-linked elastomer of size 1 to 10 μm are dispersed in a continuous thermoplastic polymer matrix and the content of the elastomeric component exceeds that of the thermoplastic polymer. Usually, such systems are cured with DP. Dynamic vulcanisation can be performed in two ways (Fig. 13). Thermoplastic elastomers offer improved processability, *e.g.*, their melts behave as thermoplastics despite the presence of the cross-linked elastomeric constituent.²¹⁹ The thermoplastic nature of the blend can be due to the curing dynamics features which prevent the formation of a three-dimensional rubber network in the dispersed phase. However, the melt viscosity of the PPC enriched with PP increases as the content of SKEPT increases up to 25%. The crystal structure of the starting PP can either change or remain unchanged depending on the procedure for preparation. The structure and properties of this type of dynamically cured polymer blends, peculiarities of their

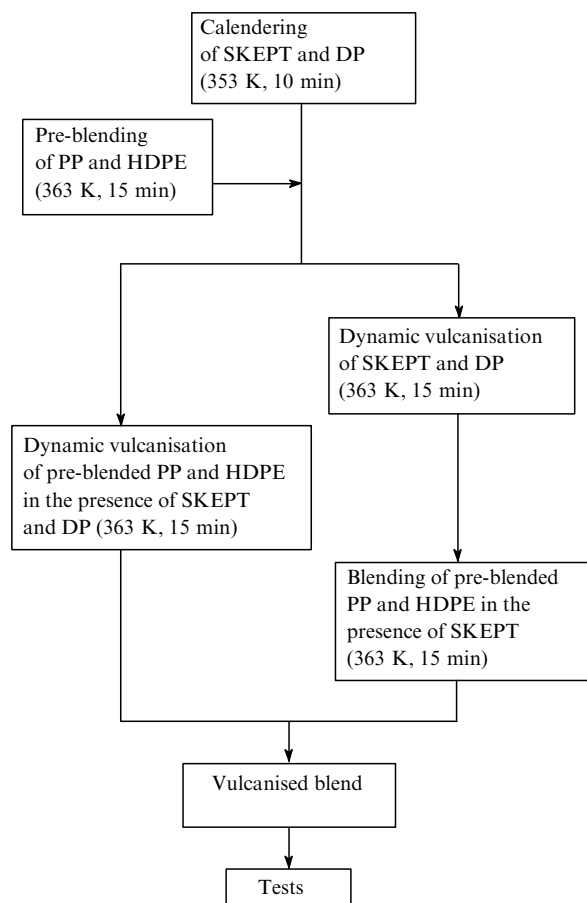


Figure 13. A scheme of dynamic vulcanisation process.

rheology and structural characteristics have been the subject of detailed studies (see, *e.g.*, Refs 220 and 221). The deformation mechanism of thermoplastic elastomers based on isotactic PP and SKEPT involves the deformation of the structure of the composition in the first stage followed by simultaneous deformation of both the cross-linked SKEPT domains and PP macromolecules; the strength and elongation at break are determined by the tension of the cross-linked elastomer.²²²

Blends of PO and SKEPT can be prepared using numerous methods that are not only of scientific, but also practical value. One of these procedures involves the formation of blends of cross-linked SKEPT (ternary SKEP) and PO using roll mills or peroxide-initiated dynamic vulcanisation in an extruder. This method was first proposed for PPC;²²³ however, at present it has found wide industrial application for production of plastics and thermoplastic elastomers. It offers such advantages as short blending time, short-term processing cycle, small energy expenditure for recycling and the possibility of easy control over the properties of products by varying the component ratio.

Main conditions for the preparation of materials based on dynamically vulcanised polymer blends with optimum properties have been formulated and a number of factors determining the structure and properties of such blends were pointed out.²²⁴ For instance, polymeric compositions with high content of rubber can be used as thermoplastic elastomers, while polymer blends with high content of plastic can be used as rigid plastics 'enriched' with rubber. Peculiarities of their morphology improve processability despite the presence of the cross-linked elastomeric component.¹⁹⁹ Dynamic vulcanisation also allows the preparation of such PPC as, *e.g.*, SKEPT–PP, SKEPT–PP–HDPE, LDPE–SKEPT, *etc.*^{225, 226}

VIII. *In situ* preparation of diblock chemical hybrids

In this section we will consider diblock polymeric compositions in which one of the block materials does not belong to the polyolefins. From the standpoint of structure and properties this group of PPC comprises diblock copolymers, namely, graft copolymers in which one component (the polymeric support) represents a macromolecular organometallic compound. These copolymers can be prepared using the Ziegler–Natta catalysts and by consecutive polymerisation of olefins.

Lithium-containing block copolymers of ethylene and butadiene²²⁷ and of ethylene and isoprene²²⁸ seem to be the first representatives of this group of PPC. The molecular mass of the PE blocks varied from 13 000 to 36 000. Since ethylene polymerisation was accompanied by cross-linking of 1,2-butadiene units, this method was found to be more appropriate for the preparation of ethylene/styrene diblock copolymers²²⁹ or blends consisting of PS blocks and blocks of ethylene/propylene copolymer (EPC).^{230, 231} The synthetic procedure involves treatment of the organolithium compound with TiCl_4 to replace lithium by titanium, reduction of titanium and the formation of the catalyst component for polymerisation of ethylene (the molecular mass was 7000–33 000 for PE blocks, 10 000–11 000 for PS blocks and 33 000 for EPC blocks).

The PS–b-poly(ethylene-co-propylene) composition was also synthesised using the PS–Li macroanion and TiCl_4 .²³² The molecular mass of the EPC blocks was as high as 500 000, the $M_w:M_n$ ratio was 2.24 to 4.23, the degree of crystallinity varied from 7% to 20% and the content of ethylene units in the block was 70% to 80%.

The efficiency of the catalyst, expressed as the number of polymer chains per Ti–C bond was rather high (0.88). According to the results of differential scanning calorimetry (DSC) studies, the thermogram (Fig. 14) exhibits a small peak of PS at $T_g = 369$ K. Both the melting temperature (410 K) and relatively low molecular mass ($M_n = 63$ 000, $M_w:M_n = 1.4$) point to a linear structure of the PE blocks.[‡]

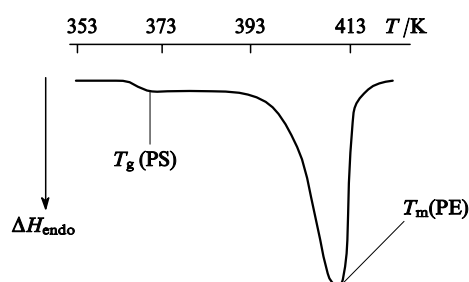


Figure 14. A DSC scan of block copolymer PS–PE.²³²

Among numerous methods for the *in situ* preparation of diblock PPC in the radical polymerisation of a particular compo-

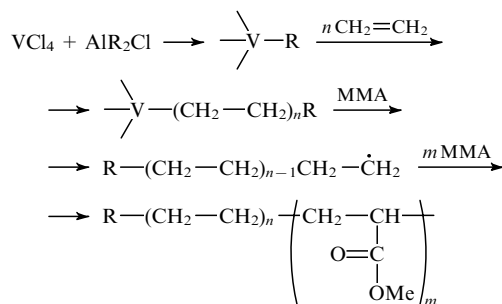
‡ For comparison, mention may be made that consecutive anionic copolymerisation of equivalent amounts of styrene and 4-vinylpyridine on LiBu at 195 K resulted in a PS–b-P4VP (PS:P4VP = 59:41) composition ($M_n = 62$ 300),⁸⁰ which was used as compatibiliser for blends of polar and non-polar polymers belonging to different classes. Anionic polymerisation of styrene in the presence of polymers is accompanied by chain entanglement of newly formed linear macromolecules and the polymer network of cross-linked chains²³³ and results in macroscopically heterogeneous gels. The formation of cross-linked or grafted chains was also observed in the anionic polymerisation (using LiBu, AlEt_3) of diisocyanates in the presence of butadiene, isoprene and butadiene-styrene rubbers.²³⁴ In the last-named case the formation of graft polymers occurs due to the involvement of the side double bonds in positions 3 and 4.

nent, two procedures are most widely used. The first method (preparation of IPN) is in essence a radical polymerisation of vinyl monomers in the presence of soluble or swollen polymers (here, a typical example is provided by the polymerisation of styrene in the presence of polybutadiene). The second procedure involves the use of polymeric peroxide or azo initiators (see, *e.g.*, Refs 235 and 236) whose concentrations are comparable with those of the components.

In situ preparation of diblock PPC can proceed either by conventional polymerisation mechanisms or as a stepwise (consecutive) process involving ‘switching’ of the polymer formation mechanisms (in this case, each block is formed on the active centres of different chemical nature). The latter can be exemplified by the preparation of diblock copolymers based on olefins and vinyl monomers in the presence of the $\text{TiCl}_3\text{--AlEt}_3\text{--ZnEt}_2$ system.²³⁷ The stage of ethylene polymerisation involves the formation of polymer chains with terminal zinc–carbon bonds that provide the possibility for the next stage, TiCl_3 -catalysed polymerisation of vinyl monomers, to proceed. By choosing the most appropriate combinations of the olefin and vinyl monomers one can prepare block, graft or block/graft copolymers representing either the end products (PPC) or compatibilisers of PO and vinyl polymers.

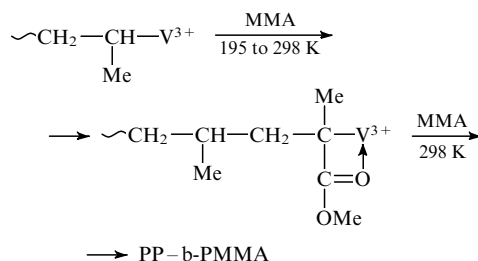
Methods for the preparation of modified poly- α -olefins by switching of polymerisation mechanisms (anionic-coordination mechanism changes to cationic or anionic mechanism, anionic mechanism is replaced by the radical one, *etc.*) have long been developed. A typical example is as follows:²³⁸ first, polymerisation of propylene is performed on the $\text{TiCl}_3\text{--Et}_2\text{AlCl}$ catalytic system. After some time, the unreacted monomer is separated and 4-vinylpyridine and SnCl_4 or Bu^nLi are added. This procedure can also be used for preparation of polyolefin chains with the MMA, vinyl ketone, acrolein and other fragments. Isotactic PP synthesised on the ethylenebis(tetrahydroindenyl)zirconium dichloride ($\text{C}_2\text{H}_4[\text{H}_4\text{Ind}]_2\text{ZrCl}_2$)–methylalumoxane catalytic system by successive treatment with the borane–dimethyl sulfide complex and pentane-1,2-diylmagnesium dibromide was transformed into PP with the MgBr terminal groups.²³⁹ The modified PP was then used as anionic initiator of polymerisation of MMA at temperatures between 195 and 318 K. ^1H NMR and gel permeation chromatography studies confirmed the formation of the PP–b-PMMA system ($M_n = 5300\text{--}3000$) which can be used as polymeric additive to blends of PP and PMMA.

It was established experimentally that the polymerisation mechanism changes from anionic-coordination to radical during the preparation of diblock copolymers of PE and PMMA.²⁴⁰ The addition of MMA to the $\text{VCl}_4\text{--AlR}_2\text{Cl}$ catalytic system in the course of anionic-coordination polymerisation of ethylene leads to its inhibition and initiation of the polymerisation of MMA (probably, as a result of radical induced cleavage of the V–C bond). The process results in the PE–b-PMMA system.



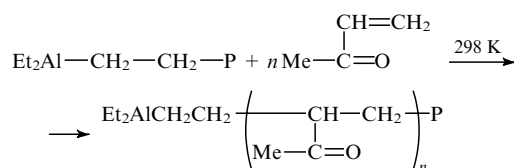
It is known that both homopolymerisation and copolymerisation of polar monomers on metal complex catalysts proceed solely by the coordination mechanism in the absence of electron-donor additives and can follow both coordination and radical pathways in the presence of such additives. It cannot be ruled out that in many instances the polar monomer itself acts as electron donor.

Kinetic studies confirmed that graft copolymerisation of MMA is radical initiated. 'Living'⁸ coordination polymerisation of propylene on the $V(acac)_3 - AlEt_2Cl$ system was used for the synthesis of a diblock copolymer of PP and PMMA.²⁴¹ The polymerisation proceeds at 195 K; raising the temperature up to 298 K in the presence of MMA leads to the formation of a radical centre as a result of homolytic cleavage of the $V - C$ bond.



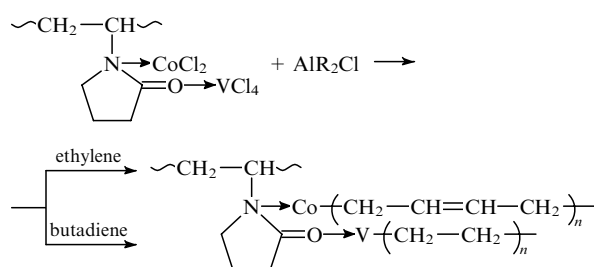
The macroradical is stabilised by the vanadium ion, which provides the possibility for 'living' polymerisation of syndiotactic PMMA blocks to proceed; chain termination in the radical polymerisation occurs on the organoaluminium compound.

Diblock copolymers of propylene and methyl vinyl ketone were synthesised using the stereospecific Ziegler–Natta catalysts.²³⁸ In first stage, a conventional anionic-coordination polymerisation of propylene proceeds, while the second stage of the process (in contrast to the radical polymerisation of MMA) represents an anionic polymerisation of methyl vinyl ketone catalysed by terminal alkylaluminium groups.



No additional treatment is required to 'switch' between the catalytically active centres in the schemes presented above since MMA itself acts as the 'switching' agent. Transformation of the anionic process into a radical one was also observed by Souel *et al.*²⁴² who studied polymerisation of isoprene in the presence of butyllithium. Treatment of the product, 'living' oligomeric isopropenyllithium, with Me_3PbCl results in an adduct whose decomposition in the presence of styrene leads to the formation of PI - b-PS.

Let us consider yet another procedure for *in situ* preparation of PPC based on polymers belonging to different classes, namely, polyolefins and polydienes. We will dwell on the copolymerisation of olefin and diene monomers under the action of bifunctional immobilised catalysts. For instance, copolymerisation of ethylene and butadiene can be performed using complexes of Co^{2+} and V^{4+} immobilised on the PE-g-poly(vinylpyrrolidone) (PE-g-PVP) system.⁴⁶ Alkylation of this heterometallic complex with AlR_2Cl leads to the formation of active centres initiating the polymerisation of ethylene (V-centres) and butadiene (Co-centres).



§ Polymerisation proceeds until complete consumption of monomer; however, the addition of a fresh portion of the monomer leads to a restart of the process at the same rate.

In the text below the combination of Co- and V-centres will be shown in a simplified form as $\begin{pmatrix} \text{Co-P}' \\ \text{V-P}'' \end{pmatrix}$. These active centres

coexist in the presence of ethylene and butadiene and retain their catalytic activity despite essential modification. Butadiene is known to be a strong inhibitor of ethylene polymerisation. The rate of copolymerisation of ethylene and butadiene on vanadium-containing active centres is low. Indeed, the rate of ethylene polymerisation decreases in the presence of butadiene (Fig. 15); however, inhibition of the reaction proceeding in the presence of heterometallic cobalt – vanadium catalysts is less pronounced. In turn, the rate of butadiene polymerisation on the Co-centres also somewhat decreases in the presence of ethylene²⁴³ whose molecules undergo insertion into the polymer chain (1 or 2 ethylene molecules per macromolecule), thus reducing the molecular mass of polybutadiene. The mechanism of this process is similar to that of chain transfer to polymer and consists in decomposition of the less stable σ -alkyl cobalt derivative that is formed from the π -allylic product upon addition of ethylene.

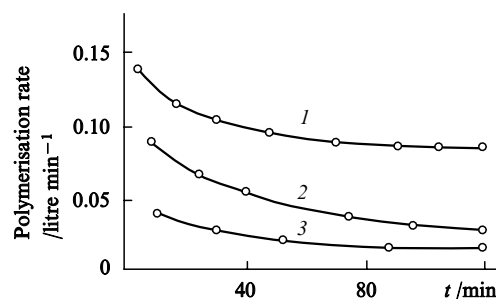
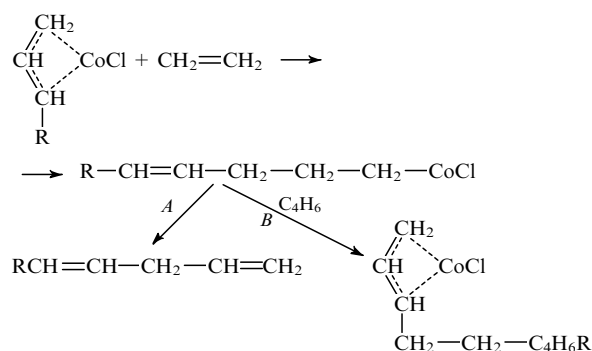
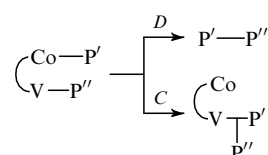


Figure 15. Kinetic curves for the synthesis of HDPE–PBd compositions under comparable conditions.

(1) Ethylene polymerisation on monometallic catalyst; (2) copolymerisation of ethylene and butadiene on bimetallic catalyst; (3) copolymerisation of ethylene and butadiene on monometallic catalyst.



Here, route *A* corresponds to chain transfer while route *B* corresponds to copolymerisation of ethylene and butadiene. However, spatial proximity of both active centres and co-operative chain propagation processes make migrations by, *e.g.*, the inter-chain exchange mechanism²⁴⁴ *via* transfer of the polybutadiene chain to PE (route *C*) or recombination of polymer chains (*D*) quite probable.



If these reactions are accompanied by chain disproportionation, the $P'-P''$ diblock copolymer is formed; persistence of

Table 8. Formation of PE–polybutadiene block copolymers in the PPC prepared by copolymerisation of ethylene and butadiene on bifunctional cobalt–vanadium catalyst.⁴⁶

Ethylene consumption for polymerisation /g	Content of polybutadiene units ^a in product (mass %)
0.5 ^b	2.7 (–)
0.5	38 (95)
1.0	24 (90)
2.0	14 (90)

^a The value in parentheses is the content of 1,4-*cis* units. ^b For copolymerisation of ethylene and butadiene on monofunctional catalyst (VCl₄ on PE–g-PVP).

ethylene polymerisation after chain transfer results in a polyblock copolymer. Such a reaction mechanism is few and far between. Obtaining convincing proof of this mechanism presents considerable difficulties, since analysis of the structure of such ‘chemical hybrids’ characterised by possible formation of interpenetrating polymer chains is a rather complicated problem. However, experiments with ¹⁴C-labelled butadiene allowed one to collect proof of the formation of block copolymers (Table 8). Quantitatively, the formation of the random copolymer was estimated by comparing its radioactivity with that of the ethylene/butadiene copolymer synthesised on the Co-containing monometallic catalyst. The stereosequence of polybutadiene units (mostly 1,4-*cis*-butadiene) in the block copolymers is such that mutual influence of the monomers is weak. Probably, this method for *in situ* preparation of diblock chemical hybrids will appear to be useful in the case of PPC based on polyolefins and polyallene and on other polymers.[¶]

Synthesis of binary polymer networks belongs to new avenues of current research. Binary networks consist of two chemically different polymer chains linked by one covalent bond, whereas IPN comprise two independent networks that cannot be separated without cleavage of covalent bonds.²⁴⁶ The distinctions between these systems are illustrated in Fig. 16.

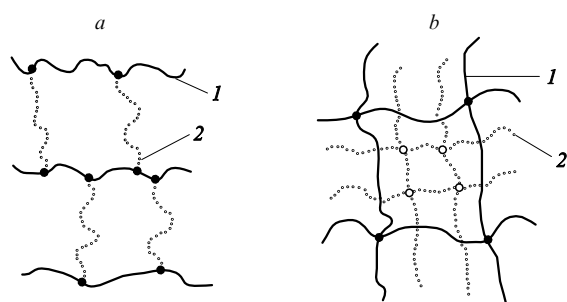


Figure 16. The structure of two-component (a) and interpenetrating (b) polymer networks; polymer A (1) and polymer B (2).

As applied to polyolefins, binary polymer networks were prepared for, *e.g.*, the poly(isobutylene)–poly(dimethylsiloxane) system.²⁴⁷ Allyl-tritelechelic PIB was synthesised by ‘living’ polymerisation of isobutylene at 193 K using the tricumyl chloride–TiCl₄–*N,N*-dimethylacetamide catalytic system. Allylation at the end groups was performed using allyltrimethylsilane. Allyl-tritelechelic PIB undergoes cross-linking with SiH-ditelechelic poly-

(dimethylsiloxane) by hydrosilylation under the action of Pt-containing catalysts. This method was used for preparation of novel thermoplastic elastomers PS–b-PIB.²⁴⁸

Thus, *in situ* prepared PPC can be synthesised from various classes of incompatible monomers following any polymer formation mechanism. The diblock copolymers considered in this section are most often used as polymeric additives that improve compatibility of immiscible polymers rather than individually.

IX. Preparation of conducting composites using the principle ‘compatibilisation *via* polymerisation’

Mixing of conducting and dielectric particles is a well known procedure used for preparation of conducting polymers.²⁴⁹ The synthesis of a conducting polymer surrounded by a dielectric matrix is often used to improve the strength and electrical conductivity of polymeric materials.^{250, 251} According to percolation theory,²⁵² an increase in the content of the conducting polymer to a particular critical value causes a sharp decrease in its electrical resistance (the so-called percolation threshold is reached).

The method for *in situ* preparation of molecular compositions containing a polyolefin as one component can also be extended to the conjugated polymers (in particular, doped PAC). Conducting PAC films are very brittle, which is detrimental to their operating characteristics, and unstable (film destruction occurs with time). Therefore, the preparation of materials that can be processed in a conventional manner requires modification of such films.

An attempt at preparing a composite material with good electrical properties by simple dispersion of powdered PAC obtained by catalytic polymerisation of acetylene according to Shirakava using the Ti(OBu)₄–AlEt₃ system in the PE matrix failed,²⁵³ since only large PAC aggregates of size 10 to 100 μm were formed. Blending of components on a molecular level can be achieved by performing direct polymerisation of acetylene on any surfaces moistened with the catalyst solution. In particular, such a polymerisation can be carried out on 300 μm-thick LDPE films impregnated with Ti(OBu)₄ and alkylated with AlR₃.²⁵³ The reaction on the surface of the PE powder impregnated with the same catalytic system is carried out in the liquid phase (in dibutyl ether)²⁵⁴ or in the gas phase.²⁵⁵ Sometimes, polymerisation is performed from the gas phase in viscous media (*e.g.*, silicon oil) in the presence of PE-supported catalysts.^{256, 257} Polystyrene solutions (5%–20%) in toluene can be considered as examples of such high-viscosity (10–400 sP) media. Suspension polymerisation allows the preparation of materials with good electrical and mechanical properties. High density PE films containing PAC (6 mass %–10 mass %) remain flexible and elastic and exhibit high strength. The conductivity of the compositions prepared by doping such films with iodine or lithium lies between 10 and 100 Ω^{–1} cm^{–1} and increases upon film drawing due to alignment effects.²⁵⁵ Polyacetylene obtained by polymerisation of acetylene on a PE matrix at 383 K has a *trans*-structure stereosequence and undergoes cross-linking with time, thus forming a three-dimensional structure in the bulk of the PE matrix. Such composite materials are characterised by a conductivity of 1 to 5 Ω^{–1} cm^{–1}. High-molecular-mass PAC latex particles are formed on the Luttinger catalysts in the presence of surfactants, mainly copolymers of styrene or PE blends and poly(ethylene oxide) (PEO).²⁵⁸

To improve the adhesion between the conducting components and the polymeric support (*i.e.*, films based on PE, PP, SKEP, PS, *etc.*, and shaped as necessary), the latter is modified by grafting of functional groups [poly(acrylic acid) (PAAc) or poly(allyl alcohol) (PAA)] that serve as ‘immobilisers’ of the catalyst of acetylene polymerisation.⁵⁸ After polymerisation these supports become coated with a dark PAC film 10–50 μm thick, which acquires conducting properties (see Table 9) after treatment with iodine vapours or other electron acceptor dopants such as SbF₅, AsF₅, FeCl₃ and perchlorates.

¶ It should be noted that copolymerisation is also performed using other catalytic systems. For instance, the microblock copolymer of butadiene and styrene is formed when the system LiR–KOR is used.²⁴⁵ In this case, butadiene undergoes polymerisation of the Li centres, while styrene is polymerised on the K centres. The microblock size is determined by the frequency of C–Li ⇌ C–K transitions.

Table 9. Properties of conducting films prepared by polymerisation of acetylene in the presence of catalytic system $\text{Ti}(\text{OBu})_4\text{--AlEt}_3$ and immobilised on dielectric supports.⁵⁸

Support	Titanium content /mmol g ⁻¹	Polymerisation time /h	PAC film thickness /mm	Specific conductivity ^a
PE	traces	3	—	1×10^{-7}
PE–g-PAA	0.04	2	0.05	6.2
PE–g-PAAc	0.06	2	0.016	4.2
PE–g-PAAc	0.10	1	0.02	14.4
PE–g-PAA	0.115	3	0.025	6.7
PTFE–g-PAA	0.4	3	0.01	2.4
PVAIc	0.20	2	0.02	3.9

^a Dimensionality is $\Omega^{-1} \text{ cm}^{-1}$.

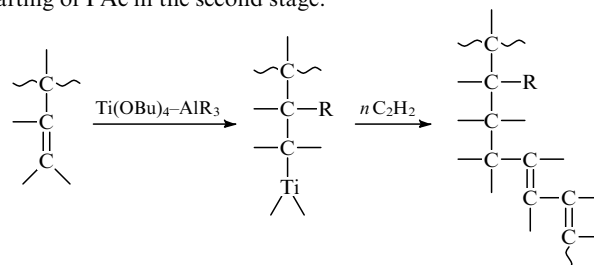
In this case, we deal with the surface conductivity of the *in situ* prepared PPC, while the polymeric supports remain dielectrics. This method can also be used for the preparation of multi-layered PPC containing a conducting layer with controllable conductivity parameters. Materials based on this type of PPC are relatively easy to produce and retain their properties on long storage (more than three years). Probably, improved stability of these materials is due to the presence of a barrier preventing the oxidation of PAC.

High-conductivity compositions, namely, block copolymers of PAC and PS are also prepared by ‘switching’ the polymerisation mechanisms,^{259,260} that is, the polymerisation of the styrene oligomer ($M_n = 1000$) obtained on LiBu in the presence of AlCl_3 and $\text{Ti}(\text{OBu})_4$ additives is followed by the polymerisation of acetylene or propyne. It is noteworthy that an increase in the content of acetylene units in the copolymer leads to changes in its morphology, *viz.*, fibrillar structures typical of PAC disappear and the polymer acquires a *trans*-structure. The syntheses of soluble block copolymers consisting of PAC blocks and polymeric support blocks (PS or polyisoprene) were reported.^{261,262} In this case, CuCl_2 in anhydrous THF at 193 K is used as catalyst. Polymeric support blocks exhibit dielectric properties; however, doping of the block copolymers allows the preparation of materials whose conductivity is comparable with the metal conductivity. This type of conducting composition can be synthesised using a terpolymer of, *e.g.*, diene, ethylene and propylene and blends of thermoplastic elastomers as well.^{253,255,263}

Bolognesi *et al.*²⁶⁴ reported an interesting method for preparation of a comb-like copolymer in which the *trans*-PAC chains are grafted onto a polybutadiene or polyisoprene matrix [this was done using the $\text{Ti}(\text{OBu})_4$ catalytic system and a mixture of tetramethylenediamine and *sec*-butyllithium].²⁶⁴ A large body of patent literature exists on this subject. For instance, the procedure for preparation of a readily processable composition of PE and PAC involved treatment of a thin PE film with the catalyst followed by polymerisation of acetylene.²⁶⁵ The conductivity of the material obtained was $5 \Omega^{-1} \text{ cm}^{-1}$. To obtain doped, high-conductivity compositions based on PO and oriented PAC, plastic fibres or ribbons were washed with a solution of the Ziegler–Natta catalyst and placed stretched in a vessel filled with acetylene gas.^{266,267} Polymer blends based on conducting material were also prepared in another manner using porous films or membranes.^{268,269} The newly formed macromolecules that fill porous matrices with uniaxially oriented pores were found to have a preferential orientation along the pore axis. The approach based on the use of porous HDPE films obtained by uniaxial drawing of the polymer in liquid media *via* delocalised crazing was used for the preparation of PE–PAC compositions.²⁷⁰ The content of PAC was at most 8 mass % and the results obtained after selective extraction of PE indicated the formation of a rigid three-dimensional PAC network reinforcing the PE matrix. However, the formation of PAC chains grafted onto PE in such systems also cannot be ruled out. This will cause the orientation of both phases,

viz., the finely dispersed porous PE matrix and rigid-chain PAC macromolecules. Doping the polymer blend with iodine led to an increase in the bulk conductivity by 14 to 16 orders of magnitude, which points to a low percolation threshold for the conductivity of the structures with marked anisotropy of the mechanical and electrophysical properties. The conductivity of compositions containing up to 3% doped PAC was described in the framework of the simple percolation model.

The structure and various (including electrical) properties of films based on PAC and polybutadiene have been studied in detail.^{271,272} It is appropriate to prepare these compositions from diene–ethylene–propylene terpolymers and PAC.²⁵⁵ Polymerisation of acetylene in the elastomeric matrix results in a product which exhibits not only high conductivity and resistance to aggressive media, but also reasonable operating characteristics. Cross-linking of these compositions leads to immobilisation of PAC. Graft polymers consisting of polydiene and PAC are relatively easy to prepare. In this case, the metal–carbon bonds formed with participation of vinyl groups of the 1,2-polybutadiene units in the first stage of the process are then involved in grafting of PAC in the second stage.²⁷³



Soluble graft block copolymers of PAC (up to 5%) and atactic PS, soluble block copolymers of PAC and polyisoprene (including doped block copolymers)²⁷⁴ and the PAC–b-poly(norbornene)–b-PAC triblock copolymers with different block lengths were synthesised. Graft copolymers are characterised by micro-phase separation.

Polymer–polymer compositions based on polyolefins and conjugated polymers can be prepared using not only PAC, but also such components as polyphenylacetylene, poly(propargyl alcohol) and poly(propargylamine), which are obtained by polymerisation of the corresponding monomers on the $\text{Mo}(\text{V})$ complexes immobilised on PE, PP or PS.²⁷⁵ Polymerisations of crystalline diacetylenes in a microporous polymeric matrix resulted in compositions of isotactic PP and substituted polydiacetylenes.²⁷⁶ Drawing the PP film in 20% solutions of substituted 2,4-hexadiynes followed by removal of the solvent allowed the preparation of a film containing up to 20% diacetylene units. Studies on the γ -radiation-induced, solid-phase polymerisation revealed an increase in the degree of conversion of the monomer in the PP matrix as compared to the reaction in solution. This was explained by a higher initiation rate rather than the mechanical effect of the matrix. A method for ‘internal’ doping of the polyconjugated system with iodine that is partially separated during the polymerisation of the iodine-containing monomer was reported.²⁷⁷

Preparation of blends of polyconjugated polymers and UMMPE by gelation^{278–280} is also of interest. For instance, a UMMPE–poly[2-butyl-5-(2-ethylhexyl)-1,4-phenylenevinylene] (70 : 30) composition was prepared from solution (more correctly, a gel) in *p*-xylene. No information on the conducting properties of such PPC was reported.

Products of the *in situ* polymerisation of pyrrole are also used as components of conducting PPC. The procedure for preparation of such PPC as PE–PAC involves immobilisation of the catalyst on the surface of functionalised PE films. This method was also used for the synthesis of PE–polypyrrole (PPr) compositions.²⁸¹ To this end, a film consisting of PE and sulfonated PS was immersed in a solution containing FeCl_2 and FeCl_3 and then polymerisation of pyrrole was performed at 275 K for 30 min in

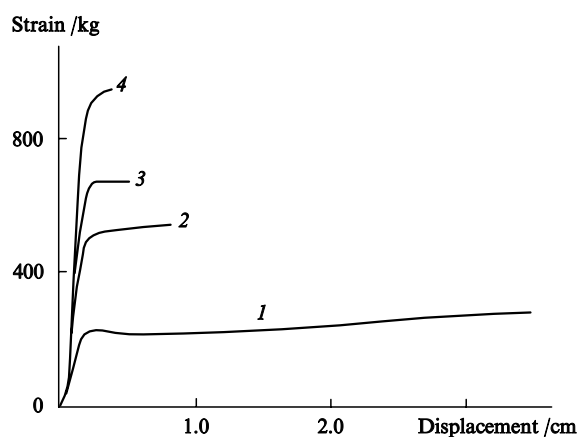


Figure 17. 'Strain-displacement' curves for double film PE-sulfonated PS (without PPr) (1) and ternary films PE-sulfonated PS-PPr (2-4) with different conductivities prepared by electrochemical polymerisation.²⁸¹ Conductivities ($\Omega^{-1} \text{ cm}^{-1}$): (2) 3.8; (3) 7.5; (4) 14.9.

the dark followed by post-polymerisation doping. The surface conductivity of the polymerisation product was $\sim 250 \Omega^{-1} \text{ cm}^{-1}$. Films prepared from this material exhibit good mechanical properties; however, the films characterised by higher conductivity are less elastic and more rigid (Fig. 17).

Conventional methods for the synthesis of conducting compositions have some inherent drawbacks, such as high rigidity and dark colour of products, a complicated procedure for preparation of samples with specified conductivity and long duration of the formation of films thicker than $10 \mu\text{m}$. To eliminate these drawbacks, it was proposed to prepare this kind of PPC in the form of PPr-based polymer alloys by chemical²⁸² or electrochemical²⁸³ polymerisation of pyrrole on polymer supports. The method involves coating an electrode with a polymeric support film $\sim 20 \mu\text{m}$ thick. The PPr chains begin to grow from the film side adjacent to the electrode surface. Therefore, initially only the 'electrode' side of the film is conducting. The opposite, 'surface' side of the film acquires conducting properties only after being penetrated by the PPr chains. Polymer alloys prepared in this manner exhibit some attractive properties including high conductivity (more than $300 \Omega^{-1} \text{ cm}^{-1}$), stability in air, good film-forming ability and high homogeneity. Werner²⁸⁴ reported the synthesis of a number of PPr-based, conducting, thermoplastic and elastic *in situ* prepared PPC including those containing PB. Methods based on the use of monomers (e.g., pyrrole or aniline) as solvents for the polymerisation have also been developed.²⁸⁵⁻²⁸⁷

Conducting compositions containing tailor-made PO can be prepared by the blending of components. In particular, microporous PE films synthesised by rapid melt extrusion followed by annealing exhibit a well-developed surface and can be used as supports for composite materials prepared by coating these films with a thin layer ($4-7 \mu\text{m}$) of conducting polyaniline (PAn) from aqueous dispersion.²⁸⁸ This kind of material is characterised by strong adhesion between their components. Despite its very small thickness, the PAn layer has the same conductivity ($0.2 \Omega^{-1} \text{ cm}^{-1}$) as that of a much thicker film cast from the PAn dispersion.

PAn-Based conducting compositions are also prepared by polymerisation of monomers in porous polymeric matrices obtained by cold drawing of polymer films (including HDPE films) in reactive liquid media by a delocalised crazing mechanism.^{289, 290} Electrochemical polymerisation in thin pores of the PE matrix in the acid-aqueous electrolytes results in the formation of oxidised PAn (emeraldine salt). The specific surface conductivity of the undoped product is $9 \times 10^{-3} \Omega^{-1} \text{ cm}^{-1}$ (the conductivity of undoped PAn is only $10^{-10} \Omega^{-1} \text{ cm}^{-1}$, see Ref. 291). Doped PAn exhibits a conductivity of $5 \Omega^{-1} \text{ cm}^{-1}$ (see

Ref. 292). In finely dispersed porous matrices, PAn forms spherulites $60-100 \text{ nm}$ in diameter (cf. 300 nm in diameter fibrillae formed outside the matrices). The films are characterised by uniform dispersion of the PAn phase in the bulk and by complete phase separation of the components. It is noteworthy that the content of non-extractable (insoluble) PE retained as the constituent of the polymer blend upon selective extraction of PE in decalin at 418 K and in xylene at 408 K lies between 20% and 30% PE. A possible explanation is as follows. Since the growing polymer particles are much larger than the effective pore diameter of the matrix ($4-15 \text{ nm}$), the fibrillae of the matrix phase penetrate the particles of the PAn phase, thus preventing them from being accessed by the solvent molecules.

In situ synthesis of conducting compositions can also be performed in the reverse order. In this case, the catalyst or initiator of polymerisation of the corresponding monomer is immobilised on the conducting component. For instance, doping of PAc with dihydronaphthalide sodium results in the formation of a charge-transfer complex²⁹³ $[\text{Na}_{0.057}(\text{CH})]_x$ which is used as initiator for grafting of blocks of PS, polyisoprene, PMMA, PEO, etc., onto the PA chains.²⁹⁴

The possibility of immobilisation of metal complex catalysts on graphite followed by the *in situ* preparation of conducting PPC²⁹⁵ makes this approach be particularly attractive. Here, the height of the potential barrier to the charge carriers injected into the dielectric polymeric component of the PPC reduces.²⁹⁶ The PE-soot composition also exhibits conducting properties;²⁹⁷ a sharp decrease in the electrical resistance begins as the content of soot reaches 6 vol.%. The conductivity of this PPC is independent of the soot particle size (on the average, 62 nm in diameter) and the melt flow index of PE. As the content of soot changes from 16 vol.% to 28 vol.%, the maximum conductivity increases from 1 to $3 \Omega^{-1} \text{ cm}^{-1}$ at a current density of up to 15 A cm^{-2} . The current-*vs.*-voltage curve passes through an extremum. The decrease in the electric current is due to stress relaxation and to scission of soot chains caused by the Coulomb forces at high voltages. The HDPE-based composition exhibits higher conductivity compared to the LDPE-based PPC; this is probably due to the lower volume fraction of the amorphous phase characterised by high concentration of soot in the former case.

Thus, different synthetic procedures developed in the framework of the *in situ* approach to preparation of PPC are convenient and promising for the synthesis of conducting composite materials.

X. Formation mechanism and the structure of *in situ* prepared polymer-polymer compositions

In the preceding sections of this review we have considered many aspects of the mechanism of formation of the *in situ* prepared PPC. In this section, we will sum up information on the morphology, formation mechanism of polyolefin molecular compositions and the role played by the interfacial layers.

The strength of adhesive interaction between the components of PPC is an important characteristic determining their mechanical properties and operating characteristics. The properties of various two-phase polyolefin-polymer compositions can essentially (and even abnormally) change irrespective of the nature of the polymeric constituents. Most often, the parameters of PPC are determined by peculiarities of the boundary (interfacial) layers characterised by effective interactions between the components of the PPC. In principle, the morphology of the interfacial layer can follow two patterns.⁷ First, the interfacial layer can comprise two regions adjacent to the one and only interface and having specific structures different from the structure of the bulk phases of each component (A and B). Second, a situation with two interfaces is possible. General and more detailed schemes illustrating the structure of the interfacial layers are shown in Fig. 18. If PPC are prepared by blending polymeric components that can be even virtually immiscible, the first pattern can be followed; however, in

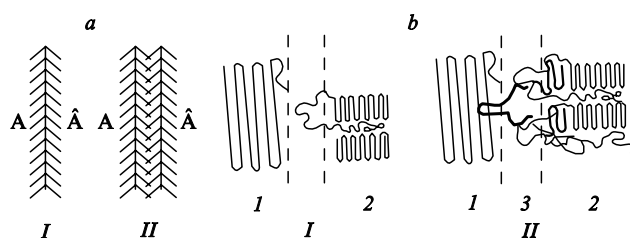


Figure 18. The structure of intermediate layers in the formation of polymer blends (I) and synthetic (II) compositions (a) and the structure of the intermediate layers in polymer blends (I) and in synthetic (II) compositions iso-PP (1), triblock copolymer (2) and PE (3) (b).

this case the interfacial layers are formed due to the physical interparticle interactions and self-diffusion of macromolecular segments. The latter process is a kind of segmental dissolution of polymers accompanied by migration of the low-molecular-mass homologues-components towards the interface (this provides an explanation for the important role of the molecular mass distribution of the starting polymers in the formation of PPC).

As mentioned above, considerable attention is given to the methods for weakening the interface stress and improving adhesion between the immiscible phases.²⁹⁸ In the course of reactive blending (polymerisation of one monomer in the presence of the other component) such boundary layers are formed as a result of the appearance of interpenetrating polymer chains and, possibly, pseudointerpenetrating polymer networks, which favours the improvement of compatibility of the components.

Often, the interface is represented as a conventional, two-dimensional geometrical surface. However, in real binary compositions the interface can be rather thick and exhibit specific properties that differ from the properties of the bulk phases. These are not only lowered segmental mobility of macromolecules, reduced number of possible macromolecular conformations and loosened macromolecular packing, but also violation of identity of the chain building blocks and changes in the translational dislocation vectors and character of relaxation processes, *etc.* The properties of PPC are strongly dependent on how the interfacial layer is distributed within the compositions, *i.e.*, is it localised only at the interface or does it extend to the bulk phases of the polymeric constituents? The interfacial layer has a complex structure. It includes the adsorbed near-surface layer with specific properties and some transition layers in which the degree of ordering of the macromolecular packing varies with the distance from the surface of the polymeric matrix. If the content of one component is low (5% to 10%), the so-called threshold space of the interfacial layer takes on particular significance, since in this case the phase continuity can be violated, thus providing the possibility of direct contact between the macromolecules of the polymeric constituents. Under certain conditions, one bulk phase can 'penetrate' through the second bulk phase (Fig. 19), which leads to the formation of interfacial structures with improved adhesion.

As a rule, the mechanical characteristics of the interfacial layer are related to its adhesive properties, that is, an increase in the modulus of elasticity corresponds to an increase in the adhesive energy and to thinning down of the interfacial layer. When estimating the contribution of the boundary layers to the properties of a multiphase system, one should know the distance from the interface at which deviation of local properties from the bulk properties can be considered insignificant; an important point is, however, that the thickness of the interfacial layer determined by different methods depends on the sensitivity of a particular method.⁸ Nevertheless, the thermodynamic approach allows one to evaluate the minimum thickness of the interfacial layer ($\delta_{\min}$), which meets the criterion for its stability.²⁹⁹

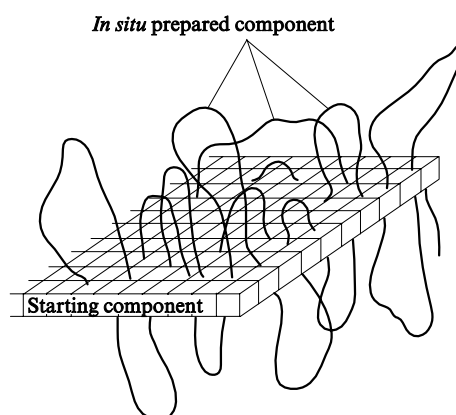


Figure 19. A scheme illustrating interpenetration of polymer chains in compositions prepared by *in situ* polymerisation.

The density of the interfacial layer changes exponentially with the distance from the interface and can be controlled in a targeted manner. The volume of the interfacial layer, V_1 , can be found using the following equation³⁰⁰

$$V_1 = \frac{\rho}{\rho_1} V (1 - e^{-\alpha N}),$$

where ρ and V are the density and volume of the polymer matrix, respectively; ρ_1 is the effective density of the interfacial layer; α is the coefficient of proportionality; and N is the number of particles of a particular component.

The density of the interfacial layers in the composition of HDPE and PVC was qualitatively assessed using positron annihilation technique.⁶⁵ It was found that the *in situ* prepared PPC are characterised by dispersion of the PVC particles in disordered PE domains. A decrease in the density of macromolecular packing upon the formation of the interface was also pointed out by Chalykh *et al.*³⁰¹ The PE component of this PPC was found to form one crystalline phase and two amorphous phases (the surface phase and the intermediate phase).³⁰² NMR studies revealed the existence of domains characterised by different free induction decay parameters and relaxation times in the bulk of the PPC. The interaction between these domains is weaker than within each of them. The formation of the transition layer leads to loosening of the near-surface layer of the PE phase. The mean correlation time of intermolecular motions in this layer is 10^{-8} s.

Similarly to the filled systems, the interfacial layer in polymer–polymer compositions serves three main interrelated functions.¹ These are (i) stress redistribution from the phase contact region to the bulk phases (reduction of stress concentration in the more flexible component), or operation as a specific structural stress concentrator during the degradation of PPC; (ii) changes in the elastic and viscoelastic properties of PPC; and (iii) suppression of both cracking and formation of other defects (the interfaces prevent the samples from microcracking).

The type of the phase structure and the sizes of corresponding structural domains depend on the nature of the polymers under study (the surface tension at the interface and the viscosities of the components and their ratios, the volume fraction of the components and blending conditions). It is these characteristics that determine the properties of PPC. In particular, the formation of amorphous-crystalline structure leads to improvement of the impact toughness (see, *e.g.*, Ref. 303); PPC with fibrillar structure exhibit higher strength and improved strain–stress properties (see, *e.g.*, Refs 304 and 305); polymer compositions with lamellar structure are characterised by improved barrier properties³⁰⁶ while continuous structure favours achievement of an optimum combination of the properties of both components.³⁰⁷

If the formation of dispersed structures has been studied in much detail, the conditions for the appearance of domains with

continuous morphology have been little studied except, probably, for the PE–PS system.³⁰⁸ Recently, Tseng *et al.*¹⁸⁶ reported the results of scanning electron microscopy studies of the changes in the morphology of compatible and compatibilised incompatible PP–PA-6 (30:70) systems. The incompatible PPC were characterised by high surface tension at the interface, which led to the formation of a coarse-grained product. Even the addition of a rather large amount of the PP/MA phase (5 parts by mass) was insufficient for inhibition of the formation of this structure. On the other hand, the addition of the PP/MA–co-PPG copolymer (5 parts by mass) led to substantial reduction of the domain size of PA-6. The reduction magnitude was found to be a function of the diamine-modified PPG chain length. Finally, the reactions involving compatibilisers containing grafted MA (0.8 mass %) followed by the formation of the PP/MA–co-PPG copolymer result in the compatible compositions for which the longer the PPG chains, the higher the dispersity. Similar results were also obtained in studies of a compatible system PP–(PP/MA)–PA-12 (65:10:25), in which all the MA groups enter into reactions with the terminal NH₂ groups of PA-12 and the particle size lies between 0.1 and 0.5 μm or less.³⁰⁹

It should be noted that the particle size distribution of the dispersed phase in compatible systems is much narrower than in incompatible systems. In the latter, coarse-grained particles of PA-12 grow in the course of annealing at 453 K. This is accompanied by grafting a larger number of the PA-12 molecules onto the PP/MA phase and by an increase in the thickness of the interfacial layer. An increase in the content of the PP/MA phase favours an increase in the dispersity of PA-12. Despite the presence of excess MA groups, the (PP/MA)–g-PA-12 system is formed in these compositions. However, it should be kept in mind that thermomechanical treatment during processing of polymers has a strong effect on the mechanochemical processes in and, hence, on the morphology of these heterogeneous systems.

In addition to the interaction between the functional groups of different components (including grafted ones) of an *in situ* prepared PPC, grafting of the newly formed polymeric constituent (a polyolefin, polydiene or polyacetylene) of the PPC onto the surface of the polar component also plays an important role in the formation of the interfacial layer in this type of PPC. Grafting can occur, first, in the initiation stage of polymerisation (the multiple bonds of the surface reactive groups can be cleaved and these groups can undergo insertion into macromolecules in the form of end groups); second, in the growth stage, when the multiple bonds of a particular component are involved in the copolymerisation; and, third, in the stage of chain transfer to the surface of the polar component (the reaction between the propagating chain end or a functional group of the polymer and the specific surface group, resulting in the formation of a covalent bond). Specific reaction mechanisms and the relative contributions of particular reaction stages depend on the nature of the constituents of PPC.

Improvement of the properties of the PO–PO compositions prepared using the principle ‘compatibilisation *via* polymerisation’ as compared to polymer blends of the same chemical composition is rationalised by higher ordering of their morphology.¹²⁸ The synthesis of the PO–PO compositions involves coating of the catalyst with the polymeric constituents in rigorous order, that is, PP, SKEP and, finally, PE. In this case the adhesive, SKEP, is localised at the interface (*cf.* polymer blends with the same structural elements, in which SKEP is much more dispersed within the bulk of the dispersed phase). Therefore, the brittleness temperature of the compatibilised composition is reduced by 16°.

As a rule, one component of a polymer blend presents no obstacles to crystallisation of the other blend component.⁹⁹ Nevertheless, there are some exceptions. For instance, the crystallisation temperature of the PA-6 phase in the PP–PA-6 compositions is 2–3° lower than that of the starting polymer, which points to a lower nucleation rate.¹⁸⁶ In other words, the product of *in situ* polymerisation, PP–(PP/MA)–PA-6, prevents crystallisation of PA-6.^{310, 311} On the other hand, the crystallisa-

tion temperature of the PP phase of the composition is appreciably higher (by 6–9°) than the crystallisation temperature of the individual polymer. This means that PA-6 acts as a promoter for crystallisation of PP in the composition under consideration. No substantial changes in the melting temperatures of these semi-crystalline polymers in both compatible (437.5 K) and incompatible (494.5 K) PPC occur; however, the degree of crystallinity of the PA-6 phase in the compositions decreases. Probably, the presence of copolymers within the interfacial layer makes the crystallisation of PA-6 more difficult to proceed. On the other hand, the degree of crystallinity of the PP phase in compatible PP–PA-6 compositions remains unchanged.

Finally, yet another important structural feature of the interfacial layer should be pointed out. The macromolecules located within this layer adopt an extended conformation due to the orientational effect of the matrix. For instance, the macromolecular segments adjacent to the PVC phase in the molecular compositions of PE and PVC are oriented.³¹² This can be rationalised by the effect of the PE chain growth conditions, namely, by high density of the growing PE chains in the thin near-surface layer. Polymer chains growing in this case in a co-operative manner adopt an extended conformation. It is assumed^{7, 8} that crystallisation of one component near the phase boundary of the other component is accompanied by the formation of transcrystallites that are stronger and more rigid than spherulites. Interpenetration of the polymer blocks into the interfacial layer provides the possibility for the adhesive interaction (anchoring) between the constituent phases to occur. Such a submicrostructure contributes largely to improvement of the impact toughness of PPC.

Orientation of macromolecules at the interface between glassy polymers leads to transition of the polymers into a state typical of liquid-crystalline polymers.³¹³ Rigorous control of crystallisation conditions also allows the preparation of highly crystalline PE films (in this case, the polar component can act as nucleating agent for crystallisation) and polymer alloys. In particular, PE can undergo epitaxial crystallisation on oriented poly(oxyethylene) in spite of different crystal structures, macromolecular conformations and polarity of both polymers.³¹⁴ However, this is impossible if PP, cellulose, PVAIc or PA-6 are used instead of poly(oxyethylene). The formation rate of the *in situ* prepared PPC also plays a significant role. If macromolecules leave the reaction medium at a rate comparable with the chain propagation rate, no stacking occurs; rather, structures with extended conformations of the macromolecules are formed.³¹⁵ The so-called occlusion effect responsible for occlusion of the growing polymer chains within the ‘dead’ polymer domains should also be taken into account. Thus, by using the ‘compatibilisation *via* polymerisation’ strategy one can prepare structures with the nonequilibrium orientation of macromolecules.

From the aforesaid it follows that the interactions between the components of PPC at the interface, especially between crystalline polymers, should be considered in close relation to the changes in the molecular and supramolecular structure and taking into account the unique topology of such polymers. Not only physical immobilisation and chain entanglement, but also chemical interactions between different-type polymeric constituents can occur in the molecular compositions. The net effect of these factors leads to the formation of a common co-operative system, which includes several types of bonds and is characterised by additional structuralisation of PPC, which favours the achievement of a high degree of homogenisation. This complex system of interactions at the interface in the *in situ* prepared PPC takes over the breaking load in the case of destruction of the composite material.

Nevertheless, an ideal type of structural organisation of the PPC in question is provided by the IPN that represent molecular compositions formed in the *in situ* polymerisation of monomer 2 in preliminarily swollen polymer 1. The major difference between the classical IPN and the *in situ* prepared compositions based on crystalline polymers lies in the fact that the formation of IPN

involves substantial swelling of the polymer in the monomer. One of the most important features of the IPN consists in extremely strong (in essence, on the molecular level) mutual dispersion of the components.

The size, D , of the polymer 1 phase domains formed in the semi-IPN in the polymerisation of monomer 2 with the molecular mass M_2 can be estimated using the semiempirical Donatelli equation.³¹⁶ This equation takes into account the changes in the free energy of the system and is written as follows:

$$D = \frac{2\gamma\omega_2}{RTv_1[(1-\omega_2)^{-2/3} + \omega_2/v_1M_2 - 1/2]},$$

where γ is the surface tension at the interface, ω_2 is the mass fraction of the monomer and v_1 is the density of cross-links in polymer 1.

Under some assumptions we can estimate the domain size of the PS phase in the blends with PP, prepared by the *in situ* polymerisation of styrene in PP deformed *via* delocalised crazing.⁷⁵ This size is nearly 100 nm, which is in agreement with the results of electron microscopy studies. The aggregative stability of these systems is provided by the strong system of entanglements between two macromolecular networks (the so-called catenane links), *i.e.*, by a specific type of anchoring. Under optimum conditions this method allows one to achieve complete interpenetration of the components on the molecular level even for thermodynamically incompatible polymers.

Morphologically, the systems under study are also relatively close to the IPN. The point is that the second polymer phase is formed in the intercrystallite domains of partially crystalline PO. At temperatures below the melting temperature, PO exhibit rather high resistance to the action of the surface forces that cause phase separation, thus stabilising the newly formed structure. In other words, the crystal structure of PO, which plays the role of cross-links in the first network, reduces the possibility of the formation of extended phase domains of the second component and determines the dispersity of the system. Indeed, the synthesis of the HDPE–PMMA compositions *via* delocalised crazing⁷⁶ resulted in the formation of the structures characterised by phase co-continuity (selective extraction of the components led to the formation of a continuous porous framework rather than to phase separation of the composition). The formation of the PO phase within the amorphous polar component occurs in a more complex manner. In this case, release of heat (its amount can be rather large) in the formation zone of the PO component leads to softening of the matrix and to penetration of the PO phase into the polar component matrix under the action of mechanical stress.

A salient feature of the formation of IPN is the imposition of microphase separation that is due to the thermodynamic incompatibility of the polymer networks formed on the chemical reactions.¹² The chemical compositions of the separating phases depend on both the stoichiometry of the components and the IPN formation rate. The microphase structure is characterised by the degree of segregation of the two-component system in which phase separation into the polymeric constituents occurred (usually, no equilibrium phase separation is reached and the phases with variable chemical composition are formed). The most sensitive characteristic of the phase separation in polymer blends is the relative elongation at break.⁸⁴ Often, passage from compatibility to incompatibility is very sharp and occurs at a particular ratio of the components. Even if specific interactions between the macromolecules of PPC can occur at ambient temperatures, their thermodynamic compatibility deteriorates on heating and they are characterised by the lower critical solution temperature.

Since the components of molecular PPC are thermodynamically incompatible, the compositions prepared from them belong to nonequilibrium systems. To convince oneself that this is true, it is sufficient to give, *e.g.*, the PE–PMMA system molecular mobility (by annealing), which leads to melting of the PE phase

and devitrification of the PMMA phase and is exactly the same as what occurs usually in the case of mixing of polymer melts.

Thus, polyolefin-based PPC prepared by *in situ* polymerisation of one component do not represent typical interpenetrating polymer networks since they can be dissolved in appropriate solvents and are characterised by a wide range of variations in the yielding and creep. On the other hand, they also differ from conventional polymer blends. These PPC can be called molecular, pseudointerpenetrating, thermoplastic chemical polymer blends³¹⁷ that exhibit homogeneity on a microscopic level. Combinations of some specific properties of their components can lead to positive synergistic effects.

XI. Fields of application of *in situ* prepared polymer – polymer compositions

Almost without exception PPC and their individual polymeric constituents have found the same fields of application, the use of the former being often more advantageous. Polymer – polymer compositions belong to the class of hybrid composite materials with improved breaking strength. A salient feature of PPC is nonlinear dependence of their properties on the chemical composition due to unique structural peculiarities. As a rule, these materials are characterised by improved impact toughness (cold resistance), strength, wear resistance and exhibit good dispersability and processability. Many of them (*e.g.*, PVC–PE compositions) are suitable for production of plastic pipes and sheets, various profiles, moulded products and antifriction materials. Polymer compositions based on syndiotactic PP exhibit radiation-damage stability and can be used instead of plasticised PVC.¹¹⁶ Improved thermal stability of the *in situ* prepared HDPE–PVC compositions is rather unusual and sets them apart from polymer blends or untreated PVC.^{49,318} This property, which is also characteristic of the PVC–PS graft copolymers,³¹⁹ is thought to be due to the fact that the mobile chlorine atoms present in the allyl groups as impurities or bound to the tertiary carbon atoms of PVC are removed in the course of grafting. This again confirms the formation mechanism of the structure of interfacial layers in the *in situ* prepared PPC. Polymer – polymer compositions PVC–HDPE can find applications as high-strength, cold resistant polymer films for enclosing greenhouses.⁶³ These materials exhibit improved thermal stability and UV and IR radiation stability, *i.e.*, they favour the ‘greenhouse effect’. The ability of the PE films used for enclosing greenhouses to keep unsweated and retain transparency for long periods under conditions of excess moisture content is also of great importance.

Modification of PP with elastomeric and thermoplastic elastomer additives allows substantial improvement of the impact toughness of the materials and reduction of the brittleness temperature. Among conventional additives are PIB, butyl rubber, SKEP, SKEPT, polybutadiene rubbers, divinylstyrene-based thermoplastic elastomers, *etc.* Polymer – polymer compositions based on PP and ternary SKEPT have superiority in cold resistance (down to 223 K) and impact toughness compared to the untreated PP.³²⁰ The rheological characteristics of these PPC allow them to be processed using conventional methods for processing of thermoplastics, *viz.*, extrusion, injection moulding, blow moulding and pressing.

Blends of different types of PE exhibit improved processability and higher impact toughness compared to the individual components. Often, this leads to enhancement of the performance of production equipment. The PE–PB and PP–PB compositions prepared using the method of ‘compatibilisation *via* polymerisation’ are characterised by high modulus of elasticity, strength, thermal stability, crack resistance and tensile creep. These materials are promising for production of hot water supply pipes, heat exchangers and cable plasticates. In addition, blends of engineering polymers and commercially available thermoplastics are used for production of, *e.g.*, bumpers.

The thickness of the LDPE film used for production of containers should be at least 50 to 60 μm ; these values are mainly determined by the low strength of the polymer. Compatibilisation of several types of polyolefins (*e.g.*, LDPE and HDPE) allows substantial improvement of the properties of the polymer films and reduction of their thickness down to 20 to 30 μm without deterioration of the film strength. This result in more than doubling the performance of extruder reactors and reducing the specific consumption of materials.³²¹ Packaging films are also produced from PPC based on blends of PE with atactic PP, PIB, *etc.* The content of the recycled materials used for production of PE packaging films and containers reaches 50%.¹⁶ Recycled materials are used for production in those cases where no heavy demands are placed on the structural strength of products, but their environmental safety characteristics should meet stringent requirements (*e.g.*, decorative, insulating and sound-absorbing panels, *etc.*). To this end, one can use wood–polymer compositions based on wood waste and recycled thermoplastics (in particular, sawdust mixed with SKEPT-modified recycled LDPE).³²²

Polyolefins, and first of all HDPE, LLDPE, LDPE, PP and its copolymers, as well as PB are the main components of the PPC used for production of pressure pipelines. The properties of polymer–polymer compositions have a strong effect on the strength characteristics of pipes and the operating conditions. New types of LLDPE-based PPC were recommended³²³ for production of hot water supply pipelines (323 K, a pressure of 5 MPa) with a service life of 50 years. Compositions based on UMMPE ($M_w = 4.5 \times 10^6$) and low-molecular-mass PE ($M_w = 8.0 \times 10^4$) are used for production of high-strength, high-modulus fibres by single-stage and two-stage drawing techniques.^{324, 325}

Dilution of the blend with the main component is also used for recycling of multicomponent compositions.³²⁶ For instance, homogenisation of blends of LDPE, HDPE, PP and PVC followed by the addition of PP ($\sim 50\%$) resulted in phase inversion, so that the properties of the end product were mainly determined by the properties of multifilled PP.

As mentioned above, PO and PA, with somewhat different polarities, represent a typical example of immiscible polymers. Blending of PO and PA in the presence of appropriate compatibilisers improves the impact toughness of materials and provides a means of protecting the polymer surface from attack by atmospheric moisture and oxygen. The latter can be illustrated taking the *in situ* prepared PPC formed immediately on polymeric fibres as an example.⁴⁹ The PETP or PA fibres become covered with a specific kind of PE ‘coat’, which protects them from wear, thus improving the wear resistance of the materials, from moisture absorption, *etc.* (Fig. 20). *In situ* prepared polymer–polymer compositions have found an unusual field of application as supports for metal complex catalysts.⁵³ Specific properties of PPC based on HDPE and metal-containing polymers, *e.g.*, titanium, nickel, cobalt and other metal polyacrylates should also be pointed out.³²⁷ Interpenetrating polymer networks can be formed not only within the interfacial layer, but also in the bulk of these PPC. This is due to the fact that not all unsaturated groups are consumed in the polymerisation of metal diacrylates in PE melts. Since the PPC are processed at temperatures above the polymerisation temperature, the unreacted functional groups can be involved in the chemical interaction to form IPN. *In situ* prepared polymer compositions can combine the advantages of thermoplastics and thermosetting polymers. Often, the *in situ* method allows recycling of thermoplastics. The use of filled PPC, *e.g.*, a ternary system PP–LDPE–short glass fibres (up to 30%–40%) whose morphology was studied by Avalos *et al.*,³²⁸ is also expected to provide a way to substantially improve their properties.

Stable conductivity, good mechanical characteristics, high homogeneity, protective effect of the matrix and good processability of the compositions of PAc and PO open the possibility of

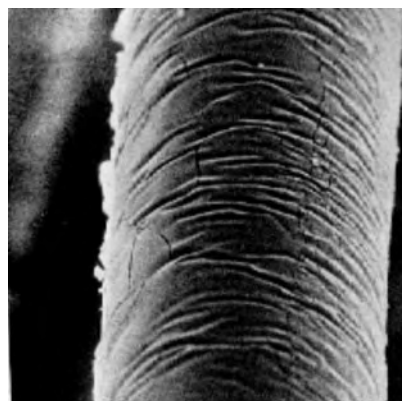


Figure 20. A SEM image of the surface of PETP fibre coated with a HDPE ‘skin’.

their use for production of moulded products, *e.g.*, semiconductor relays, thermistors, solar batteries, *etc.*³²⁹

The operating characteristics of PPC including their photo-degradation and photo-oxidation behaviour under natural conditions have been the subject of intensive research. For instance, it was found that the rate of ozone oxidation of oriented HDPE–PP compositions decreases as the content of PP increases.³³⁰ In studies of the blend of isotactic PP and SKEPT† it was shown that an increase in the content of PP leads to enrichment of the interfacial layer with rubber and that the structure of the interfacial layer is the determining factor in the thermal oxidation of blends and vulcanisates.³³¹ This manifests itself as changes in both the mechanism and kinetics of radical steps in the initial stage of oxidation which can affect inhibition of the oxidation process. Photo-induced oxidation of PPC based on commercially available LDPE and LLDPE is accompanied by scission of the polymer chains and cross-linking of the molecules, as indicated by the changes in the molecular mass and molecular mass distribution. If PPC contain polymeric sensitizer constituents, chain scission reactions become more important, while cross-linking of polymer chains, which can also occur, appears to be less significant. No preferential degradation of a particular component was observed in studies of the blends of LLDPE³³² or LDPE^{333, 334} and styrene–butadiene copolymer.

A unique possibility of controlling the properties of polymers has arisen after the preparation of blends of PO with non-olefin components by reactive blending. In particular, polyolefins co-calendered with PVC without using volatile plasticisers can be given such useful properties as elasticity and strength.³³⁵

Of course, the entire spectrum of applications of molecular polyolefin–polymer compositions is much broader.

XII. Conclusion

The use of molecular polyolefin–polymer compositions allows to a great extent the increasing industrial demands for novel materials to be met with reasonable cost:property ratio. Studies on interrelations between the compatibility of polymeric constituents, structure and properties of these PPC are of great theoretical and practical importance. In addition, the preparation of this type of PPC by reactive blending opens the possibility of re-use of plastic waste and degraded polymeric materials. Compatibilisation of the components of PPC requires improvement of interfacial adhesion and an increase in the phase dispersity, which can often be achieved by using interfacial modifiers. PO-Based compositions prepared by *in situ* polymerisation of one component do not belong to typical representatives of interpenetrating polymer

† SKEPT composition is ethylenenorbornene (4.0 mol %), propylene (32 mol %) and ethylene (the rest).

networks; on the other hand, they differ from conventional polymer blends. They can be classified as molecular, pseudointerpenetrating, thermoplastic chemical polymer blends.³¹⁷ In some optimum cases the *in situ* prepared PPC are characterised by homogeneity on a microscopic level, a valuable combination of specific properties of their constituents and by positive synergistic effects.

The structure of a real particle of the *in situ* prepared PPC is shown in Fig. 21. The particle is composed of the catalyst component or another precursor (1) coated with the newly formed polymer (3) and the interfacial layer (2). The topology and phase structure of the PPC can be controlled in the design stage. Determination of the structure of the PPC and finding out the methods for its control will allow targeted design of polyolefin-based composite materials with desired properties. Unfortunately, no analytical expressions relating the molecular parameters and the composition of a system to its properties have been derived as yet. Would they be proposed, this will favour the refinement and generalisation of the experimental relationships and the development of a well-substantiated approach to the preparation of PO compositions with desired properties.

A great advantage of the methods for preparation of PPC considered in this review is that they allow one to prepare operationally compatible polymer compositions from thermodynamically

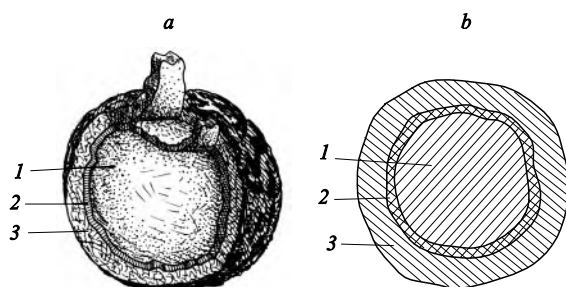


Figure 21. General view (a) and simplified scheme (b) of the structure of a particle of molecular PPC (for details, see text).

cally incompatible components. These compositions exhibit stable properties and have superiority in some characteristics compared to traditionally used polymer blends. This approach follows a recent trend, according to which polymeric materials are given the desired properties by choosing appropriate combinations of the known components rather than by polymerisation of new monomers, since the potential of the organic synthesis of new monomers and polymers based on them are, after all, limited.

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^d — *Chem. Phys. Rep. (Engl. Transl.)*

Mechanisms of asymmetric induction in catalytic hydrogenation, hydrosilylation and cross-coupling on metal complexes

V A Pavlov

Contents

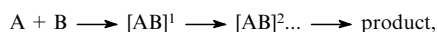
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Abstract. The current state of studies on the mechanisms of asymmetric hydrogenation, hydrosilylation and cross-coupling induced by metal complexes is considered. The possibilities for the identification of stages of catalytic reactions involving asymmetric induction are analysed. The classification of the types of asymmetric induction according to the differences in these stages is proposed. In most cases, asymmetric induction occurs in the stage of substrate coordination by catalytic complexes (the key–lock interaction). Evidence is presented in favour of the assumption that the asymmetric carbon atom is formed in the product in the stages of transformations of the asymmetric intermediate, even though the starting chiral catalytic complex is C_2 -symmetric. The bibliography includes 118 references.

I. Introduction

Asymmetric catalytic reactions involving prochiral substrates on chiral metal-complex catalysts proceed through the interaction of these species to form diastereomeric intermediate complexes. The rational description of the phenomenon of asymmetric induction (or diastereoselectivity)[†] in asymmetric synthesis can be given using empirical stereochemical rules and models¹ analogous to those proposed by Prelog, Cram, Cornforth, *et al.* Asymmetric induction can take place either in the stage of interaction (coordination) of a metal-complex catalyst with a substrate to form an intermediate complex or in the course of subsequent transformations of the resulting complex. The first alternative is sometimes called the steric control or the ‘key–lock’ interaction (the terms ‘chiral recognition’ and ‘chiral discrimination’ are also used).

For the reaction



where A is the substrate and B is the reagent (catalyst), the following general classification of the types of asymmetric induction is proposed:

- (1) prior to the reaction (due to a chiral medium);

- (2) the stage involving the interaction of A with B (coordination of the substrate by the catalyst);

- (3) transformations of the first ($[AB]^1$), second ($[AB]^2$) and subsequent intermediates already involving the coordinated substrate;

- (4) nonbonded diastereomeric interactions analogous to those existing between enantiomers in racemates.

Asymmetric induction of the first type is observed in reactions performed in a chiral matrix [for example, in cholesteric liquid crystals (CLC) in the mesophase temperature range, where a chiral helical structure is formed] or in a chiral solvent and, probably, under the combined action of the electric and magnetic fields.^{2,3} Asymmetric induction of the second type takes place in asymmetric metal-complex catalysis, in particular, on hydrogenation and hydrosilylation of aromatic ketones. Asymmetric induction occurring in the course of transformations of the first and second intermediates (the third type) has been examined in detail for catalytic allylic alkylation.⁴ The nature of asymmetric induction, which is caused by interactions between enantiomers in racemates (the fourth type) and due to which the racemates differ from the constituent individual enantiomers in some chemical and physical properties, is poorly known.

Asymmetric induction, if considered as a way of communicating stereochemical information, involves two components, *viz.*, static discrimination due to steric hindrance and dynamic discrimination resulting from kinetic or thermodynamic factors.⁵

Hydrogenation, hydrosilylation and cross-coupling are of importance from the practical standpoint because they comprise a minimal set of reactions, which provide the preparation of chiral products bearing many functional groups involved in pharmaceuticals.⁶ Because of this, the present review deals with the mechanisms of asymmetric induction occurring in these three reactions.

II. Asymmetric induction prior to the catalytic reaction

Asymmetric induction prior to the reaction should be considered as a manifestation of the chiral action of a medium both on the catalyst, which in this case can be achiral, and the prochiral substrate. Asymmetric reactions can proceed in a CLC medium

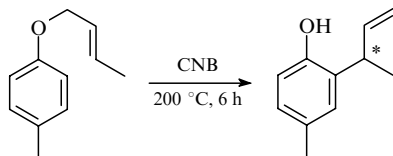
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[†] The enantioselectivity can be considered as a measure of asymmetric induction in asymmetric catalysis where the enantiomeric product is isolated from a diastereomeric intermediate complex.

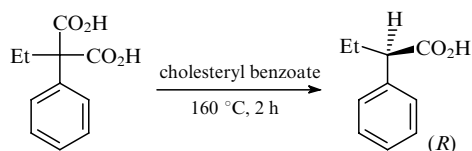
in the mesophase temperature range where a chiral helical structure is formed (for more detailed arguments in favour of asymmetric induction prior to the reaction, see below). However, the published data on asymmetric synthesis in a CLC medium as a chiral matrix are contradictory. The enantioselective Claisen rearrangement performed in a CLC mesophase has been reported.⁷



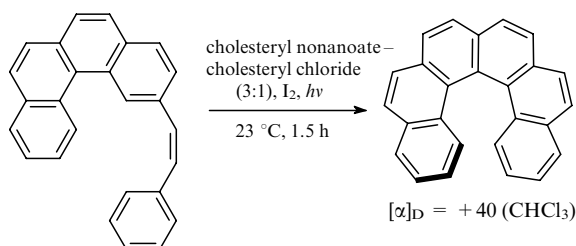
CNB is cholesteryl *p*-nitrobenzoate.

The authors judged the enantioselectivity of the reaction from the CD spectra of the product.

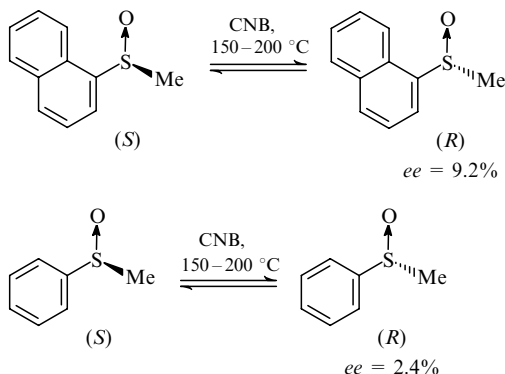
Ethyl(phenyl)malonic acid was decarboxylated in a CLC mesophase in an optical yield (*p*) of 18%.⁸



In the photochemical synthesis of hexahelicene performed in CLC within the mesophase temperature range of 20–25 °C, the enantioselectivity of the process was 1%, which was confirmed by the presence of a CD maximum in the absorption band of the hexahelicene obtained.⁹



However, photocyclisation of α -(*N*-methylanilino)styrene into *N*-methyl-2-phenylindoline in various CLC mesophases afforded a racemic product.¹⁰ When studying thermochemical interconversions of sulfoxides in a cholesteryl *p*-nitrobenzoate mesophase, a small enantiomeric excess (*ee*) of the product was observed.¹¹



It was concluded^{10,11} that asymmetric transformations in cholesteric mesophases, like those in standard chiral solvents, proceed in low optical yields. However, the authors of the cited papers noted that exceptions are possible in the case of strong specific interactions between the dissolved compound and CLC.

In another study,¹² even the theoretical possibility of the manifestation of the asymmetric effect in a CLC mesophase was

denied because the helical step of CLC (300–400 nm) is incompatible with the molecular sizes of standard reagents. These molecules do not ‘notice’ the helical structure of CLC, much as people do not notice the curvature of the earth’s surface. Nevertheless, CLC, owing to the chirality of their molecules, can exert a slight asymmetric effect on chemical reactions, if only as optically active solvents.

The asymmetric influence of the magnetic field is poorly known.[‡] Pasteur was the first to take an interest in this problem. He believed that if the magnetic field can induce rotation of the polarisation plane of light in the case of achiral compounds (the Faraday effect), it can generate the dissymmetry analogous to that possessed by chiral molecules. Kelvin reasoned that this idea is in error because the magnetic rotation does not possess the right- or left-handed quality, *i.e.*, it is not chiral. However, P Curie noted that the magnetic field parallel to the electric field can induce chirality because the mirror operation (which provides interchangeability of components) is applicable to the parallel and antiparallel molecular arrangements in this combined field.¹⁴ The above-considered enantiomorphism and the enantiomorphism of chiral molecules are distinguished as the ‘false’ and ‘true’ chirality, respectively.^{2,3} This raises the question of whether the ‘false’ chiral effect can cause asymmetric induction. It is known that the symmetry is broken at the level of elementary particles. It is assumed that the ‘false’ chiral effect can induce analogous symmetry distortions in chemical reactions. Changes in the symmetric (in the absence of this effect) energy barriers in the path of formation of enantiomers of the product can lead to differences between the rate constants of formation of enantiomers in the chemical reaction away from the equilibrium.^{2,3}

This theoretical reasoning has been supported experimentally. Thus Gerike¹⁵ discovered the enantiomeric enrichment (although small and irregular) of the product (*ee* < 1%) in alkylation of prochiral ketones with Grignard reagents, the addition of bromine at the double bond and some other reactions using various combinations (parallel, antiparallel and orthogonal mutual arrangements) of the electric (15–8100 V cm^{–1}) and magnetic (constant and alternating, 8 × 10³–1.17 × 10⁵ A m^{–1}, 0–50 Hz) fields. It was reported that reduction of ketones with Grignard reagents and lithium aluminium hydride in a constant magnetic field proceeded with high enantioselectivity.¹⁶ However, this conclusion was disproved by one of the authors.¹⁷ It is agreed^{2,3} that the concept of the asymmetric influence of the constant magnetic field is reasonable, but this influence can serve only as a ‘starter’ and must be combined with a chiral autocatalytic process. Apparently, this problem calls for further careful experimental investigation.

We also examined asymmetric induction in catalytic reactions proceeding in a liquid-crystal chiral matrix^{18,19} by studying hydrogenation of α -acetamidocinnamic acid (ACA) in the presence of achiral Wilkinson’s catalyst RhCl(PPh₃)₃ possessing a substantial molecular volume (this fact is of importance in imparting the helical ordering of the CLC molecules to the molecules of the catalyst). Since RhCl(PPh₃)₃ and ACA are insoluble in a CLC melt, *viz.*, in cholesteryl tridecanoate (CTD), the reaction was carried out in a CTD–BuⁿOH–C₆H₆ mixture. In this solution, the molecules of CTD, the substrate (ACA) and the catalyst RhCl(PPh₃)₃ have helical ordering at the mesophase temperature of 60–70 °C. This is evidenced by the fact that the CD spectra show maxima of induced circular dichroism of the same sign in the absorption bands of the substrate and the catalyst. Probably, the same sense of helical ordering of the substrate and catalyst molecules facilitates discrimination between the *Re*- and *Si*-sides of the C=C bond in the substrate coordinated to the catalyst in an intermediate complex. Actually, a moderate temperature-dependent enantioselectivity was observed in the reaction under consideration (Fig. 1).

[‡] The non-asymmetric influence of the magnetic field on chemical reactions has long been known (see, for example, the review¹³).

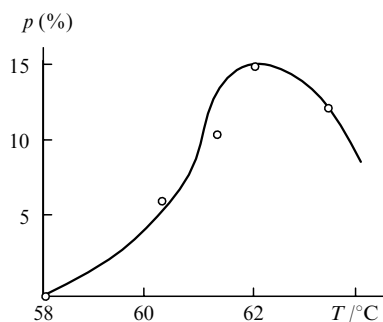


Figure 1. Temperature dependence of the optical yield of *N*-acetylphenylalanine in hydrogenation of ACA.

The dependence has a maximum in the middle of the temperature range of the CTD mesophase where the cholesteric liquid crystal is helically ordered. This effect could also be attributed to the effect of CLC as a chiral solvent. However, the fact that the maximum of enantioselectivity coincides with the middle of the temperature range of the liquid crystal mesophase counts in favour of the former explanation.

With the aim of investigating the effect of a combination of the electric and constant magnetic fields on chemical reactions, we[§] used a solenoid.²⁰ Acid- and base-catalysed mutarotation of D-glucose in water was examined. In the mutarotation of monosaccharides, the equilibrium was established between the α and β forms, which are diastereomers. In the initial stage, the reaction was far from the equilibrium (this is a necessary condition for the magnetic field to exert the asymmetric effect^{2,3}). The reaction was carried out in a temperature-controlled polarimetric tube placed in a solenoid and its course was followed from the change in the optical rotation. The rate constant of mutarotation k was calculated according to the first-order equation. The magnetic field strength (H) was calculated from the magnetic rotation of the polarisation plane of light under the action of water at $\lambda = 589$ nm. The direction of magnetic field was judged from the direction of the observed rotation of the plane of polarisation induced by water. To obtain a more accurate estimate of the dispersion of the rate constants, some experiments were repeated several times at the same temperature. The results are given in Table 1.

Presently, one cannot give an unambiguous answer to the question of how the rate constant is changed depending on the direction of magnetic field. However, the reaction at low temperatures in the field with (+)- α_D H₂O proceeds somewhat more rapidly than that in the field with (–)- α_D H₂O. At the same time,

Table 1. Rate constants of mutarotation of D-glucose at different temperatures depending on the direction of magnetic field in a solenoid.²⁰

$T/^{\circ}\text{C}$	H/G	$10^3 k/\text{min}^{-1}$		$10^3 \Delta k/\text{min}^{-1}$
		(+)- α_D H ₂ O	(–)- α_D H ₂ O	
6.2	1266	3.73 ± 0.04	3.69 ± 0.02	+0.04
		3.74 ± 0.03	3.42 ± 0.08	+0.32
10.2	1265	6.01 ± 0.02	5.65 ± 0.03	+0.36
		5.81 ± 0.04	5.59 ± 0.02	+0.22
20	1262	6.02 ± 0.01	5.50 ± 0.04	+0.52
		16.68 ± 0.05	16.72 ± 0.05	–0.04
30	1259	16.80 ± 0.03	16.82 ± 0.06	–0.02
		43.57 ± 0.29	41.57 ± 0.08	+2.00
38.3	1256	42.50 ± 0.39	43.10 ± 0.20	–1.60
		90.87 ± 0.49	83.58 ± 0.62	+7.29

§ The experiment was carried out in collaboration with E I Klabunovskii.

it can be said with reasonable confidence that the effect of a constant magnetic field (without combining with the electric field) is absent. The results of the investigation of D-glucose mutarotation in water in a constant magnetic field demonstrated that the changes in the rate constants depending on the direction of the magnetic field are comparable in value to the errors of the measurements (Table 2).

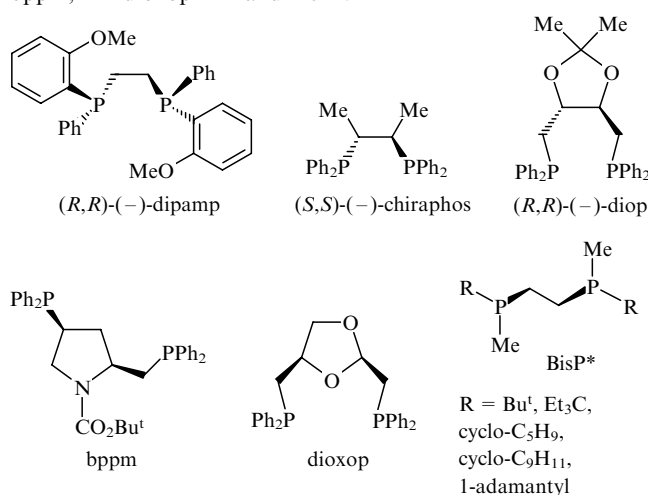
Table 2. Rate constants of mutarotation of D-glucose at $20 \pm 0.1^{\circ}\text{C}$ depending on the direction of constant magnetic field ($H = 7490$ G).

$10^3 k / \text{min}^{-1}$		$10^3 \Delta k / \text{min}^{-1}$
(+)- α_D H ₂ O	(-)- α_D H ₂ O	
13.73 ± 0.85	14.67 ± 0.29	-0.94 ± 0.85
14.84 ± 0.26	15.03 ± 0.07	-0.19 ± 0.26
14.17 ± 0.41	15.19 ± 0.23	-1.02 ± 0.41
15.14 ± 0.56	14.85 ± 0.11	$+0.29 \pm 0.56$
15.00 ± 0.42	15.07 ± 0.11	-0.07 ± 0.42

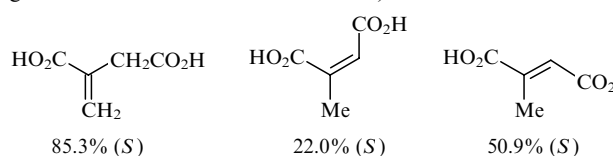
III. Asymmetric induction in the stage of substrate coordination by catalytic complexes

The elucidation of the nature of asymmetric induction and the identification of the stage where it takes place are closely related to the investigation of the general mechanism of asymmetric reactions. For the latter problem to be solved, it is necessary to reveal individual elementary stages, determine their rates, detect and characterise intermediates (including the establishment of their absolute configurations) and, finally, identify the key stage of asymmetric induction. If asymmetric induction occurs in the stage of substrate coordination by a chiral catalytic complex, this fact can be established using rather simple logical approaches considered below.

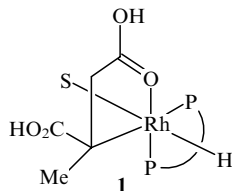
The mechanism of hydrogenation of the C=C bond in substrates was studied using rhodium phosphine catalysts, involving such ligands as dipamp,^{21–25} chiraphos,^{26–29} diop,^{21,29} bppm,^{30,31} dioxop^{32,33} and BisP*.³⁴



In studies on hydrogenation of itaconic, citraconic and mesaconic acids in the presence of [Rh(bppm)]⁺ giving rise to 2-methylsuccinic acid, an attempt was made to reveal the stage involving asymmetric induction (the optical yields of the products are given below the formulae of the acids).³⁵



In the event that the enantioselectivity of the reaction is controlled by intermediate **1** common to all the three substrates (which follows from Halpern's theory discussed below), the optical yields must be close, which is contradictory to the experimental data considered above. Hence, it was concluded that asymmetric induction occurred in the stage of substrate coordination (the 'key-lock' interaction).

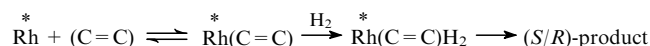


S is the solvent

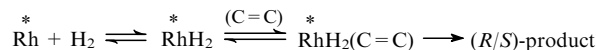
It should be noted that the chiral catalytic complex with the bppm ligand does not possess symmetry elements (except for C_1) and, hence, asymmetric induction in the stage of substrate coordination is performed by the asymmetric complex.

The hydrogen pressure influences the enantioselectivity of hydrogenation of acetyl- and benzoylaminocinnamic acids and their esters in the presence of rhodium complexes with the bppm, diop or dipamp ligands (with NEt_3 and without it). To explain this fact, Ojima *et al.*³⁵ offered the hypothesis that two reaction pathways compete with each other:

Path A



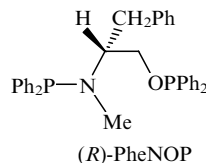
Path B



Paths A and B are favourable at low and high hydrogen pressures, respectively. Path B has been found previously in the studies of hydrogenation of alkenes on Wilkinson's catalyst. The authors of the cited study postulated³⁵ that paths A and B afforded different enantiomers. Hence, an elevation of the pressure, which facilitates path B, would be expected to decrease the enantioselectivity up to the inversion of the configuration. It is this situation that was experimentally observed. Interestingly, the addition of triethylamine weakened the influence of the hydrogen pressure on the enantioselectivity. The anion, which is generated upon the addition of NEt_3 to acid (the substrate), has a much higher tendency to form an adduct with the rhodium phosphine complex than the corresponding acid. Consequently, the contri-

bution of path B in the presence of a base is insignificant, which agrees with the experimental evidence that the enantioselectivity remained virtually unchanged at different hydrogen pressures. Hence, the hypothesis under consideration provides an adequate explanation for the effect of the hydrogen pressure and the influence of the addition of a base on the enantioselectivity.

However, this scheme, as applied to the hydrogenation of derivatives of amidocinnamic acid, does not allow one to reveal the stage responsible for asymmetric induction due to a lack of detailed stereochemical information on two competitive reaction pathways. Nevertheless, the hypothesis for two competitive reaction pathways is fruitful. It was found^{36–39} that the enantioselectivity of hydrogenation of ACA in the presence of the $[\text{Rh}((R)\text{-PheNOP})(\text{cod})]\text{ClO}_4$ complex



depends on the hydrogen pressure, the temperature, the ratio of the concentrations of ACA and the complex and the dielectric constant of the solvent (Fig. 2). These dependences can readily be explained within the framework of the above-considered concept. The contribution of the reaction path B becomes more significant and, correspondingly, the higher enantiomeric excess of the product adopting a certain configuration, *viz.*, (*S*)-AcPhe, is achieved as the hydrogen pressure is elevated, the concentration of the substrate with respect to the catalyst is decreased, the temperature is lowered and the dielectric constant of the solvent decreases. The role of the first two factors follows directly from the schemes of the reaction paths A and B. The influence of the two last-mentioned factors is in agreement with the observations made in the study.³⁵ The proposed explanation is also confirmed by the fact that rhodium hydride was observed in the reaction mixture at low temperature (-20°C).³⁷

Upon hydrogenation of the enamide substrate on complexes with bppm and PheNOP, asymmetric induction occurs during the transformation of an asymmetric intermediate.

The pure dihydride mechanism (path B), which is realised even at low temperature and hydrogen pressure, was considered in the study³⁴ devoted to hydrogenation of methyl α -acetamidocinnamate ($\text{Ac}\Delta\text{PheOMe}$) on a rhodium complex containing (*S,S*)-1,2-bis(*tert*-butylmethylphosphino)ethane (Scheme 1).

Asymmetric induction takes place during substrate coordination by the dihydride complex (major intermediate) present in an

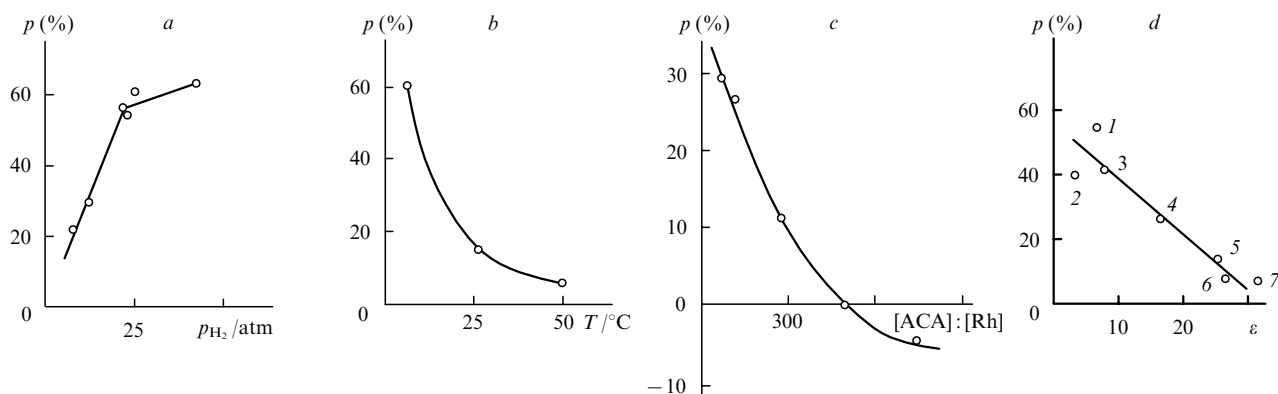
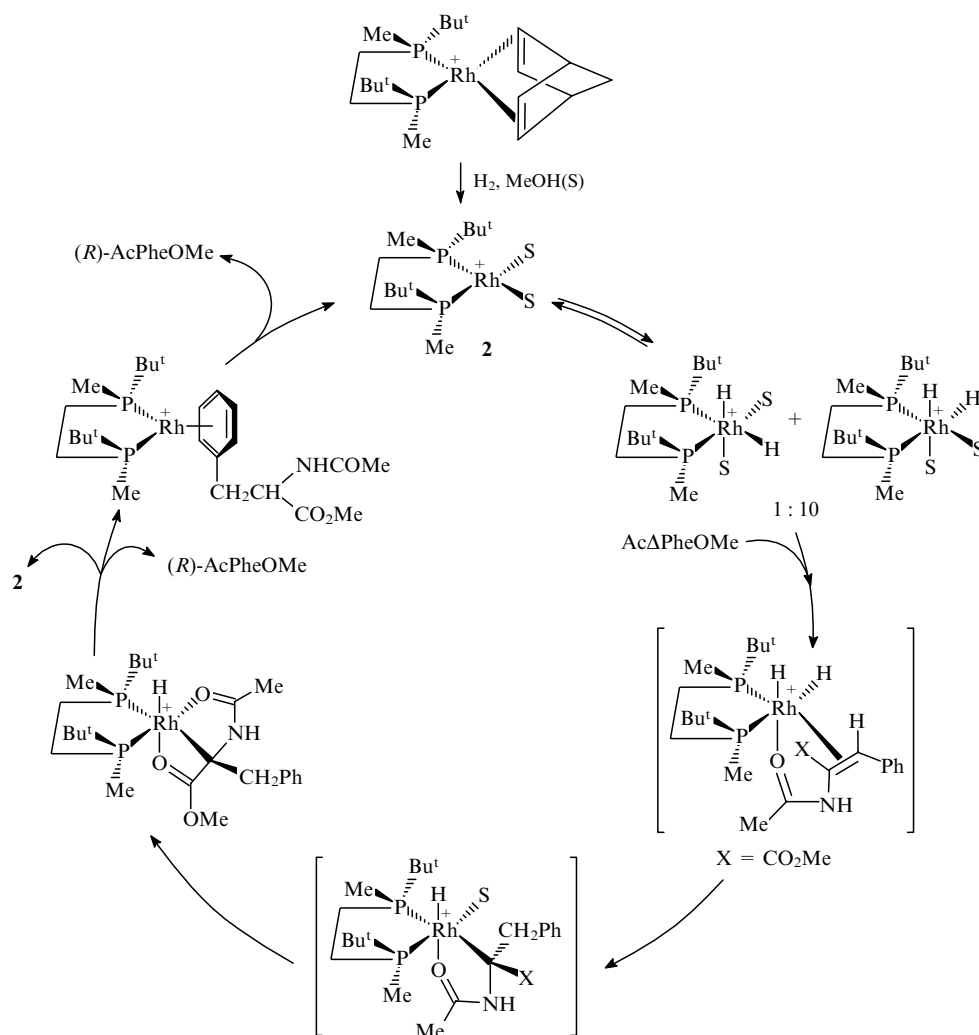


Figure 2. The optical yield of the product (*S*)-AcPhe in hydrogenation of ACA vs. the hydrogen pressure (*a*), the reaction temperature (*b*), the ratio of the concentrations of ACA and the catalytic complex (*c*) and the dielectric constant of the solvent (*d*).

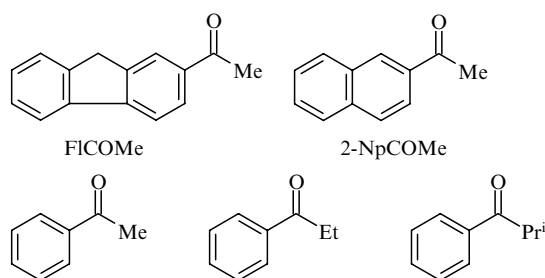
The reaction conditions: (*a*) — $T = 20^\circ\text{C}$, $[\text{ACA}]:[\text{Ph}] = 100:1$, $\text{C}_6\text{H}_6\text{--MeOH}$ (1:1); (*b*) — $p_{\text{H}_2} = 1$ atm, $[\text{ACA}]:[\text{Ph}] = 100:1$, $\text{C}_6\text{H}_6\text{--MeOH}$ (1:1); (*c*) — $T = 50^\circ\text{C}$, $p_{\text{H}_2} = 1$ atm, $\text{Pr}^\text{i}\text{OH}$; (*d*) — $T = 25^\circ\text{C}$, $p_{\text{H}_2} = 1$ atm, $[\text{ACA}]:[\text{Ph}] = 100:1$, the solvent: (1) DMF; (2) dioxane; (3) THF (4) EtOH — C_6H_6 ; (5) MeOH — C_6H_6 ; (6) EtOH; (7) MeOH.

Scheme 1

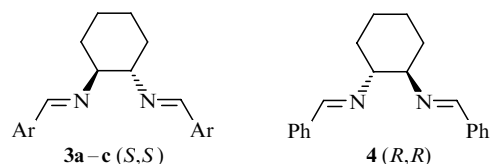


excess. As can be seen from Scheme 1, this intermediate is devoid of symmetry elements, *i.e.*, the asymmetric carbon atom is generated in the product in the stage of the transformation of the asymmetric intermediate although the starting chiral catalytic complex **2** possessed the symmetry C_2 .

The mechanism of asymmetric induction was investigated for hydrogen-transfer hydrogenation of aromatic ketones R^1COR^2



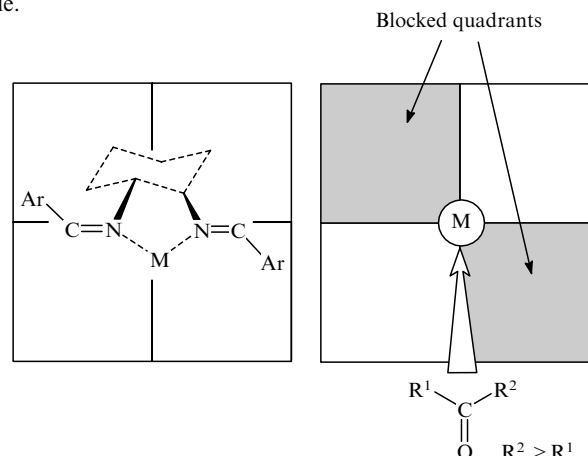
on rhodium and iridium complexes, which were generated *in situ* and contained Schiff bases, *viz.*, derivatives of (*S,S*)- (**3a–c**) and (*R,R*)-1,2-diaminocyclohexane (**4**).⁴⁰



3: Ar = Ph (**a**), C₆H₄OMe-*o* (**b**), Np-2 (**c**).

In all cases, the configuration of the product was determined by the configuration of the ligand and was independent of the nature of the metal atom. If ketones as substrates of this reaction are arranged in order of decreasing difference between the molecular volumes of two substituents (Fig. 3), it can be seen that *ee* tends to decrease in the series FICOMe > 2-NpCOMe > PhCOMe > PhCOEt > PhCOPrⁱ. In the case of rhodium complexes with the ligand **3a**, the corresponding series is as follows: FICOMe > 2-NpCOMe ≈ PhCOMe ≈ PhCOEt ≈ PhCOPrⁱ.

The most pronounced difference in *ee* is observed for FICOMe and PhCOMe. This fact can be interpreted using the quadrant rule.



The metal atom in the C_2 -symmetric chelate chiral complex (the catalyst) is oriented toward the intersection point of the

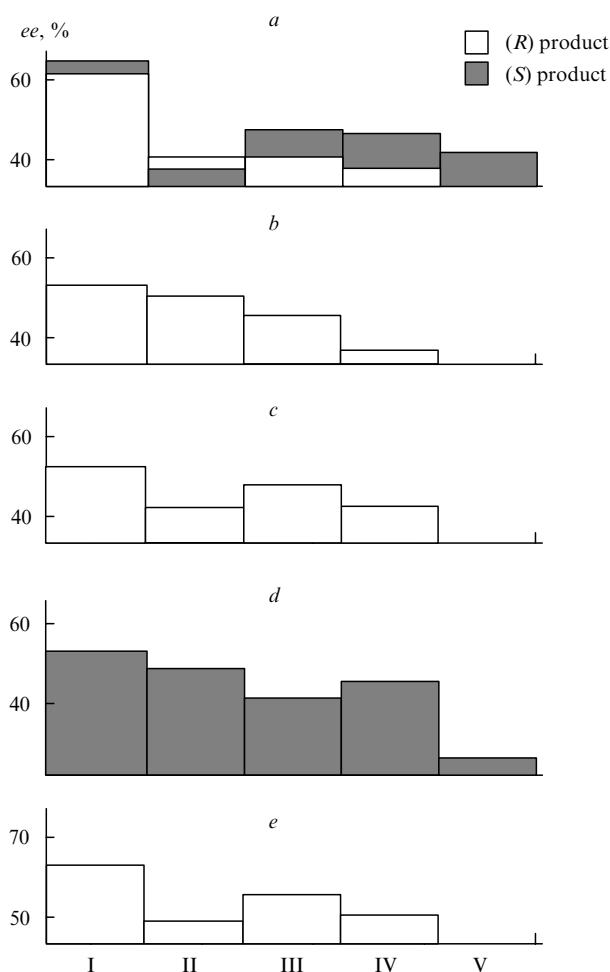


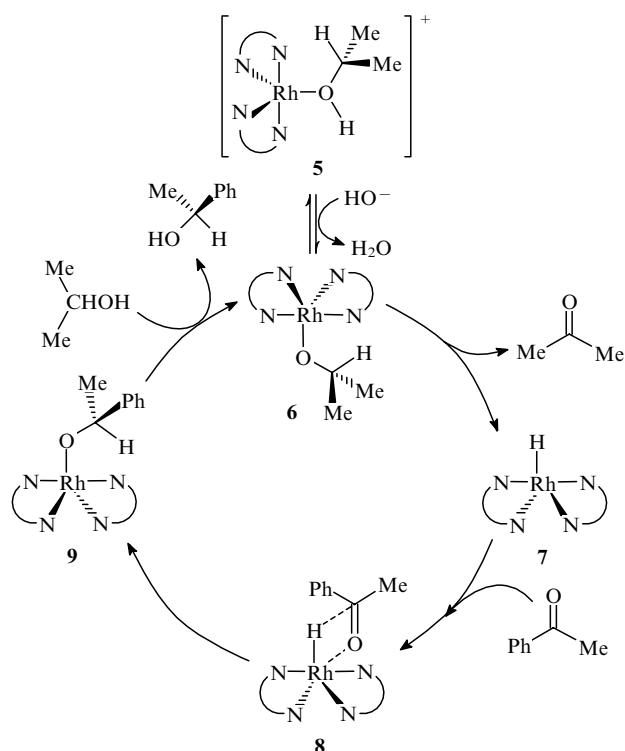
Figure 3. Influence of the difference between the molecular volumes of the substituents R^1 and R^2 in ketone R^2COR^1 ($R^2 > R^1$) on the enantioselectivity of hydrogenation.

(The catalytic system: (a) Rh/3a, Rh/4; (b) Rh/3b; (c) Rh/3c; (d) Ir/4; (e) Ir/3b. Ketone: (I) FlCOMe; (II) 2-NpCOMe; (III) PhCOMe; (IV) PhCOEt; (V) PhCOPrⁱ).

quadrants and the C_2 -symmetrically arranged aryl substituents fall in the quadrants related by the symmetry C_2 (left upper and right lower), thus 'blocking' them. The larger the difference between the molecular volumes of the substituents in the ketone involved in the intermediate complex (the average of two possible positions, which can occupy the ketone in the intermediate, is indicated by an empty arrow), the higher the probability of the bulky substituent of the carbonyl group of the ketone being located in the free quadrant and, correspondingly, the larger the chiral discrimination and, consequently, the higher the enantioselectivity. It is this situation that was experimentally observed and, hence, the data obtained can be considered as an argument in favour of the fact that asymmetric induction (chiral recognition) takes place in the stage of substrate coordination in an intermediate complex.

Other authors also support the idea that asymmetric induction in hydrogenation with the hydrogen transfer catalysed by rhodium and iridium complexes occurs in the stage of ketone coordination. Thus the following catalytic cycle (Scheme 2) was proposed⁴¹ for hydrogen-transfer hydrogenation of acetophenone catalysed by (S)-(+)-3-*sec*-butyl-, (S)-(-)-3-(1,2,2)-trimethylpropyl- or (S,S)-(+)-3,8-di-*sec*-butyl-1,10-phenanthroline complexes of rhodium(I) in a $Pr^iOH-KOH$ medium.

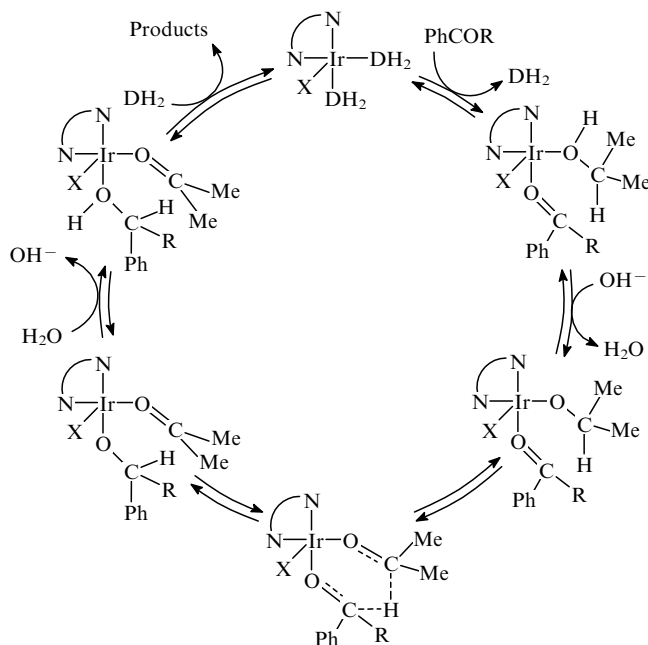
Scheme 2



As can be seen from Scheme 2, asymmetric induction occurs upon substrate coordination by asymmetric intermediate 7. However, this mechanism of hydrogenation needs additional evidence.

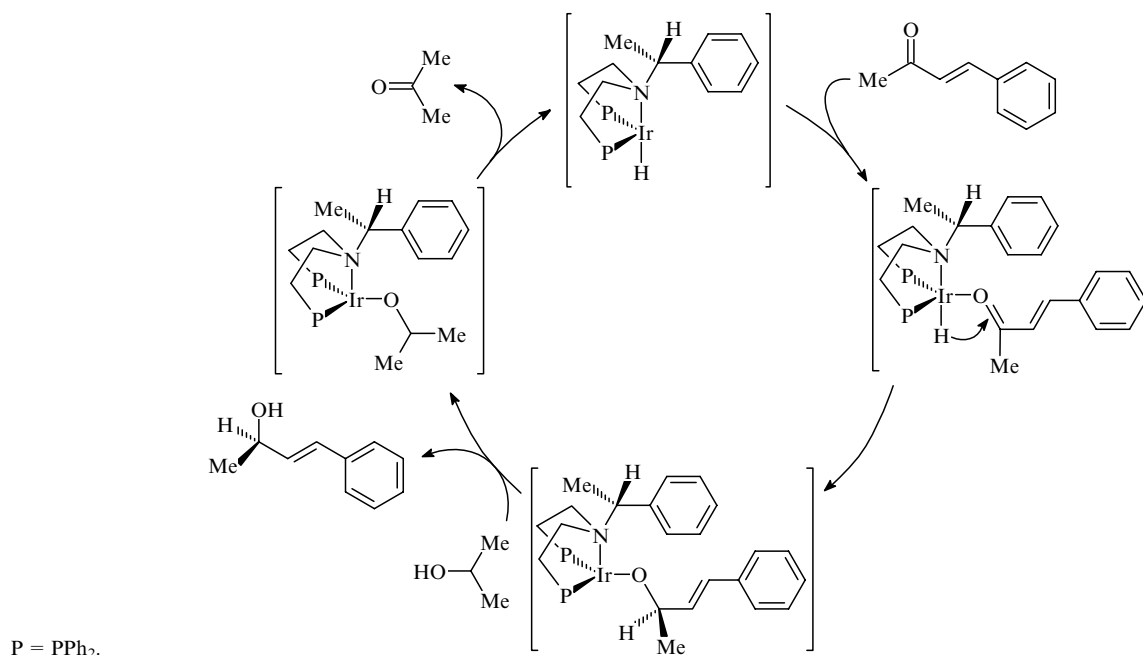
For the reactions catalysed by iridium complexes with Schiff bases, which were prepared from pyridine-2-carbaldehyde and α -phenylethylamine, a mechanism was proposed according to which asymmetric induction takes place in the stage of the hydrogen transfer from the donor (isopropyl) group to the acceptor molecule (ketone subjected to hydrogenation) in the cyclic transition state (Scheme 3).^{42,43}

Scheme 3



DH₂ is propan-2-ol; X = DH₂, OH⁻; R = Me, Et, Prⁿ, Prⁱ.

Scheme 4

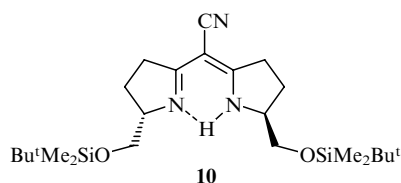


The catalytic cycle proposed⁴⁴ for hydrogenation of benzylideneacetone in the presence of the $\text{HIr}[(R)\text{-Ph}.\text{CH}(\text{Me})\text{N}(\text{CH}_2\text{CH}_2\text{PPh}_2)_2]$ complex is shown in Scheme 4. The structure of the intermediate was established by X-ray diffraction analysis. According to this scheme, asymmetric induction occurs in the stage of coordination of the ketone by the asymmetric complex.

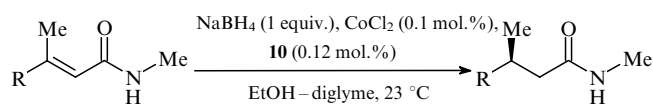
Scheme 3 involves direct hydrogen transfer, whereas Scheme 4 implies that the transfer proceeds with the participation of metal hydride.⁴⁴ Both schemes are to a large extent conventional, but the latter scheme seems to be better justified[†] because the hydride intermediate was found experimentally.⁴⁴

Therefore, there is some evidence that asymmetric induction takes place in the stage of ketone coordination by an asymmetric intermediate complex, which lost the symmetry C_2 (if it was present in the starting catalytic complex).

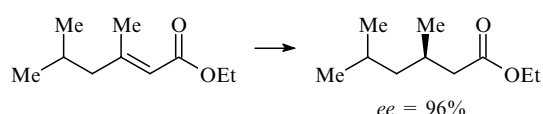
The complex, which is formed *in situ* based on CoCl_2 , semi-corrin ligand **10** and NaBH_4 in alcohol, serves as an efficient catalytic system for asymmetric reduction.^{46, 47}



Amides and esters of α,β -unsaturated acids are reduced by this system with high enantiomeric excess ($ee = 90\% - 99\%$).



$ee = 98.7\%$ ($R = (\text{CH}_2)_2\text{Ph}$), 98.9% ($R = \text{C}_6\text{H}_{11}$), 92.4% ($R = \text{Ph}$);



[†] At the same time, Scheme 4 ignores the reversibility of the reaction involving the hydrogen transfer from isopropanol⁴⁵ and, hence, Scheme 3 seems to be preferable.

The investigation of the reaction mechanism followed with the use of NaBH_4 in an $\text{EtOD} - \text{DMF}$ medium or using NaBD_4 in an $\text{EtOH} - \text{DMF}$ medium demonstrated that borohydride and EtOH serve as sources of hydrogen atoms at the β - and α -carbon atoms of the product, respectively.⁴⁷ Hydrogenation of substrates bearing a prochiral carbon atom in the α -position proceeds non-enantioselectively with respect to this atom.^{47, 48} The assumed structure of the intermediate complex is shown in Fig. 4.

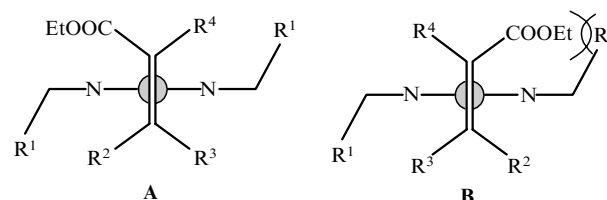
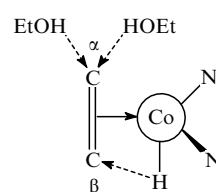
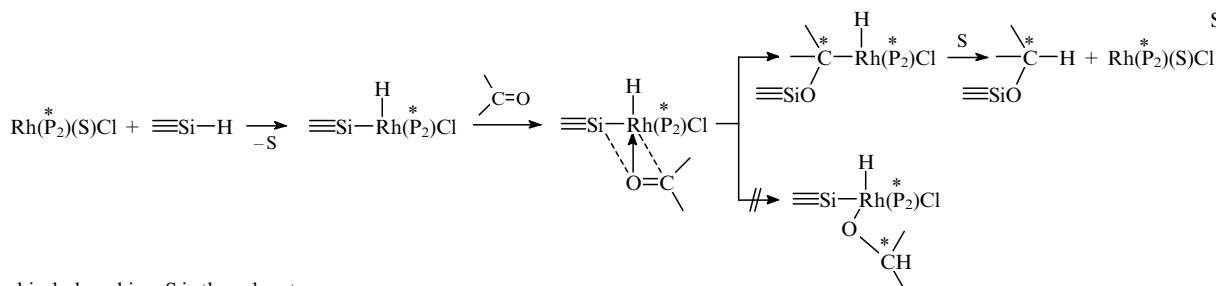


Figure 4. Possible structures of the intermediate complex in reduction reactions on a cobalt-containing catalyst (the cobalt-hydride bond is omitted for clarity).⁴⁷

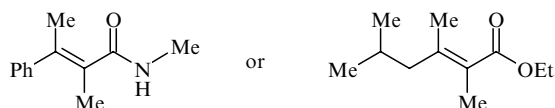
The involvement of the coordinated alkene in structure **B** is sterically hindered so that the transition state **A** is more favourable. Unfortunately, the authors did not indicate the $\text{Co}-\text{H}$ bond, whereas the latter, probably, provides an explanation for the fact that the asymmetric carbon atom is generated only in the β -position of the alkene and hydrogen is generated from NaBH_4 . Actually, the experimental observations mentioned above can readily be explained by assuming that the alkene containing the non-equivalent α - and β -carbon atoms is coordinated to the cobalt atom (whose hydride ion is, undoubtedly, generated from NaBH_4) as shown below





* P is chiral phosphine, S is the solvent.

Reduction of the C = C bond in substrates of the types

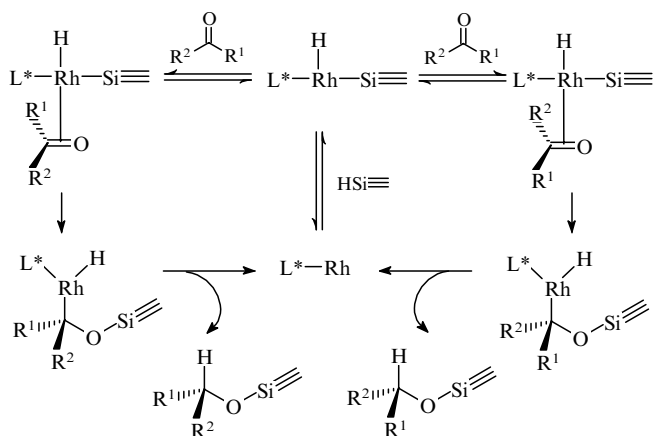


involves the enantioselective addition of the hydride ion at the C_β atom, which is controlled by an asymmetric Co hydride complex, whereupon the intact chiral C₂-symmetric metal complex fragment, apparently, cannot ensure the enantioselective attack on the α-carbon atom. This explanation agrees well with the conclusion made previously that asymmetric induction is realised in the stage of the transformation of an asymmetric intermediate. Hence, turning back to Fig. 4, it can be said that asymmetric induction takes place in the stage of coordination of alkene by the asymmetric monohydride complex of cobalt.

The mechanism of asymmetric hydrosilylation has been studied less thoroughly than the mechanism of asymmetric hydrogenation. It was suggested⁴⁹ that the enantioselectivity results from the competition between diastereomeric silyloxyalkyl(aryl)-rhodium intermediates (Scheme 5).

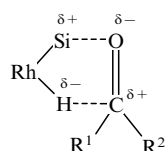
According to another assumption, asymmetric induction takes place in the stage of the addition of ketone to an intermediate complex^{50, 51} (Scheme 6).

Scheme 6



L* is (S,S)-(+)-2,3-O-isopropylidene-2,3-dihydroxy-1,4-bis(diphenylphosphino)butane [(S,S)-(+)-diop].

This scheme is similar to that proposed in the study⁵² where the following structure of the five-membered transition state was assumed



In all the above-considered cases, asymmetric induction is realised in the stage of substrate coordination by an asymmetric intermediate.

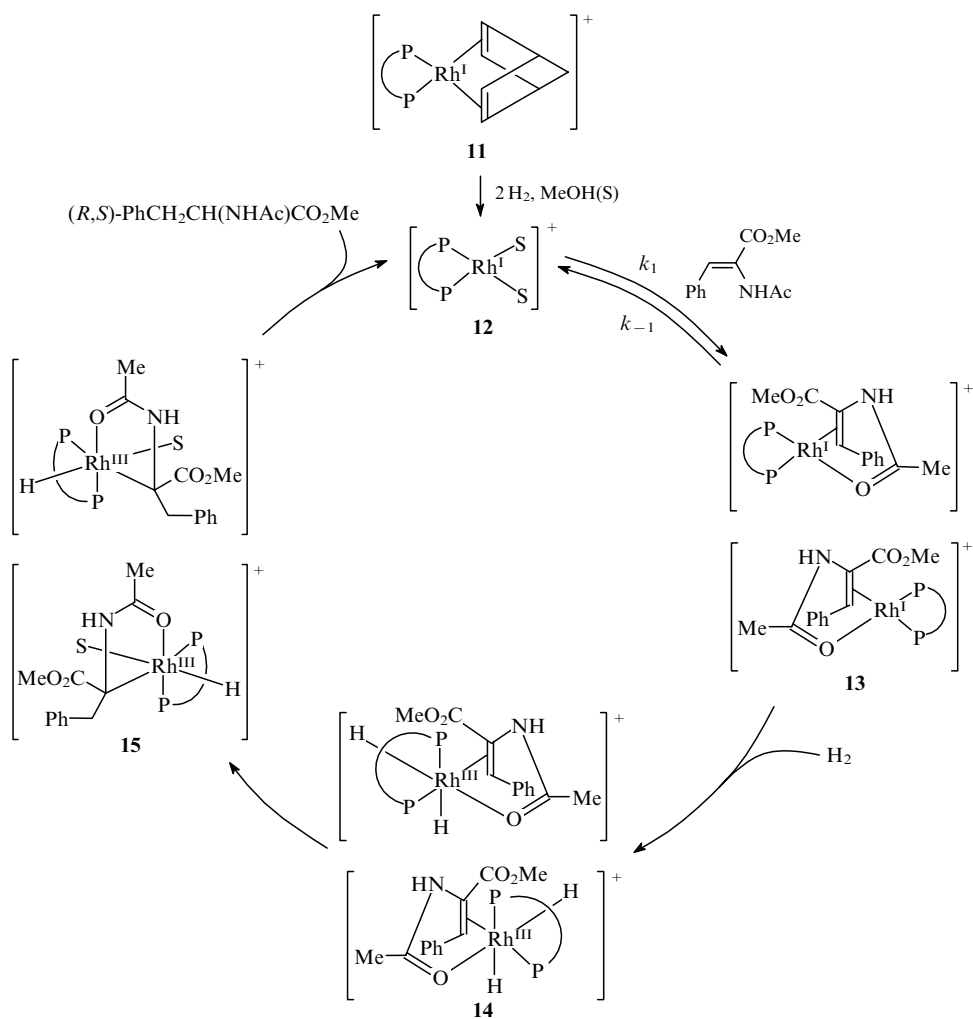
IV. Asymmetric induction in the course of transformations of the first or subsequent intermediates of the catalytic reaction

Research on the mechanism of catalytic hydrogenation of substrates like (Z)-α-acetamidocinnamic acid in the presence of rhodium phosphine complexes was started with the detailed investigation of the kinetics of hydrogenation of methyl (Z)-α-acetamidocinnamate catalysed by a rhodium complex containing achiral diphosphine, viz., 1,2-bis(diphenylphosphino)ethane (diphos).^{27, 53–55} The catalytic cycle of this reaction is shown in Scheme 7. The precursor of the catalytic complex, viz., an ionic adduct of diene with a catalyst (**11**), is involved in the catalytic cycle after reduction of the diene. The structure of complex **12** was determined by ³¹P NMR spectroscopy⁵³ and the structure of complex **13** was established by ³¹P, ¹³C and ¹H NMR spectroscopy and X-ray diffraction analysis.²⁴ At room temperature, the oxidative addition of hydrogen to the complex **13** is the rate-limiting step of the reaction, whereas reductive elimination of the product becomes the rate-limiting step at –40 °C. As a result, alkyl hydride complex **15** at –75 °C was accumulated in a concentration sufficiently high for analysis by ³¹P, ¹³C and ¹H NMR spectroscopy.^{29, 54}

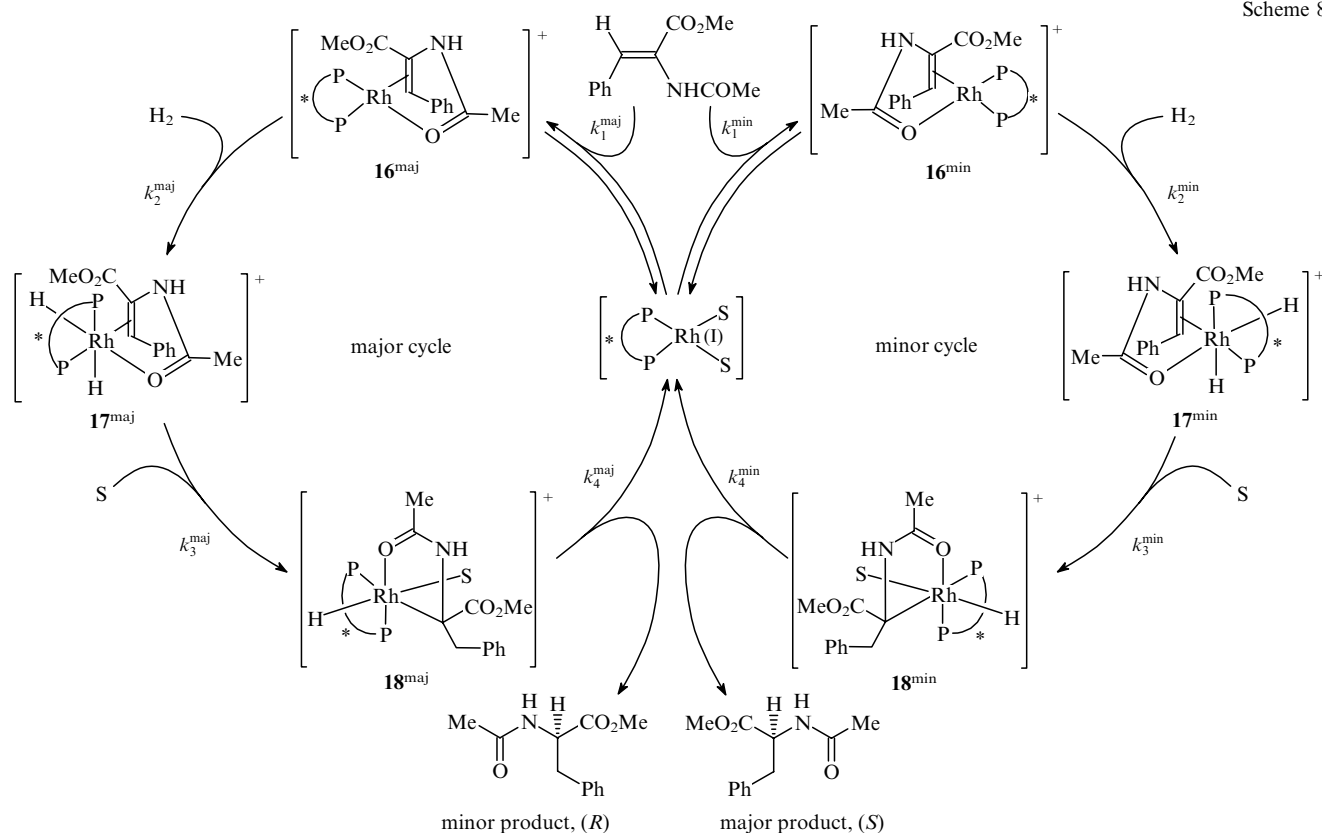
Of compounds presented in Scheme 7, only intermediate **14** was not identified and its structure was proposed 'by analogy'.^{56, 57} Later on, the dihydride intermediate was found experimentally.⁵⁸ The intermediates **13**, **14** and **15** as well as the reaction product are racemates (both enantiomers of these intermediates are shown in Scheme 7).

The catalytic cycle of hydrogenation of the same substrate catalysed by {Rh[(R,R)-dipamp]}⁺ is shown in Scheme 8. In this catalytic cycle, the corresponding intermediates are diastereomers and it is reasonable that the reactions involving these intermediates proceed at different rates.⁵⁹ An analogous catalytic cycle was proposed^{26, 27} for hydrogenation in the presence of {Rh[(S,S)-chiraphos]}⁺. In both cases, ³¹P NMR spectroscopic studies demonstrated^{26, 29, 55, 59} that one of the diastereomers (**16**^{maj}) was present in a high excess with respect to the other diastereomer (**16**^{min}). The structure of the major diastereomer (**16**^{maj}) obtained in the reaction in the presence of {Rh[(S,S)-chiraphos]}⁺ was established by X-ray diffraction analysis²⁶ and circular dichroism spectroscopy.²⁷ However, the configuration of the resulting product was opposite to that, which would be expected to be realised if the reaction proceeds through this intermediate.^{23, 26, 60, 61} Hence, it was suggested^{26, 55} that the enantioselectivity is associated with the difference between the constants $k_2^{\min}$ and k_2^{maj} ($k_2^{\min} \gg k_2^{\text{maj}}$, see Scheme 8) due to which the reaction proceeded predominantly through the intermediate **16**^{min} whose concentration was small compared with that of **16**^{maj}. In the case of hydrogenation of methyl (Z)-α-acetamidocinnamate in the presence of {Rh[(R,R)-dipamp]}⁺ at 0 °C, the ratio of the constants $k_2^{\min} : k_2^{\text{maj}} \approx 1000$.⁵⁹ Halpern⁵⁵ assumed that this situation follows the Curtin–Hammett principle according to which

Scheme 7



Scheme 8



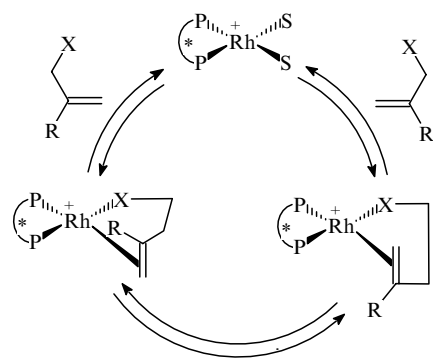
the ratio of the products depends only on the difference between the free energies of the transition states and is independent of the ratio of the conformers (intermediates). According to Halpern's theory, the chiral recognition (asymmetric induction) takes place in the transformation $16 \rightarrow 17$ involved in the catalytic cycle. Unfortunately, no explanation was offered for the differences in stability and reactivity of the intermediates 16^{maj} and 16^{min} , which could allow an understanding of the reason for the substantial difference in the rates of their transformations.

Halpern's theory provides an explanation for the effects of hydrogen pressure and temperature on the enantioselectivity of the reaction. It was demonstrated³⁵ that the enantioselectivity decreased and even the configuration of the product was changed as the hydrogen pressure was increased. According to Halpern's mechanism (see Scheme 8), the formation of the intermediates 17 is accelerated as the hydrogen pressure is increased. At some time, this step ceases to be rate-limiting and the process is controlled by the reversible formation of the diastereomeric adduct 16 , i.e., the enantioselectivity is determined by the ratio $k_1^{\text{min}}:k_1^{\text{maj}}$. Since $k_1^{\text{maj}} > k_1^{\text{min}}$, another catalytic cycle, which affords an opposite isomer of the product, becomes more favourable and the enantioselectivity is decreased. It is this situation that was experimentally observed.

The formation step of adduct 16 is characterised by a substantially higher enthalpy of activation than the next step of the addition of hydrogen (in the presence of $[\text{Rh-dipamp}]^+$ as the catalyst, 18.3 and 6.3 kcal mol⁻¹, respectively). What this means is the rate of the first step is decreased much more rapidly than that of the second step as the temperature is decreased and, consequently, the first step can become rate-limiting. Hence, the enantioselectivity would be expected to decrease with decreasing temperature. This situation was observed in reactions involving some phosphine catalysts.^{32,35}

Since Halpern's theory provides an explanation for many experimental observations, it was commonly accepted in the 1980s.^{62–65} However, this theory has a number of drawbacks.

1. According to Scheme 8, the coordination mode of enamide is not changed (*Re-Si*) and, consequently, the balance between the major and minor catalytic cycles remains unchanged on going from the planar-square complex 16 containing the C_2 -symmetric chiral (diphosphine)Rh(I) fragment to the octahedral complex 17 containing the asymmetric (diphosphine)Rh(III)H₂ fragment.



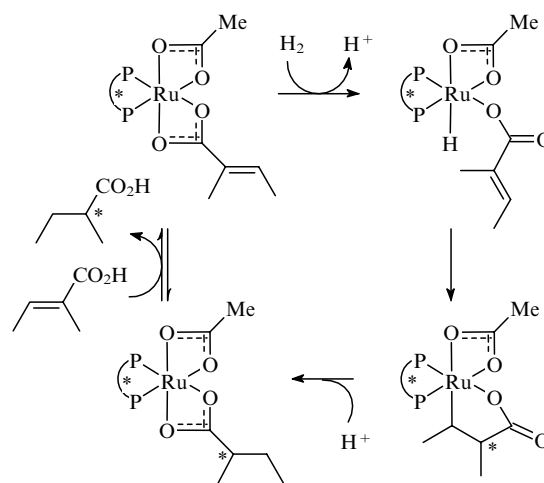
However, the real situation may be different. Moreover, intramolecular interconversions of the complex 16 are quite possible and even (see Ref. 66) the energy barrier for these interconversions is low. It is conceivable that the interconversion *Re-Si* occurs in the step $16 \rightarrow 17$, in which case the major enantiomer is formed in the major catalytic cycle.

2. Most likely, Halpern's theory is inapplicable in the case of rhodium complexes serving as catalysts of hydrogenation of enamides with *ee* = 99.0%–99.9%. In this case, with the generally observed ratio between the major and minor intermediates (10:1), the ratio of the rate constants $k^{\text{min}}:k^{\text{maj}}$ must be even several orders of magnitude larger than that in the case of the rhodium complex with the chiraphos ligand (*ee* = 88%,

$k^{\text{min}}:k^{\text{maj}} \approx 1000$). This difference in the rate constants of the transformations of diastereomeric intermediates seems to be unlikely. For the reaction involving the rhodium complex with the BisP* ligand, another mechanism was proposed³⁴ (see above).

3. Halpern's scheme provides no explanation for some experimental evidence, for example, for the difference in enantioselectivity of hydrogenation of the *E* and *Z* isomers.^{67,68} The enantioselectivities of hydrogenation of (*Z*)- and (*E*)- α -benzoylaminocinnamic acids using the Rh/(*S,S*)-diop system differ not only in magnitude but also in sign.⁶⁹ This may be associated with the different modes of coordination of the above-mentioned substrates by the rhodium atom (the *E* isomer is coordinated through the carboxy carbonyl group, whereas the *Z* isomer is coordinated through the amide carbonyl fragment).⁷⁰ Apparently, the *Re*- or *Si*-side of the coordinated double bond of the substrate may also be changed. Halpern's theory provides no explanation for the influence of bases on the value of *ee* in the reactions performed in the presence of catalysts for which this theory has been initially proposed.³⁵ Thus according to Halpern's hypothesis, the enantioselectivity of hydrogenation in the presence of diphosphine catalysts decreases as the temperature is decreased; however, this is not necessarily the case. Thus in hydrogenation of dehydroamino acids in the presence of rhodium complexes with the prophos, cycphos or diop ligands, the optical yields decreased as the temperature was raised.^{42,71} Apparently, Halpern's mechanism is only a special case.

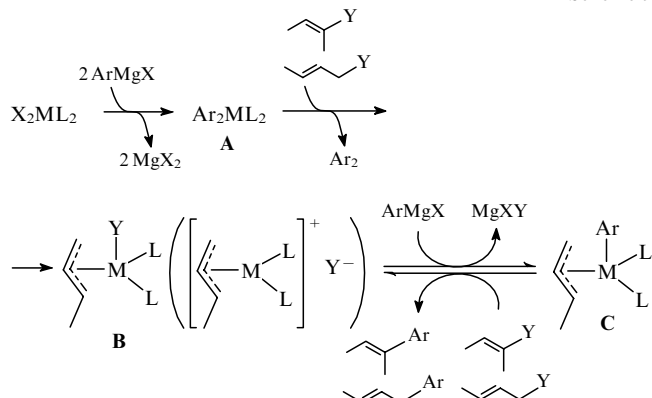
The mechanism of hydrogenation of substrates, such as tiglic acid, catalysed by the Ru(OAc)₂[binap] complex has been studied in sufficient detail. It was demonstrated that hydrogenation proceeded through the formation of a ruthenium monohydride complex.⁷² The mechanism of hydrogenation of tiglic acid on this catalyst was detailed in the study.⁷³



The bis(carboxylato)ruthenium complex involving a substrate performs the heterolytic splitting of H₂ giving rise to a hydride. The hydride ion reduces the C=C bond in the coordinated substrate to form the chelate which contains the chiral product in the half-hydrogenated state. Protonolysis of the newly formed Ru–C bond affords the target product. According to this scheme, asymmetric induction takes place in the formation of the chelate complex with the substrate hydrogenated, i.e., in the step of the transformation of the intermediate devoid of symmetry elements (except for *C*₁). An analogous mechanism for hydrogenation of tiglic acid on the catalytic methallyl complex [binap]Ru. [η³-(CH₂)₂CHMe]₂ was proposed in the study.⁷⁴ In the cited study, it was also assumed that asymmetric induction occurs in the step of the transformation of the asymmetric intermediate, which already involves the substrate in the coordination sphere.

Asymmetric cross-coupling of Grignard reagents with alkenes has been less well studied. According to the presently accepted mechanism, the reaction proceeds through the formation of the intermediate π -allyl(aryl)ML₂ (Scheme 9).^{75–79}

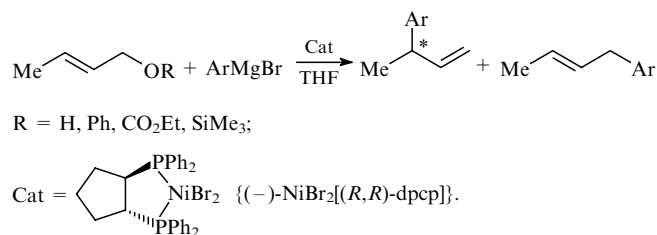
Scheme 9



X = Hal; M = Ni, Pd; L₂ = P₂, P, P;

Y = Br, OH, OPh, COMe, OSiMe₃, CO₂Me.

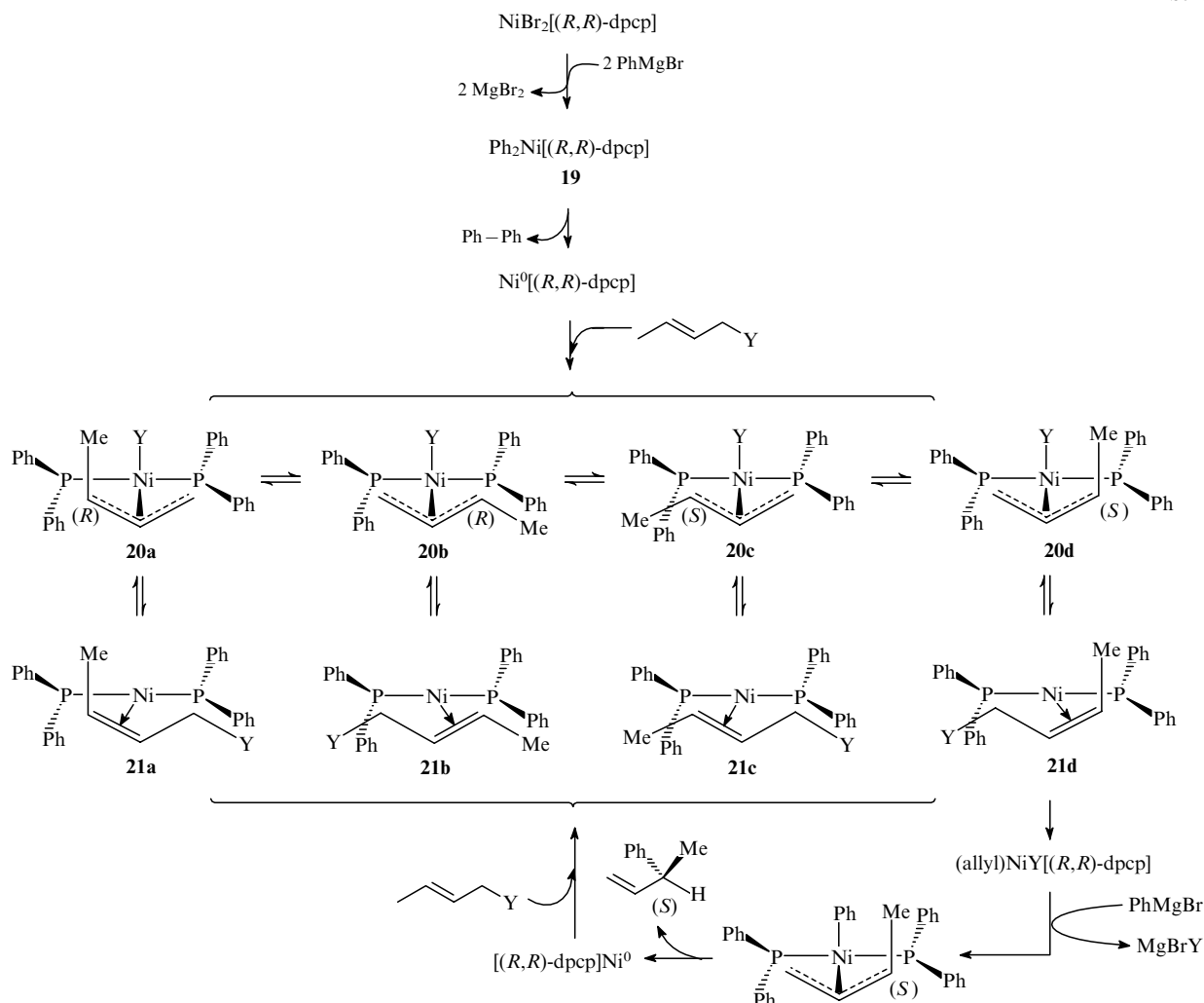
The stages A → B, B → C or C → products may be responsible for asymmetric induction. With the aim of elucidating this problem, we studied the reaction of arylmagnesium bromides with derivatives of crotyl alcohol under the action of a nickel catalyst by increasing successively the molecular volume of the leaving group (OR).⁸⁰



Among the intermediates which confirmed the general reaction mechanism proposed previously, species involving π -coordinated alkene (the substrate) were identified by ³¹P NMR and CD spectroscopy. Probably, these intermediates, which exist in the equilibrium with intermediates **20**, are involved in the overall reaction (Scheme 10).

The chiral arrangement of the phosphine phenyl groups of the coordinated dpcp ligand presented in Scheme 10 is based on the results of X-ray diffraction analysis of the complex⁸¹ (the cyclopentane ring of the dpcp ligand is omitted). The crotyl ligands in the intermediates **20a–20d** involve the stereogenic⁸² carbon atom whose configurations are symbolised as (*R*) and (*S*). The π -coordinated crotyl ligand of this type can be subjected both to the (*R*)-(*S*)-inversion of the π -allylic chirality and the *syn-anti* transformation according to the π - δ - π mechanism.^{83–85} Hence, it can be assumed that all possible forms of the intermediate **20** (**a–d**) exist in the equilibrium. In turn, each intermediate can exist in equilibrium with the intermediates **21a–21d**. The interconversion **20d** ⇌ **21d** experiences the smallest of steric

Scheme 10

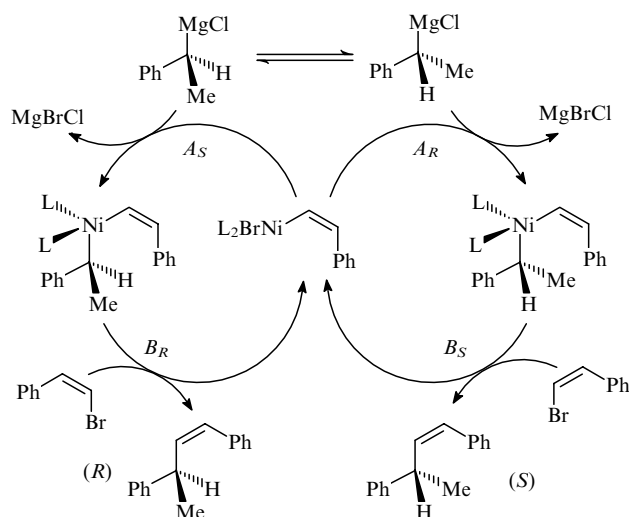


hindrances. The reaction proceeding through these intermediates affords a product whose configuration is identical with that observed experimentally. The larger the molecular volume of the leaving group, the more favourable this path and the higher the expected enantioselectivity. This fact was confirmed experimentally. Hence, asymmetric induction in the reaction under consideration takes place in the stage of the interconversion of the asymmetric intermediates $20(a-d) \rightleftharpoons 21(a-d)$.

This mechanism allows one to explain rather readily the characteristic features of the reaction observed experimentally, *viz.*, the dependence of the enantioselectivity on the molecular volume of the leaving group (the larger the molecular volume, the more favourable the path through the intermediate **21d** and the higher the enantioselectivity) and the fact that the enantiomeric excess of the product is independent of the temperature (because the equilibrium can be established even at low temperatures). Both intermediates responsible for asymmetric induction already involve the coordinated substrate and are asymmetric.

Another type of cross-coupling, for example, the reaction of a racemic mixture of 1-phenylethylmagnesium chloride with (*Z*)- β -bromostyrene catalysed by nickel complexes (the dynamic kinetic resolution) can be represented by Scheme 11.⁸⁶

Scheme 11



Asymmetric induction can take place both in steps *A* and *B* (in both cases, the intermediates are asymmetric).

V. Asymmetric induction caused by nonbonded diastereomeric interactions

Solutions containing one enantiomer or a mixture of enantiomers (a racemate) may differ in physical properties. Thus the NMR spectra of the racemate differ from those of the optically active compounds comprising this racemate.^{87,88} Analogous effects were also observed in calorimetric studies. These effects are attributable to diastereomeric interactions between enantiomers in solutions.^{89,90}

The enthalpies of interactions of amide derivatives of L- and D-alanine as well as of dipeptides containing the terminal L- and D-alanine residues in aqueous solutions are given in Table 3.

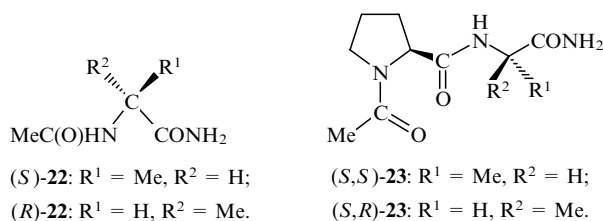
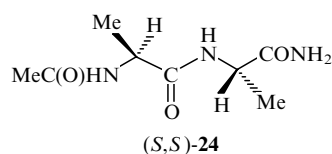


Table 3. Enthalpies of interactions of peptide fragments containing the terminal L- and D-alanine residues.⁹¹

Solution A	Solution B	$H_{AB} / \text{J kg mol}^{-2}$ (see ^a)
(<i>S</i>)- 22	(<i>S</i>)- 22	269 ± 5
(<i>R</i>)- 22	(<i>R</i>)- 22	277 ± 5
(<i>R</i>)- 22	(<i>S</i>)- 22	337 ± 10
(<i>S,S</i>)- 24	(<i>S</i>)- 22	488 ± 17
(<i>S,S</i>)- 24	(<i>R</i>)- 22	578 ± 9
(<i>S,S</i>)- 23	(<i>S</i>)- 22	769 ± 49
(<i>S,S</i>)- 23	(<i>R</i>)- 22	748 ± 16
(<i>S,R</i>)- 23	(<i>S</i>)- 22	803 ± 22
(<i>S,S</i>)- 23	(<i>S,S</i>)- 23	1629 ± 24
(<i>S,R</i>)- 23	(<i>S,R</i>)- 23	1399 ± 8
(<i>S,S</i>)- 23	(<i>S,R</i>)- 23	1515 ± 43

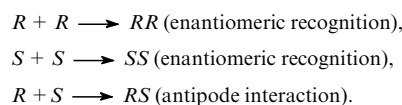
^a This dimension was used by the authors of the cited study.⁹¹



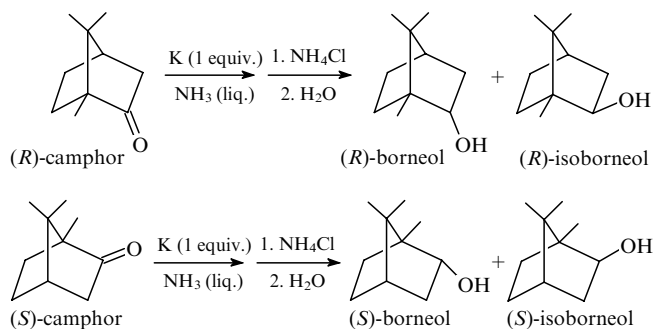
The observed differences in *H* are indicative of the presence of nonbonded interactions between enantiomers in solutions, such as monomer–monomer, monomer–dimer and dimer–dimer containing the terminal L- and D-alanine residues.⁹¹

An impressive example of the separation of an enantiomer and a racemate by fractional distillation was reported.⁹² It appeared that the boiling point of the racemate of trifluorolactic acid differs from that of its enantiomers. This is indicative of the presence of strong nonbonded diastereomeric interactions. However, this effect was not observed for the ester of lactic acid. The differences in the physical properties of enantiomers and the racemate in solutions are generally rather small,[†] but they are sufficiently large for these substrates to exhibit different chemical activities.⁹⁴

The following general principle was stated: the reaction rate for a chiral compound and the ratio of the resulting products depend, among other things, on the enantiomeric composition of the starting compound.⁹⁵ The following reactions can be distinguished:



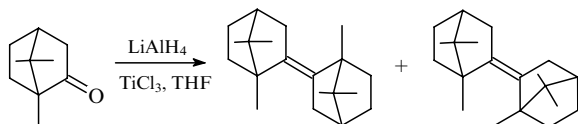
Below examples are given of reactions where one of the nonbonded interactions (or all these interactions taken together) leads to different compositions of the products.



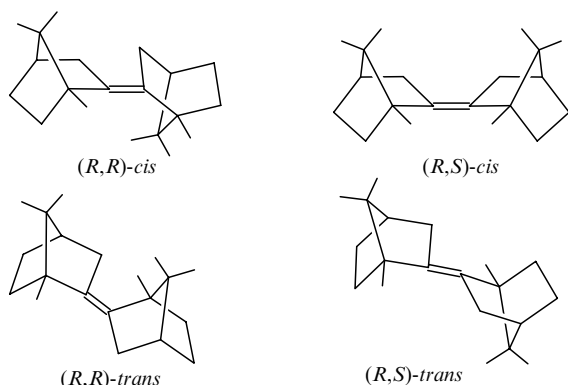
[†] Differences in the physical properties of the enantiomers and the racemate in crystals have long been known and were described in handbooks (for example, see Ref. 93). These differences are due primarily to the differences in the molecular packings in the crystals.

If (*R*)- or (*S*)-camphor was used as the starting substrate, the excess of borneol in the resulting mixture was insignificant. However, the reaction starting from racemic camphor afforded borneol as the major product.⁹⁶ In contrast, reduction of (*R*)-camphor with LiAlH_4 gave rise predominantly to isoborneol, whereas borneol was obtained as the minor product (90.2% and 9.8%, respectively).^{95,97} A somewhat different composition of the mixture was obtained in the reaction starting from (*R,S*)-camphor (88.7% and 11.3%, respectively).

Reductive dimerisation of camphor

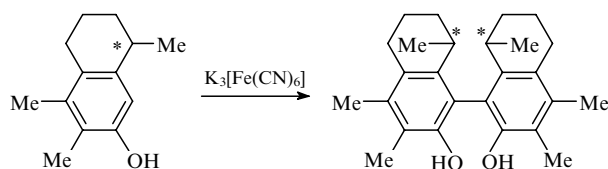


afforded a mixture of isomers

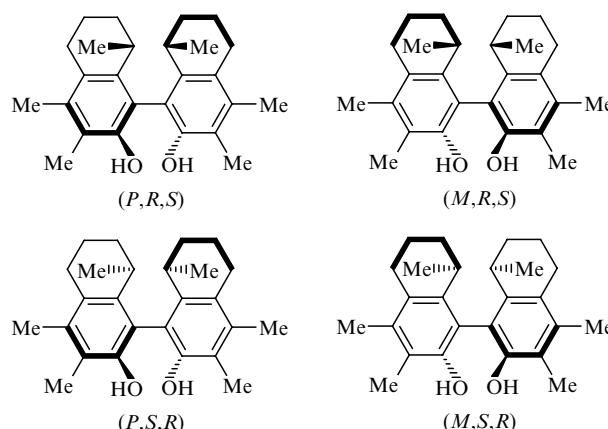
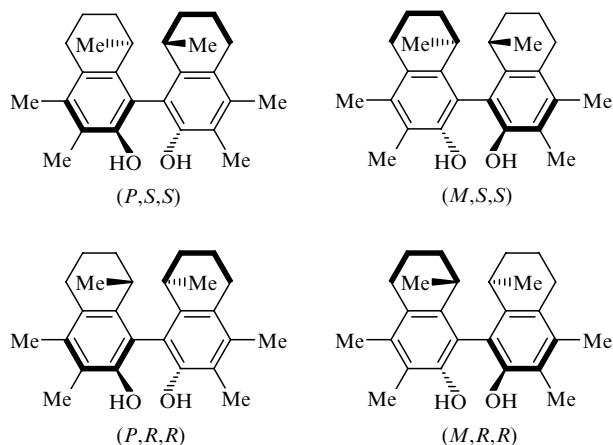


The reaction involving the (*R*)-monomers of camphor gave rise to the (*R,R*)-cis and (*R,R*)-trans dimers in a ratio of 34.8 : 65.2. In the product obtained from the racemate of camphor, (*R,S*)-cis [(*R,R,S,S*)-cis] and (*R,S*)-trans [(*R,R,S,S*)-trans] isomers were present in a ratio of 37.4 : 62.6.⁹⁵

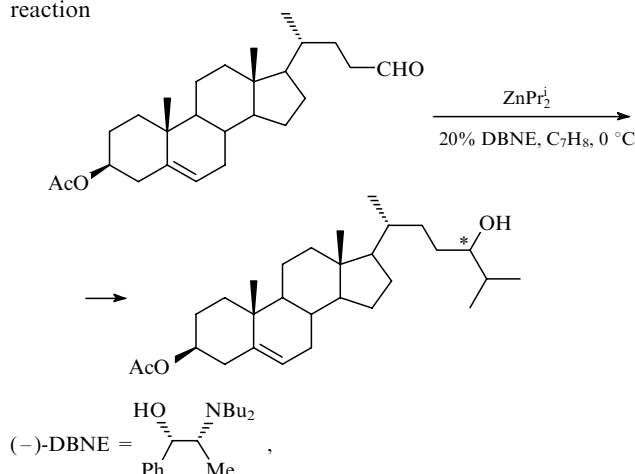
Oxidative dimerisation of the (*S*)-monomer of a phenol derivative



afforded the (*P,S,S*) and (*M,S,S*) diastereomers in a yield greater than 97.5%.⁹⁵ The racemic monomer can, in principle, give eight diastereomers:



However, dimerisation of this monomer produced a mixture of the (*P,S,S*), (*M,S,S*), (*P,R,R*) and (*M,R,R*) diastereomers (*trans* dimers) in 66% yield, whereas the theoretically possible yield is 50%. This inconsistency can be considered as an argument in favour of active interactions between the enantiomers. The reaction



catalysed by chiral aminoalcohol yielded a chiral compound bearing an asymmetric centre in the terminal fragment.⁹⁸ (-)-Aminoalcohol catalysed the formation of (*R*)-alcohol with the diastereomeric excess $de = 97\%$ independently of its enantiomeric purity (100% and 21%), whereas the (*S*) product with $de = 87\%$ was obtained in the presence of (+)-aminoalcohol ($ee = 100\%$). This result is attributable to nonbonded diastereomeric interactions between the chiral substrate and the aminoalcohol.

The non-linearity of the changes in the optical and enantiomeric purities, which was observed in some cases, is accounted for by similar reasons.

The effect of the non-linear dependence of the enantiomeric excess of the product on the enantiomeric (or diastereomeric in the case of a diastereomer) purity of the catalyst (the reagent) can be manifested in asymmetric catalysis⁹⁹ (in asymmetric synthesis and in stereoselective reactions¹⁰⁰) if a chiral catalyst (or a reagent) can form a dimeric diastereomeric complex with one of the reagents of the catalytic (or non-catalytic) reaction.

Possible dependences of the enantiomeric excess of the product on the enantiomeric excess of the catalyst (the reagent) are shown in Fig. 5. A wide range of such reactions is presently known.^{99,100} These effects are attributed to the differences in the reactivity of homochiral and heterochiral dimeric complexes.

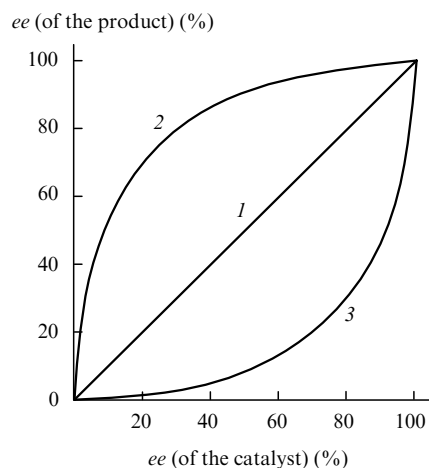
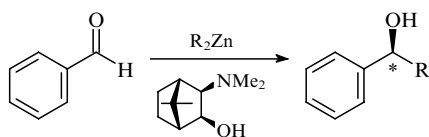
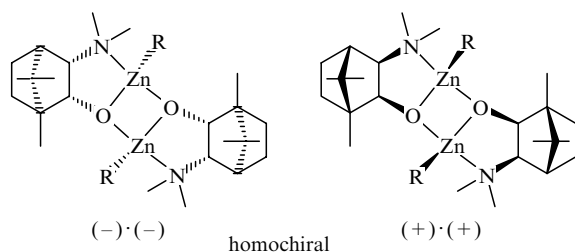


Figure 5. Possible deviations from the linear dependence of *ee* of the product on *ee* of the catalyst. (1) the linear dependence, (2) the positive non-linear effect, (3) the negative non-linear effect.

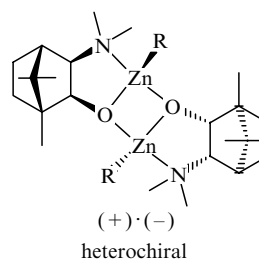
For example, in the reaction



the homochiral (–)·(–) dimer



is 1200 times more active than the heterochiral dimer,



which gives rise to the positive non-linear effect.^{101–103}

VI. Conclusion

Recent investigations demonstrated that the enantioselectivity of some metal-complex catalysts approaches 100%. Ligands for complexes, which ensure the record-breaking enantiomeric purity of the products in various reactions, are given in Table 4. All the listed ligands are conformationally rigid and possess a pronounced helical component bearing bulky groups at the ends of an incomplete helical turn.⁶

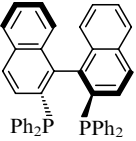
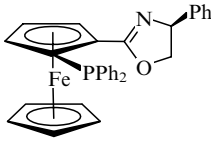
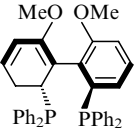
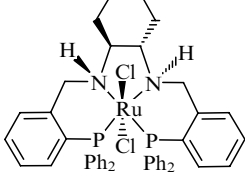
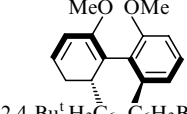
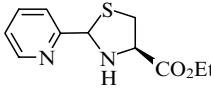
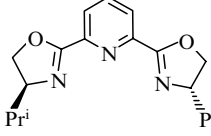
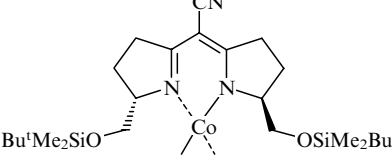
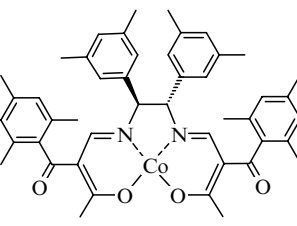
The investigation into the mechanism of hydrogenation of enamides in the presence of one of such complexes (the octahedral asymmetric rhodium dihydride complex containing the BisP* ligand) demonstrated that asymmetric induction takes place in the stage of substrate coordination by the complex. The high enantioselectivity of this catalytic reaction (99.9%) is determined by the 99.95% probability of the coordination of enamide by one side {the *Re*-side in the case of the Rh[(*S,S*)-BisP*] complex}.¹⁰⁶ This is indicative of a large difference between the free activation energies of substrate coordination through the favourable and unfavourable sides. The probability of the substrate being coordinated through a particular side is, evidently, determined by the helical component of the conformationally rigid ligand of the complex bearing bulky groups at the ends of the incomplete turn of the helix.

As an alternative mechanism for improving the diastereomeric purity of an adduct of a dihydride complex with enamide, intramolecular isomerisation is less probable due to the high reactivity (short lifetime) of this intermediate (such an isomerisation is more likely in the case of an adduct of the starting complex with the substrate,⁶⁶ which is not involved in the catalytic cycle³⁴).

Table 4. Ligands involved in catalytic complexes, which are used in various reactions.

Ligand, complex	<i>ee</i> (%)	Ref.	Ligand, complex	<i>ee</i> (%)	Ref.
Hydrogenation of enamides catalysed by rhodium complexes			Hydrogenation of enamides catalysed by rhodium complexes		
	98–100	20, 81		99.9	107
	99	104		98.1	108
	100	105		99.8	108
	> 99.9	106			

Table 4 (continued).

Ligand, complex	ee (%)	Ref.	Ligand, complex	ee (%)	Ref.
Hydrogenation of ketones, ketoesters and aminoketones catalysed by ruthenium complexes			Hydrogen-transfer hydrogenation of ketones catalysed by ruthenium complexes		
	99–100	109, 110		97	114
	98	111		97	115
	97.8	112	Hydrosilylation of ketones catalysed by rhodium complexes		
2,4-Bu ₂ H ₃ C ₆ C ₆ H ₃ Bu ₂ -2,4				98	116
Reduction of enamides and imines catalysed by cobalt complexes				95	117, 118
	98.9	40, 47			
	98	113			

The relationship between the sense of the helical component of a ligand in a rhodium complex involved in hydrogenation of enamides and the configuration of the product⁶ either results from asymmetric induction taking place in the stage of substrate coordination or is a consequence of an alternative mechanism, which is most likely common to the overall series of reactions in which this regularity is observed.

The available experimental data indicate that the reactions proceeding under the action of chiral C₂-symmetric metal-complex catalysts generate the asymmetric carbon atom in the product in a step involving an asymmetric intermediate. Apparently, the Curie–Pasteur principle, which states that there is ‘no asymmetry without asymmetry’, has a literal sense.

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Controlled synthesis of stereoblock polypropylene. New trends in the development of elastomers

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Abstract. The review generalises published data on the synthesis of elastomeric stereoblock polypropylene, a representative of thermoplastics, which are prepared by random or block copolymerisation of various co-monomers and are widely used in the manufacture of diverse mechanical rubber goods. New unique applications of metallocene and post-metallocene catalysts in the design of polyolefin elastomers with a broad spectrum of physico-mechanical characteristics are discussed. Particular attention is given to modern homogeneous catalyst systems based on Group IVB element metallocene complexes, which ensure highly efficient synthesis of polypropylene elastomers with various stereoblock structures. Data on the specific features of the structure and properties of the elastomeric stereoblock polypropylene are analysed. The bibliography includes 160 references.

I. Introduction

Homo- and copolymers of α -olefins currently rank as one of the most important industrial polymeric materials. The world manufacture of polyolefins such as high-density polyethylene (HDPE), linear low-density polyethylene (LLDPE), and isotactic polypropylene (IPP), estimated as tens million tons a year, constantly increases and now it accounts for more than 50% of the output of all manufactured plastics.¹ Expansion of the production of these materials was promoted by the discovery of metal complex Ziegler–Natta catalysts with high activity and regio- and stereospecificity.^{2–4} At present, industrial processes, mainly, the synthesis of IPP, make use of fourth-generation heterogeneous Ziegler–Natta catalysts containing TiCl_4 , $\delta\text{-MgCl}_2$, Et_3Al , and modifying additives.^{5–7} Due to replication (the reproduction of the shape of a catalyst particle by the growing polymer particle), the catalysts used ensure the formation of spherical polymer particles with specified size and porosity.

The range and the fields of application of homo- and copolymers of α -olefins are constantly extending. The consumption of

binary ethylene–propylene and ternary ethylene–propylene–diene copolymers permanently increases.^{1, 8, 9} The production volume of these materials exceeds a million tons a year. The industrial synthesis is performed most often using vanadium metal complex systems.^{10, 11} Highly effective two-stage processes for the production of heterophase copolymers based on IPP (1st stage) and ethylene–propylene copolymers (2nd stage)¹ are widely used in industry. By controlling the fraction and the composition of the copolymer and the molecular masses of polypropylene (PP) and the copolymer, one can obtain materials with enhanced elasticity and impact strength, thermoplastic polyolefins (TPO) and thermoplastic elastomers (TPE).^{2–6}

A special position among polyolefins is held by elastomers. They are usually prepared by statistic or block copolymerisation of various co-monomers. Elastomers are capable of being rapidly stretched and contracted; they exhibit high strength and high modulus of elasticity in the stretched state and return to the initial size as the load has been removed. The elastic properties of these materials are due to the formation of chemical or physical networks. The physical network junctions can be represented by crystalline regions joined by the transient chains of the amorphous polymer (Fig. 1). The fractions of amorphous and crystalline phase, the average size, the size distribution, the shape of crystallites, the network density, the possibility of changing the network structure under the action of load and several other factors determine the properties of elastomeric materials.

In the last two decades, the discovery of new highly effective homogeneous systems based on metallocene complexes of Group

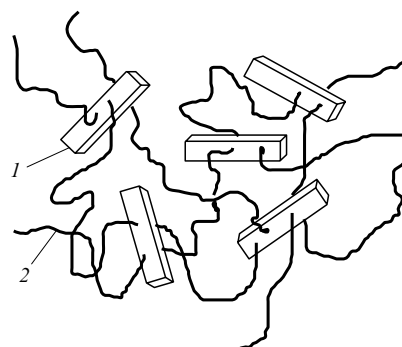


Figure 1. Schematic representation of the microstructure of elastomeric stereoblock polypropylene.

(1) Crystallites formed by isotactic blocks; (2) amorphous sections consisting of irregular blocks.

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IVB elements activated by poly(methylaluminoxane) (MAO) or by other compounds opened up new opportunities for the development of polymer technologies and for extension of the range and applications of homo- and copolymers of α -olefins. Various aspects of metallocene and post-metallocene catalysis of olefin polymerisation have been covered in monographs, special editions and reviews.^{12–20} Due to the uniformity of active centres, these catalysts make it possible to produce polymers with a narrow molecular mass distribution (MMD) and copolymers with a homogeneous composition. The narrow molecular mass distribution and structural and compositional uniformity result in enhanced mechanical strength, impact strength and clarity of materials and determine specific properties of homo- and copolymers. The successive or simultaneous conduction of polymerisation in the presence of a mixture of complexes having different structures ensures the synthesis of polymers with bi- or polymodal MMD and with a controllable composition.

When metallocene catalysts are used, the differences between the reactivities of ethylene, propylene, higher α -olefins and a number of other monomers are much less pronounced²¹ than in the case of heterogeneous or vanadium systems.²² By varying the composition, structure and the type of symmetry of metallocenes, one can control the stereospecificity of metallocene systems and prepare PP and higher poly- α -olefins with various microstructures. The use of metallocene systems not only ensures the formation of PP having different stereochemical compositions (iso-, syndio-, hemicis- and atactic polymers) at satisfactory rates but also extends the range of applicable monomers (for example, cycloolefins and polar monomers can be involved in reactions). A large number of new materials are currently produced in industry by metallocene-catalysed processes.^{23,24}

Metallocene catalysts also open up the way for the preparation of new polymers with diverse stereo- and regiochemical structures, in particular, synthetic blends of various PP, or for the selective synthesis of stereoblock PP (SBPP). The SBPP macromolecules either consist of alternating stereoblocks with different structures or have a uniform structure separated into blocks by regularly arising ‘errors’.

If the length of the co-crystallised stereoregular sequences (i) is relatively short, for example, $i \leq 10–12$ (Fig. 2 *a–d*), and the molecular mass of the polymer is high, the polymer exhibits elastomeric properties. The interest in the production of elastomeric stereoblock polypropylene (eSBPP) is caused by the fact that this is a way of one-pot synthesis of TPE from a single monomer, which has obvious advantages over the processes that require the use of at least two monomers. Due to the specific properties of metallocene catalyst systems and the possibilities they provide, the number of papers and patents devoted to various processes of eSBPP synthesis has substantially increased during the last five years. Quite recently, the range of PP-based elastomeric materials, presented in Fig. 2 and considered in this review, was extended by elastomeric PP (ePP), which is branched atactic PP with short regular, ordered (isotactic or syndiotactic) side chains.²⁵ These branches are organised in well dispersed crystal-

line domains connected by amorphous sections of the backbone, their presence preventing ‘sliding’ of the atactic chains under load, which is typical of atactic PP. Investigations by a number of companies aimed at the development of eSBPP-based materials which could replace plasticised PVC, and some other expensive elastomers are in progress, and this is largely related to the possibility of designing macromolecules in the presence of metallocene catalyst systems.^{25,26}

The present review surveys data on the influence of the structure of catalysts and conditions of synthesis of polypropylene on the activity of catalyst systems and the structure of eSBPP; the relationship between the structure and properties (strain, relaxation, thermal, *etc.*) of the SBPP produced. The attention is focused on the homogeneous catalyst systems based on metallocene complexes of Group IVB elements.

II. Catalyst systems for the synthesis of elastomeric stereoblock polypropylene

This section considers views on the mechanism of catalytic and stereospecific action of metal-complex catalysts and on the development of methods for the analysis of polymer microstructure and its relationship with the properties of catalysts; it describes the history of the discovery of eSBPP and the development of heterogeneous catalysts and highly effective homogeneous catalyst systems for the synthesis of eSBPP.

1. Characteristics of the mechanisms of catalytic and stereospecific action of metal complex catalysts

Elucidation of the mechanisms of catalytic and stereocontrolling action of catalysts is very significant for the target-directed and controlled synthesis of polyolefins. Research into the mechanism of action of Ziegler–Natta metal complex catalysts of polymerisation is the subject of a number of monographs and reviews.^{12,13–17,20,27}

The currently accepted mechanism of formation of an active centre (AC) based on Shilov’s and Dyachkovskii’s concept²⁸ includes the steps of coordination of catalyst components, alkylation and ionisation of a transition metal compound to give a coordinatively unsaturated cation containing an active metal–carbon bond. These views have been further developed after the discovery of highly effective homogeneous catalyst systems based on metallocenes in combination with MAO or weakly coordinating anions such as $B-(C_6F_5)_4$.^{13–20,24} The mechanism of action of the specific activating agents for metallocene systems is extensively studied.

Several alternative mechanisms of chain growth are described in the literature, namely, the coordinate-anionic mechanism, direct insertion of the monomer into the active metal–carbon bond and migration mechanism. On the basis of the results of recent investigations into propylene polymerisation catalysed by homogeneous syndio- and hemicispecific metallocene catalysts, preference is given to the migration mechanism. According to this mechanism, growth of the polymer chain occurs through its migration to the coordinated monomer and insertion of the monomer. The next monomer molecule is coordinated to the newly appeared vacancy, and migration of the polymer chain and insertion are repeated; thus, after each monomer insertion event, the growing polymer chain and the coordination vacancy exchange places (the Cossee mechanism). This mechanism also assumes the possibility of chain migration to the initial position without monomer insertion with retention of the AC geometry (the Cossee–Arlman mechanism). The symmetry of the AC and the ratio between the rates of the ‘monomer insertion–chain migration’ and ‘chain migration without monomer insertion’ processes largely determine the polymer microstructure.

In terms of the two-step mechanism of chain growth, the stereocontrol can take place both at the coordination step and during monomer insertion into the metal–carbon active bond.^{29–33} The insertion of the first monomer is usually not

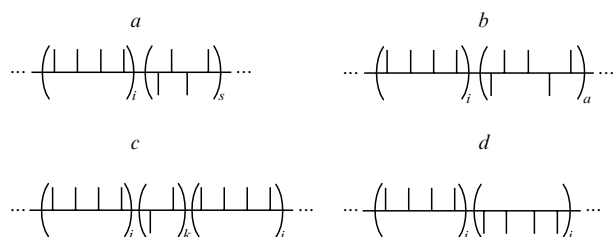


Figure 2. Schematic views of various types of SBPP.

(*a*) Alternation of isotactic and syndiotactic blocks; (*b*) alternation of isotactic and atactic blocks; (*c*) isotactic blocks with a correcting ‘error’; (*d*) isotactic blocks with an extending ‘error’.

stereospecific.³¹ Stereocontrol is enhanced as a result of cooperative action of the AC, the ligand and the growing polymer chain. The views on the mechanism of stereocontrol by metal complex heterogeneous catalysts is based on the detailed investigation of the polymer microstructure and the properties of separate polymer fractions.

In conformity with the Bovey statistics,^{34,35} a polymer chain is regarded as a sequence of isotactic dyads characterised by identical arrangements of methyl groups relative to the plane of the carbon chain of the macromolecule (*m*-dyads) and syndiotactic dyads in which the methyl groups of propylene are located on different sides of this plane (*r*-dyads). Methods for determination of the contents of *m*- and *r*-dyads, triads (*mm*, *rr*, *mr*), tetrads (*mmm*, *rrr*, *mmr*, *rrm*), various pentads (iso — *mmmm*; syndio — *rrrr*, and hetero — *rmmr*, *mmrr*, *mrrr*, *rmrr*, *rrmr*, *mrmm*, *mrrm*, *mmrm*) and higher sequences (hexads, heptads, etc.) based on the use of high-resolution ¹³C NMR spectroscopy have been developed.^{12,13,17,29,33,36–38}

Analysis of the configuration statistics allows one to identify the stereocontrol mechanism. Two key mechanisms are possible according to which stereocontrol is determined either by the chirality of the catalytic site or by the last inserted monomeric unit in the growing polymer chain. Correspondingly, two simple statistical models have been developed to interpret the distribution of the stereosequences in the polymer, known as the enantiomorphic model and the Bernoullian model. According to the enantiomorphic model, high stereospecificity is attained when an accidental 'error' arising during the polymer chain growth is corrected in the next step. The following ratios hold in this case: *rr* : *mr* = 1 : 2 or *mmmr* : *mmrr* : *mrrm* = 2 : 2 : 1. When the stereocontrol is accomplished by the last incorporated unit of the polymer chain, $4[mm][rr][mr]^{-2} = 1$.³⁷

Methods for estimating the length of continuous isotactic sequences and the regiospecificity of catalyst systems have been developed. The degree of regiospecificity is normally determined from the ¹³C NMR spectra of polymer solutions by analysing the proportion of abnormal patterns of monomer addition (2,1- or 1,3- instead of the 1,2-addition). Depending on the type of system and polymerisation conditions, the frequency of abnormal addition patterns can vary from fractions of a percent to tens of percent.^{29,33}

The fraction of isotactic sequences with different numbers of monomer units and the pentad composition of the polymer can vary over a broad range, depending on the stereocontrol capacity of catalyst systems, while in the case of stereoblock polymers, it is determined by the content of monomer units in regular and atactic sequences. The formation of stereoblock fractions with the use of heterogeneous catalyst systems is usually explained by the presence of highly coordinatively unsaturated AC the structure of which changes repeatedly over the period of polymer chain growth, for example, due to different ways of coordination of the cocatalyst and modifying additives. The microstructure of these materials is described using parametric models, in particular, the enantiomorphic model, the Bernoullian statistic model and the first- and second-order Markov chains.

In analysis of the mechanism of the stereocontrolling action of catalyst systems, the method of polymer fractionation by extraction with solvents having increasing boiling points is often used. The fractionation at rather high molecular masses (> 50 000 g mol⁻¹) is mainly determined by the stereoregular structure of polymer chains, while at lower molecular masses, it is determined simultaneously by the molecular mass and the microstructure.³⁹

When polymerisation takes place under the action of modern highly active titanium magnesium catalysts (TMC), the content of irregular fractions in the product reaches ~ 50%. However, the introduction of electron-donating modifiers, for example, dibutyl phthalate as an internal donor or various dialkoxysilanes as external donors, markedly increases the isospecificity of the systems. High isospecificity of TMC is also attained by using

2,2-substituted dialkoxypyrans as modifying additives.⁶ The isotactic fractions of polymers obtained with these catalysts are characterised by high contents of *mmmm* pentads (≥ 94%–98%).

The discovery of highly effective stereospecific homogeneous catalysts made it possible to establish the relationship between the metallocene structure, the nature of the ligands, the type of symmetry, the mechanism of polymerisation and the microstructure of the resulting PP.^{37,40,41} An advantage of homogeneous metal complex systems is the possibility of direct investigation of the AC nature by various physical methods. Ewen⁴² has formulated the symmetry rule which establishes the relationship between the structure of the initial catalyst and the microstructure of PP synthesised using this catalyst. Thus *ansa*-metallocenes of C₂ symmetry can ensure the synthesis of IPP with a content of *mmmm* pentads of up to 99%, those of C_s symmetry provide the synthesis of syndiotactic PP with up to 94% of *rrrr*-pentads, C_{2v} symmetry leads to atactic PP, and C₁ symmetry provides hemi-isotactic, isotactic or stereoblock PP depending on the type of π-bonded ligands and substituents in them. Catalysts with C₂ symmetry are characterised by homotopic, C_s, by enantiotopic, and C₁, by diastereotopic coordination positions of the olefin and the growing polymer chain. The knowledge of the mechanistic details of the stereo- and regiocontrol of the polymer gives a key to the rational design of homogeneous catalysts. By changing the metallocene structure, the type of symmetry, the ligands and substituents in the ligands and in bridges and by varying the conditions of polymerisation, one can control the microstructure, the molecular mass, and the terminal groups of polymers in the desired direction and produce materials with necessary properties. In the case of metallocene catalysts, unlike heterogeneous catalyst systems, polymerisation conditions (reaction temperature and monomer concentration) influence appreciably the stereo and regio structure of the resulting polymers.

2. Heterogeneous Ziegler–Natta catalyst systems for selective synthesis of elastomeric stereoblock polypropylene

It was found in the first of Natta's studies that PP formed in the presence of isospecific catalyst systems based on the layered violet modifications of α- or δ-TiCl₃ and Et₃Al (or Et₂AlCl) as a cocatalyst contains ~ 80 mass % of the major substance, isotactic crystalline PP insoluble in boiling n-heptane,^{43,44} ~ 5% of amorphous low-molecular-mass atactic PP soluble in ether, and ~ 15% of an intermediate fraction soluble in boiling n-heptane. It was shown that fractions with degrees of crystallinity of 15%–30% and an intrinsic viscosity of ~ 1 dl g⁻¹, unlike isotactic fractions, exhibit 'stress–strain' curves typical of elastomers, namely, a low initial modulus of elasticity, its substantial decrease upon stretching to 200%–300% and an increase in the modulus and strength upon further stretching (Fig. 3). A number of other properties typical of elastomers have been noted. A stereoblock structure has been proposed for this polymer.^{43,44}

In 1982, the synthesis of high-molecular-mass elSBPP induced by tetraalkyl or tetraaryl derivatives of titanium, zirconium and

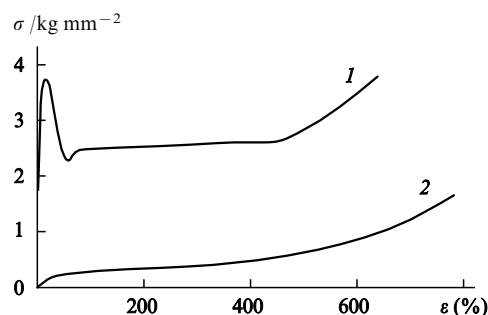


Figure 3. Stress (σ)–strain (ϵ) curves for highly isotactic (1) and stereoblock (2) fractions of PP.⁴³

Table 1. Polymerisation of propylene catalysed by Collette catalyst systems (liquid propylene, 50 °C, 1 h).^{45–47}

Row	Catalyst	[Cat.] (see ^a)	<i>A</i> (see ^b)	10 ^{−3} <i>M</i> _n (see ^c)	<i>D</i> ₉₉₃ / <i>D</i> ₉₇₅ (see ^d)	<i>T</i> _m /°C (see ^e)	<i>C</i> (%) (see ^f)	<i>F</i> _{Et₂O} (%) (see ^g)
1	ZrBn ₄	0.3	0.08	2450	0.40	148	7	—
2	ZrBn ₄ (see ^h)	0.4	0.17	520	0.53	155	23	41
3	Zr(C ₅ H ₅ CM ₂) ₄	0.5	0.15	1430	0.57	153	27	—
4	Zr(C ₅ H ₅ CM ₂) ₄ (see ^h)	0.2	0.53	376	0.46	149	11	54
5	Zr(C ₅ H ₅ CM ₂) ₄ (see ^h)	0.6	0.12	456	0.55	155	24	42
6	Zr(C ₅ H ₅ CM ₂) ₄ (see ^{h,i})	0.2	0.59	395	0.56	156	27	—
7	Zr(Bu ⁱ CH ₂) ₄	0.2	0.23	2737	0.30	144	9	—
8	Zr(Bu ⁱ CH ₂) ₄	0.6	0.12	2016	0.52	153	20	—
9	TiBn ₄ (see ^h)	0.2	0.18	1163	0.53	150	29	37
10	TiBn ₄ (see ^j)	0.2	0.29	1287	0.56	153	20	—

^a Catalyst loading expressed in mmol (g Al₂O₃)^{−1}. ^b Catalyst activity expressed in kg of PP (mmol M)^{−1} h^{−1}, where M is a transition metal. ^c Viscosity-average molecular mass (in g mol^{−1}) calculated from the intrinsic viscosities (taken from Ref. 46) using the Mark–Houwink equation with the parameters $K = 1.58 \times 10^{-4}$, $\alpha = 0.77$. ^d Macroscopic index of polymer samples determined from the intensities of the absorption bands at 993 and 975 cm^{−1} in the IR spectra. ^e Melting temperature. ^f Degree of crystallinity calculated from the heats of melting (taken from Ref. 46): $C = (\Delta H_m/209) \times 100$, where ΔH_m is the heats of melting (in J g^{−1}), 209 J g^{−1} is the specific heat of melting of crystalline polypropylene. ^g Content of the fraction soluble in diethyl ether. ^h During polymerisation, hydrogen was introduced (~3 atm). ⁱ Polymerisation was carried out with the addition of triisobutylaluminium (TIBA), Al:Zr = 1. ^j The catalyst was preliminarily hydrogenated for 20 min at 25 °C.

hafnium immobilised on Al₂O₃ [with a specific surface area (*S*_{sp}) of 100–150 m² g^{−1}] has been patented.⁴⁵ These catalyst systems allow the preparation of high-molecular-mass PP (with an intrinsic viscosity of 1.5–13.0 dl g^{−1}) with low or moderate degrees of crystallinity (5%–30%) and high melting points (135–155 °C).^{46,47} The glass transition temperature (*T*_g) of the polymers varies from −7 to −10 °C. The content of fractions soluble in ether and heptane ranges from 30% to 50%, depending on the catalyst and polymerisation conditions. The polydispersity coefficients of the polymer samples also vary over wide limits, $M_w : M_n = 6–23$ (M_w and M_n are the weight average and number average molecular masses of the polymer, respectively).

The influence of the nature of the transition metal, the ligands attached to it and polymerisation conditions on the activity and properties of the resulting polymer is illustrated by the data of Table 1.^{45–47} Zirconium complexes with bulky ligands (neopentyl or neophyl) lead to the formation of PP with a higher degree of isotacticity than ZrBn₄ (see Table 1, rows 8, 3, 1). The stereospecificity of tetranephyl and tetranepentyl complexes of zirconium depends appreciably on the concentration of the supported catalyst. An increase in the content of the complex on the support (correspondingly, an increase in the Zr:Al ratio) is accompanied by an increase in the isotacticity of the resulting polymer and simultaneous decrease in the catalyst activity (see, for example, rows 4, 5 and 7, 8).

When the zirconium complex is pre-hydrogenated, or polymerisation is conducted in the presence of hydrogen (to control the molecular mass of polymers), the catalyst activity substantially increases and the crystallinity of the resulting polymer decreases due to the increase in the content of the elastomer fraction. It should be noted that upon the addition of stoichiometric amounts of triisobutylaluminium or diisobutylaluminium hydride, the crystallinity of polymers markedly increases (see Table 1, rows 6, 4). Titanium complexes are more active than zirconium complexes. In the presence of hydrogen, the activity of titanium complexes decreases by about 20% and becomes comparable with the activity of zirconium complexes under similar conditions. The molecular mass of PP obtained under the action of titanium complexes is much higher. The crystallinity of polymers synthesised using titanium complexes in the presence of hydrogen is relatively high (see Table 1, rows 9, 10).

To characterise the elastomeric properties of polymers, most researchers use either the recovery or the residual elongation, which are determined by the following relations

$$\frac{l_{\max} - l_1}{l_{\max} - l_0} \cdot 100\% \quad \text{or} \quad \frac{l_1 - l_0}{l_0} \cdot 100\%,$$

where $l_{\max}$ is the maximum elongation, l_1 is the sample length after relaxation, l_0 is the length of the initial sample.

The results of mechanical tests of samples of elastomeric PP obtained in the studies by Collette are presented in Fig. 4. It can be seen that the polymers synthesised possess good elastomeric properties. Upon stretching by 300%, the residual elongation is 93%. However, it was found that mechanical compositions obtained by blending the high-molecular-mass fraction soluble in ether with the fraction insoluble in hexane exhibit similar properties (see Fig. 4, dashed lines). After blending for 10 min at 180 °C, the percentage of the ether-soluble fraction decreased from 69% to 37%.⁴⁶ It was concluded⁴⁶ that the key role is played by the high-molecular-mass atactic fraction, which can be co-crystallised with a more stereoregular fraction to give cross-linked structures, and the following criterion was introduced: a catalyst effective for the formation of elSBPP should possess relatively low

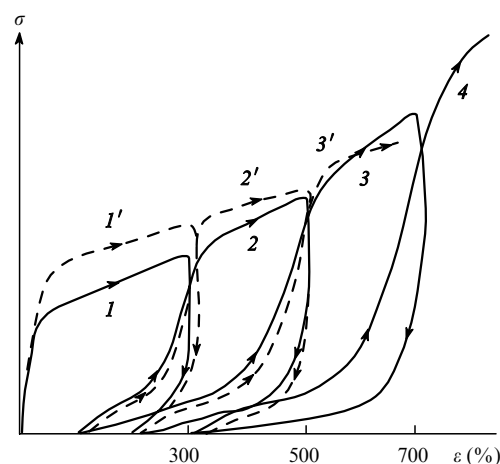


Figure 4. Hysteresis tests of elastomeric SBPP (1–4) and mechanical mixtures (1'–3') of ether-soluble ($M_n = 284\,000$ g mol^{−1}) and hexane-insoluble ($M_n = 1\,478\,000$ g mol^{−1}) fractions.⁴⁶ The rate of sample drawing and unloading is 51 cm min^{−1}. Draw ratio (%): (1, 1') 300; (2, 2') 500; (3, 3') 700; (4) 820.

stereospecificity and ensure the production of a high-molecular-weight polymer.

Later, Job⁴⁸ developed modified heterogeneous titanium magnesium catalysts for the synthesis of stereoblock ePP. The catalysts were prepared by the reaction of TiCl_4 with $\text{Mg}(\text{OAlk})_2$ in the presence of electron-donating substances (dialkyl phthalates) and activated by an organoaluminium compound with addition of a reagent to control stereoselectivity (heterocyclic aromatic nitrogen-containing compounds: 2,6-lutidine or pyrazine). In the absence of a nitrogen-containing modifying agent, these catalyst systems allow the synthesis of isotactic PP, while in the presence of this agent, stereoblock PP with short syndiotactic blocks is obtained. The specific activity (per g of the catalyst) of the TMC is 50–100 times as high as that of the Collette catalysts: $\sim 9 \text{ kg PP (g Cat.)}^{-1} \text{ h}^{-1}$ and $\sim 200 \text{ g PP (g Cat.)}^{-1} \text{ h}^{-1}$, respectively. The PP samples contained $\sim 50\%$ of isotactic pentads, the elongation at rupture reached 1000%, and the residual elongation after stretching to 300% was $\sim 70\%$ –85%.

It was shown^{49,50} that the use of heterogeneous vanadium systems, for example, VCl_3 together with TIBA, results in the formation of PP with an increased proportion of abnormal additions of the monomer (2,1- or 1,3- instead of the typical 1,2-addition) due to the lower stereo- and regioselectivity of vanadium systems. The resulting polymer possesses a number of properties typical of elastomeric PP, namely, low Young's modulus, the absence of yield point and high impact strength. In addition, it has a high frost resistance.

The elastomeric SBPP synthesised on heterogeneous catalyst systems has a broad MMD (Fig. 5) and can be separated into fractions by treatment with various solvents. The broadest MMD is observed for the most stereoregular fractions (see. Fig. 5). This property, common to heterogeneous catalyst systems, is a consequence of the multi-site nature of the AC formed in heterogeneous catalysts; it hampers the target-directed synthesis of polymers with specified characteristics.

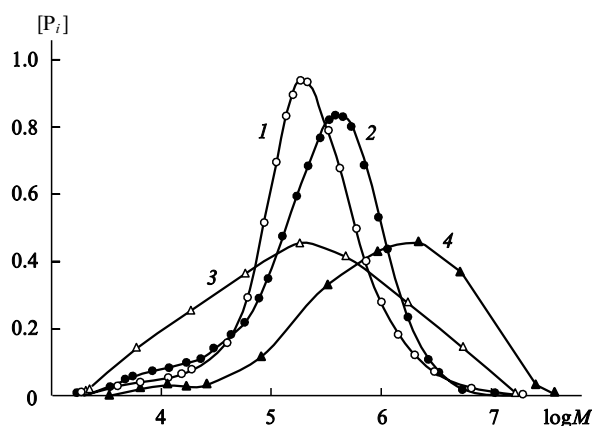


Figure 5. The molecular-mass distributions of the fractions of elSBPP prepared with the Collette catalysts (1,3,5-trichlorobenzene, 135 °C).⁴⁶ (1) elSBPP soluble in ether; (2) non-fractionated elSBPP; (3) elSBPP soluble in heptane; (4) elSBPP insoluble in hexane, $[P_i]$ is the proportion of the polymer fraction.

3. Metallocene catalysts for the synthesis of elastomeric polypropylene

The next generation of catalysts used for the synthesis of elSBPP are homogeneous catalyst systems based on metallocene complexes of Group IVB elements activated by MAO. Advantages of these systems include high activity and the possibility of obtaining

elSBPP as the only reaction product or as the predominant fraction. In addition, by selecting metallocenes and polymerisation conditions, one can control the microstructure of the growing polymer chain and change the molecular-mass characteristics of PP over wide limits.¹⁹

There are several types of homogeneous metallocene catalyst systems efficient in the synthesis of elSBPP, which differ in the mechanism of action. Since the AC structure, the stereocontrol mechanism and the properties of the resulting polymer are interrelated for these catalysts, it is expedient to consider various types of catalyst systems and the proposed mechanisms of polymerisation and to analyse the properties of the resulting elSBPP. It should be noted, however, that most of the mechanisms, although based on modern views and confirmed by some experimental results and model calculations, are still under discussion and require more detailed experimental evidence.

The main types of homogeneous catalyst systems for the synthesis of elSBPP include *ansa*-metallocenes with C_1 symmetry in the presence of the MAO cocatalyst; bisindenyl 2-aryl-substituted metallocenes in the presence of MAO; 'hybrid' metallocene systems in which metallocenes of several types are used simultaneously; alkylated bisindenyl 2-aryl-substituted metallocenes activated by TIBA, and post-metallocene catalyst systems.

a. *ansa*-Metallocenes with C_1 symmetry activated by polymethylaluminoxane

The synthesis of elSBPP with macromolecules consisting of alternating short stereoregular crystallisable and atactic sequences catalysed by MAO-activated asymmetric titanocenes **1** and **2** was first reported by Chien and coworkers.^{51–55} Under certain conditions, the reaction gave PP completely soluble in ether. For the polymer obtained at 25 °C, analysis of the density of amorphous and crystalline PP blocks⁵² made it possible to estimate the lengths of atactic and isotactic blocks; they were 50 and 20 monomer units, respectively. Propylene polymerisation catalysed by a series of structurally homogeneous metallocenes **3–7** in the presence of the MAO cocatalyst has also been studied.^{56–58} The catalytic properties of these systems, their dependence on the nature of the metallocene and on the polymerisation conditions and some characteristics of the resulting elSBPP samples are presented in Table 2.

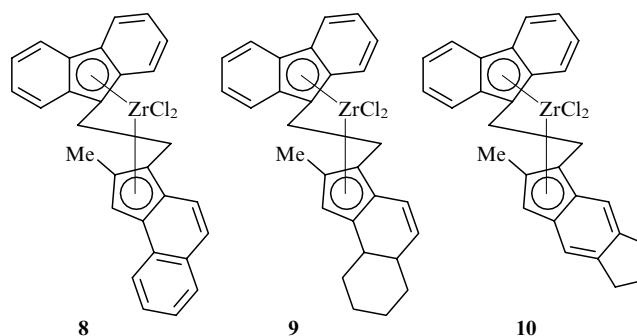
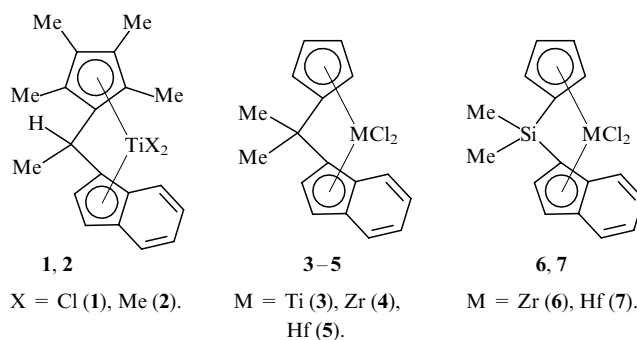
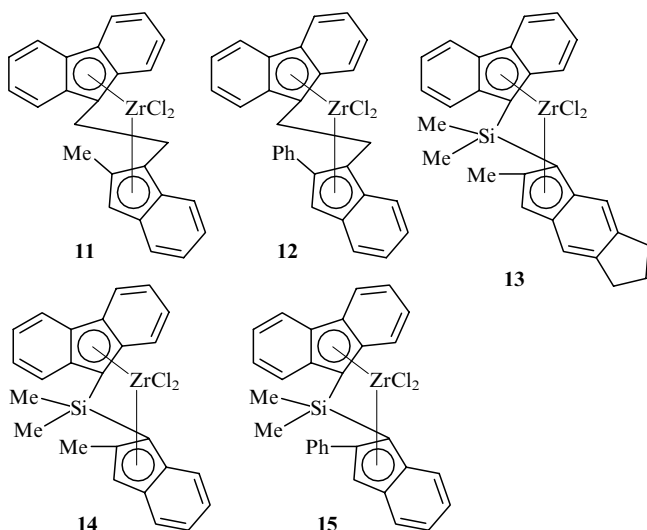


Table 2. Polymerisation of propylene induced by *ansa*-metallocenes with C_1 symmetry (MAO cocatalyst, Al: M = 2000),^{51–53, 56–59}

Row	Complex	$p_{C_3H_6}$ /atm	T_p /°C (see ^a)	A^b	$10^{-3} M_w$ /g mol ⁻¹	$M_w : M_n$	[<i>mmmm</i>] (%) (see ^c)	T_m /°C (see ^d)	<i>C</i> (%)
1	1	1.0	25	—	127	3.0	40	51/66	7
2	3	1.0	–25	0.001	—	—	72	—	—
3	3	see ^e	25	0.002	70	2.3	42	—	—
4	4	1.0	25	1.0	22	2.0	15	—	—
5	6	1.0	25	1.1	9	1.8	30	—	—
6	5	1.0	25	1.9	30	2.1	38	47/61	—
7	5	3.0	25	1.6	43	2.1	32	see ^f	—
8	5	3.0	0	0.01	75	2.1	30	see ^f	—
9	7	1.0	25	2.4	49	1.7	54	54/93	19
10	7	4.0	25	—	140	1.9	45	50/79	15
11	7	3.0	0	—	380	1.9	52	53/74	17
12	10	2.0	30	2.0	55	1.8	43	—	—
13	10	6.5	30	2.3	171	2.0	37	50	—
14	10	7.5	50	4.6	46	1.9	49	—	—
15	13	2.0	30	see ^g	103	1.8	62	—	—
16	13	8.5	30	see ^g	158	1.9	44	—	—
17	13	7.5	50	see ^g	85	1.9	67	—	—

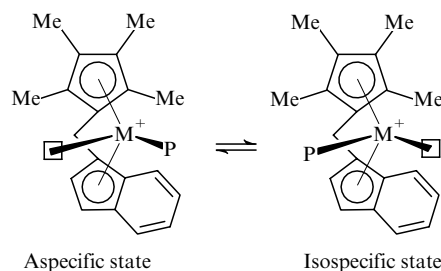
^a Polymerisation temperature. ^b Here and in Tables. 3, 7 and 8 the activity is expressed in kg PP (mmol M)⁻¹ [C₃H₆]⁻¹ h⁻¹, where M is a transition metal. ^c Content of isotactic pentads determined from the ¹³C NMR spectra. ^d Here and in Table 6, two T_m values are presented corresponding to two melting peaks observed in the DSC curves. ^e Polymerisation was carried out in the liquid monomer. ^f Amorphous polymer. ^g The sample is unstable.



Of the series of catalysts **1–7**, the hafnium complexes **5** and **7** are the most effective. They combine rather high activity and stability; they catalyse the formation of PP with fairly high molecular mass and good elastomeric and strength characteristics. An increase in the monomer concentration, all other conditions being the same, induces an increase in the molecular mass and some decrease in the content of isotactic pentads (see Table 2, rows 6, 8 and 9, 10). Note that in the presence of titanium metallocenes of this type, eSBPP is formed only in a narrow temperature range, 25 to 30 °C.⁵⁵ At –25 °C, the content of isotactic pentads reaches 72% (see Table 2, row 2). In addition, titanium complexes are much less stable than zirconium and hafnium analogs. Hafnium complexes give rise to PP with higher molecular masses than zirconocenes (see Table 2, rows 4, 6 and 5, 9); this is typical of metallocene catalysis. An unusual feature is that the activities of zirconocenes and hafnocenes are comparable. In the case of hafnium complexes, all other factors being the same, PP samples with higher degrees of isotacticity are formed (see Table 2, rows 4, 6 and 5, 9). The replacement of the propylidene bridging groups by dimethylsilylene groups results in an increase in the molecular mass and isotacticity of the PP (see Table 2, rows 6, 9; 7, 10 and 8, 11). An increase in the monomer concentration is

accompanied by a decrease in the isotacticity of the polymer for both hafnium and zirconium catalysts (see Table 2, rows 6, 7 and 9, 10), whereas an increase in the reaction temperature from 0 to 25 °C markedly decreases the isotacticity of the PP formed with the hafnium complex (see Table 2, rows 11, 10).

In a study of a stereoblock polymer prepared by anionic polymerisation of acrylates, an idea was put forward that two different states of the AC, aspecific (non-selective) and isospecific ones, may exist.⁶⁰ Subsequently, these views have been often used as the basis of the mechanisms of formation of stereoblock PP, in particular for the catalysts of C_1 symmetry.^{51–58} The key feature of asymmetric *ansa*-metallocenes is the presence of two inequivalent vacancies in the AC accessible for the monomer coordination and growth of the polymer chain. Usually, one vacancy is aspecific (non-selective) and the other one is isospecific. Chien and Collins explained the formation of a sequence of atactic and isotactic blocks in the presence of these catalysts in terms of models which take into account polymer chain growth in the active centre (the small square shows a coordination vacancy), whose stereospecific action changes as a result of slow (see Refs 51–55) or fast (see Refs 56–58) inversion (on the time scale of olefin coordination and addition), for example, due to migration of the polymer chain (P).



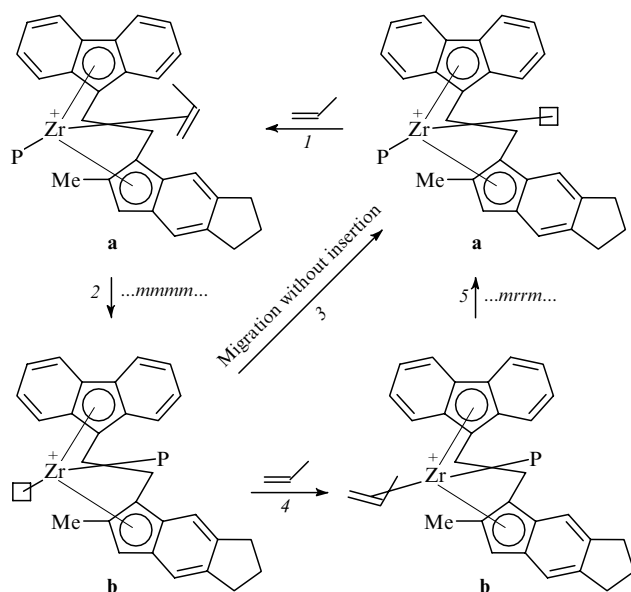
According to the Chien model, several steps of olefin coordination and insertion occur in turn in either of the active sites until its inversion takes place. However, within the framework of this model, it is difficult to explain the decrease in the content of the *mmmm* pentads following an increase in the monomer concentration on structurally similar Collins complexes. In conformity with the Collins model, the monomer is randomly coordinated

and inserted at the first or second accessible reactive active site. When two competing reactions are involved, namely, olefin insertion and chain isomerisation (migration without insertion), short isotactic sequences would regularly arise in the macromolecule; this would determine the elastomeric properties of the resulting PP; the length of these sequences would depend on the type of the coordination vacancies and the ratio of the chain growth rates in each site to the rate of active centre isomerisation. This model is also supported by the fact that hafnium complexes exhibit more pronounced stereocontrol action than the zirconium analogues, all other conditions being the same. The rate of polymer chain growth for hafnocenes is much lower than that for zirconocenes. Within the framework of this model, the replacement of zirconium by hafnium can result in a decrease in the ratio of the chain growth rate to the inversion rate.

A similar mechanism of the action of complexes with C_1 symmetry assuming the presence of two sites with different stereospecificities and competition between chain growth and migration without insertion (which also gives rise to elSBPP) has been proposed recently^{59,61} for a series of structurally rigid zirconocenes **8–15**.

A characteristic feature of these zirconocenes, as noted above, is 'stereoduality', i.e., the existence of two different coordination vacancies **a** and **b** (Scheme 1, small squares) in the cationic metal alkyl active site formed under the action of MAO.

Scheme 1



The non-selective coordination vacancy **b** is sterically less crowded than the isospecific vacancy **a**, and the processes of monomer coordination and chain migration to coordination vacancy **b** without insertion compete in the active centre. When the monomer concentration is low, chain migration without insertion can kinetically predominate. In this case, the reactions 'monomer insertion at vacancy **a** with chain migration (**a** → **b**) and subsequent chain migration without insertion (**b** → **a**)' will result in the formation of ...mmmm... sequences (see Scheme 1, cycle 1 → 2 → 3). When the monomer concentration increases, the probability of coordination and insertion at the sterically less hindered vacancy **b** becomes higher. The chain migration to the monomer that has added non-selectively gives rise to 'errors,' which are 'corrected' at the next step of monomer addition at vacancy **a**, and the...mrrm... sequences are thus formed (see Scheme 1, cycle 4 → 5 → 1). This type of polymer chain growth virtually excludes the propagation of 'errors' and, depending on the conditions, it can result in alternation of short isotactic sequences separated by single stereodeflects. Polypropylene formed by this mechanism is an isotactic macromolecule divided into short continuous isotac-

tic segments by regularly arising 'errors' (see Fig. 2 c, elSBPP with $k = 1$).

An increase in the polymerisation temperature and a decrease in the monomer concentration lead to a relative increase in the rate of chain migration without insertion and, correspondingly, to a higher content of isotactic pentads (see Table 2, rows 13, 14; 16, 17; 12, 13 and 15, 16). Conversely, an increase in the monomer concentration increases the probability of monomer insertion at coordination vacancy **b**, resulting in a decrease in isotacticity. It will be shown below that, in conformity with the proposed mechanism, the PP samples prepared with these catalyst systems are characterised by either the absence or low content of pentads of the ...mrrm... type with double 'errors'.⁶¹

It was also found for these types of catalyst systems that no 'errors' caused by isomerisation of the growing chain unit attached to the catalyst *via* β -hydride shift or the formation of allylic intermediates, typical of catalysts with C_2 symmetry,^{62–66} arise in this case. The absence of these reactions was confirmed experimentally by analysis of the pentad composition of the PP synthesised by polymerisation of $\text{CH}_2=\text{CDMe}$.⁵⁹

The catalysts of C_1 symmetry substituted at the 2-position make it possible to prepare PP with a very broad range of properties. Some parameters of the resulting polymers are presented in Table 2. An increase in the monomer concentration entails an increase in the molecular mass and a decrease in the content of isotactic pentads and in the degree of crystallinity of the polymer, while an increase in the reaction temperature is accompanied by lowering of the polymer molecular mass and an increase in the crystallinity. The best catalysts are 2-methyl-substituted complexes **8–10** with ethylene bridges because they exhibit high activity and ensure the formation of elSBPP with a relatively high molecular mass and a content of isotactic pentads at a level of 30%–50%.

These catalyst systems allow effective preparation of PP the properties of which vary over very broad limits, from those typical of highly crystalline rigid thermoplastics to those peculiar to low-crystallinity elastomers, which behave as viscous liquids under the action of load (Fig. 6). The samples combining high molecular mass ($\sim 200\,000\text{ g mol}^{-1}$) and moderate isotacticity ($[\text{mmmm}] = 30\%–40\%$) display good elastomeric and strength properties. The elongation at rupture for some samples reaches 1700%–2000%. However, a characteristic feature of elSBPP prepared on catalysts with C_1 symmetry is a relatively low melting

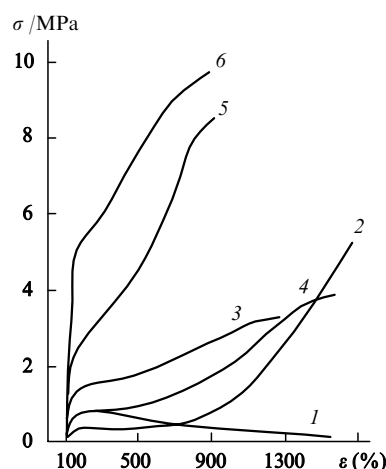


Figure 6. Drawing curves of PP samples prepared on the **10**–MAO catalyst system and exhibiting properties of viscoelastic (**1**), elastomeric (**2–4**) and stiff thermoplastics (**5, 6**).⁵⁹ M_w (g mol^{-1}): (**1**) 134 000; (**2**) 170 000; (**3**) 96 000; (**4**) 63 000; (**5**) 48 000; (**6**) 48 000.

$[\text{mmmm}]$ (%): (**1**) 20; (**2**) 37; (**3**) 38; (**4**) 37; (**5**) 60; (**6**) 57.

point.⁵⁹ This indicates the presence of a substantial number of regiodefects in the polymer chain.

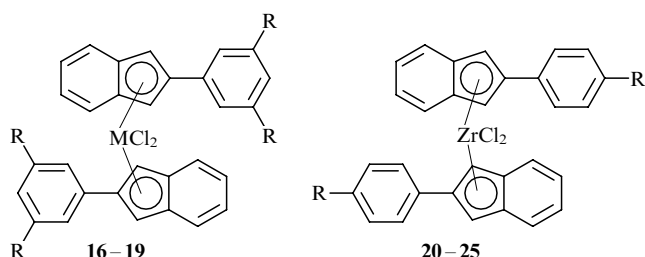
New metallocene complexes of C_1 symmetry for the synthesis of elastomeric PP have been described.²⁶ These *ansa*-metallocenes with strap-type $-(CH)_2-$ or $-(CH_2)_2-$ substituents at the 4- and 5-positions of the fluorenyl ligand possess high activity, 20–70 kg PP (g Cat.)⁻¹ h⁻¹ or 1–5 kg PP (mmol M)⁻¹ [C₃H₆]⁻¹ h⁻¹ (polymerisation in the liquid monomer medium); they provide the synthesis of PP with a molecular mass of 8×10^4 to 1.4×10^6 g mol⁻¹ and ensure very good elastomeric properties. Indeed, the residual elongation after stretching the sample by 300% is only 2.5%–10.0%. The greatest observed elongation of the sample reaches 5200%, the tensile strength is 0.8–2.5 MPa, and Young's modulus is 2.1–9.0 MPa. It has been assumed²⁶ that the unique properties of eSBPP prepared with these catalysts are determined by ultrasmall (nano-sized) crystallites which form the junctions of the polymer network.

A criterion of a 'good catalyst' of this new type for the synthesis of elastomeric PP has been proposed,²⁶ determined by the ratio between the parameters of the catalyst asymmetry (ratio of the van der Waals areas of the larger ligand and the smaller one) and parameters of stereoregularity of the synthesised PP (the ratio of *mm*- to *rr*-triads). The proportion of the *mmmm* pentads in the resulting polymers does not exceed 31%; however, unlike eSBPP formed in the presence of C_1 -symmetric catalysts considered above, these polymers contain substantial numbers of syndiotactic pentads ($[rrrr] \approx 28\%$).

b. The 'bis(2-substituted indenyl) metallocene – polymethylaluminoxane' catalyst systems

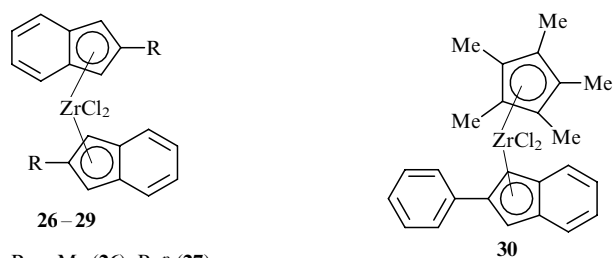
Bisindenyl metallocenes with aryl (**16–25**) and alkyl (**26–29**) substituents at the 2-position of the indenyl ring represent the most extensive and thoroughly studied class of metallocenes effective in the synthesis of eSBPP. In recent years, this series has been extended by zirconocenes with mixed hapto-bonded (**30–35**) and heterocyclic (**36–38**) ligands. Due to the intensive research, one can expect that new catalyst systems of this class effective in the synthesis of stereoblock PP would appear in the near future.

The 2-aryl-substituted dichloride complexes **16**, **19** were the first of the series of 'oscillating' metallocenes.^{67–72} Upon activation with MAO, these catalysts ensure the formation of stereoblock PP with high molecular masses.

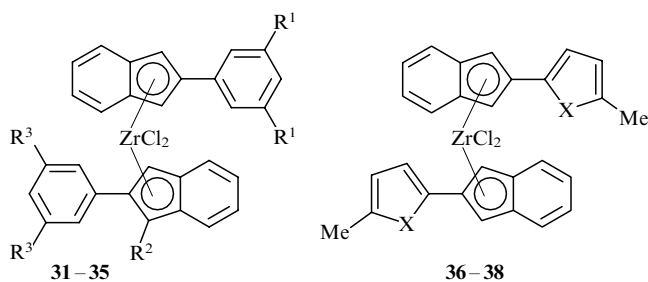


M = Zr: R = H (**16**), Me (**17**), CF₃ (**18**); M = Hf, R = H (**19**).

R = Me (**20**), Et (**21**), Buⁿ (**22**), SiMe₃ (**23**), CF₃ (**24**), Cl (**25**).



R = Me (**26**), Buⁿ (**27**), cyclo-C₆H₁₁ (**28**), Bn (**29**).



R¹ = R² = H, R³ = CF₃ (**31**);

R¹ = R³ = H, R² = Me (**32**);

R¹ = H, R² = Me, R³ = CF₃ (**33**);

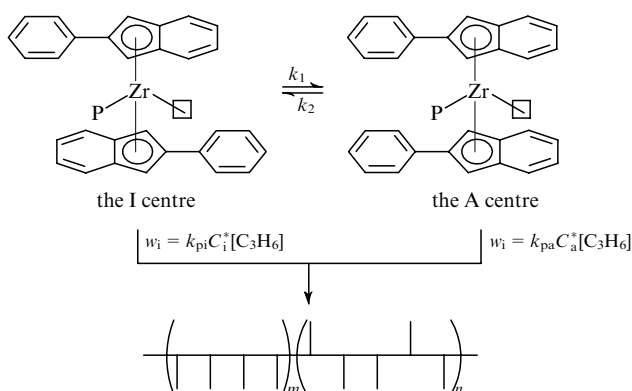
R¹ = CF₃, R² = H, R³ = Me (**34**);

R¹ = R³ = CF₃, R² = Me (**35**).

X = O (**36**), S (**37**), NMe (**38**).

X-Ray diffraction studies^{67, 73–75} showed that both the zirconocene **16** and the hafnocene **19** exist as two rotation isomers relative to the metal–hapto-ligand bond in the crystal unit cell. This attests to the energetic equivalence of both forms. This fact served as a pre-requisite for the proposed⁶⁷ 'oscillation' mechanism of the formation of stereoblock PP on catalysts of this type (Scheme 2, where the I and A stand for the isospecific and aspecific centres, respectively, k_{pi} and k_{pa} are the rate constants for polymerisation at the I and A centres, C_i^* and C_a^* are the concentrations of the I and A centres; and w_i and w_a are the rates of chain growth at the I and A centres, respectively).

Scheme 2



It was assumed that during polymerisation, the active cationic alkyl metal complex retains the ability to undergo barrier-free rotation. During the growth of the polymer chain, reversible isomerisation of the complex from the isospecific *rac*-form to the aspecific *meso*-form takes place repeatedly. The insertion of propylene during the period of existence of the *rac*-form of the active centre (the I centre) gives rise to isotactic sequences. On the *meso*-form of AC (the A centre), propylene insertion yields atactic blocks. To obtain the stereoblock structure of the polymer, it is necessary that the isomerisation rate be lower than the rate of olefin insertion but higher than the chain growth rate. Thus, chain growth on the 'oscillating' type AC gives macromolecules of the stereoblock structure. The length of the isotactic sequences is usually rather small and the stereoblock PP synthesised under the action of these metallocenes is distinguished by a low degree of crystallinity with a rather high molecular mass.

For a large number of complexes of this type, the influence of polymerisation conditions on the catalyst activity and characteristics of the resulting polymers (microstructure and fractional composition, molecular mass, MMD, elasticity) has been studied.^{67, 70, 72, 73, 76–78} Typical properties of catalyst systems and eSBPP prepared on these catalysts, and their dependence on the reaction conditions are presented in Table 3.

Table 3. Polymerisation of propylene induced by 'oscillating' catalysts (MAO cocatalyst).

Row	Complex	Al:Zr	$p_{C_3H_6}$ /atm	T_p /°C	A	$10^{-3} M_w$ /g mol ⁻¹	$M_w : M_n$	[<i>mmmm</i>] (%)	Ref.
1	16	1000	see ^a	0	0.20	556	2.8	38	76
2	16	2200	see ^a	8	0.10	411	4.0	29	70
3	16	1000	see ^a	20	0.19	539	4.7	39	76
4	16	1000	see ^a	40	0.35	163	3.4	30	76
5	20	1840	see ^a	30	0.18	360	4.5	—	72
6	20	1550	see ^a	50	0.40	37	2.6	30	72
7	16	4800	see ^a	30	0.54	145	3.0	31	70
8	16	10 000	see ^a	20	1.02	549	3.5	—	79
9	16	31 600	see ^a	20	1.77	236	2.4	16	80
10	19	1000	2.5	20	0.54	345	2.3	8	73
11	16	1000	2.5	20	0.50	232	3.8	23	73
12	19	1000	7.0	20	0.21	486	2.1	9	73
13	16	1000	7.0	20	0.17	435	3.0	31	73
14	18	1000	6.3	25	0.37	332	3.7	73	68
15	16	1000	1.8	25	0.32	179	3.0	20	68
16	16	1000	3.5	25	0.36	241	3.5	26	68
17	16	1000	6.3	25	0.54	369	3.9	32	68
18	26	3500	1.0	−20	0.03	600	3.5	11	81
19	27	3500	1.0	−20	0.004	260	2.1	16	81

Note. The catalyst concentration was varied in the range of 10^{-5} – 10^{-6} mol litre⁻¹. ^a Polymerisation was carried out in the liquid monomer.

The catalyst systems in question are characterised by a slight increase in the activity and a sharp decrease in the molecular masses with an increase in polymerisation temperature^{67, 70, 72, 73, 76–78} (see, for example, Table 3, rows 1, 4 and 2, 7). The temperature at which a high-molecular-mass eSBPP can be prepared usually does not exceed 30–40 °C. It has been noted⁷⁰ that the yield of the solid polymer formed upon polymerisation in the liquid monomer medium at 50 °C equals 30% based on the monomer consumed; the rest falls to low-molecular-mass products. The same sharp decrease in the molecular mass of the polymer upon an increase in the reaction temperature has been observed⁷² for the **20**–MAO catalyst system, which induces the formation of eSBPP with a higher molecular mass and a higher degree of crystallinity (see Table 3, rows 5, 6). From the temperature dependence of the activity of the complex **16** (liquid propylene, 0–40 °C) measured in several studies,^{70–72} the effective activation energy of polymerisation was found to be $E_a \approx 4$ kcal mol⁻¹.

Unlike a number of other metallocene catalyst systems, for these complexes, a marked decrease in the polymerisation rate with time was observed, even for low reaction temperatures (Fig. 7).⁷² The activity of catalyst systems and the molecular-

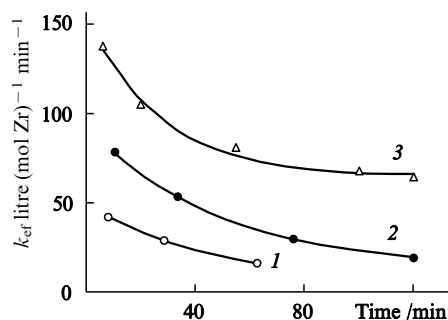


Figure 7. Effect of conditions of propylene polymerisation on the variation of the catalytic activity of the **16**–MAO system with time.⁷⁰ Polymerisation was carried out in the liquid monomer medium; $k_{cat} = w_p[C_3H_6]^{-1}[M]^{-1}$, where w_p is the rate of polymerisation. T_p (°C): (1) 2; (2) 8; (3) 30.

mass characteristics of eSBPP largely depend on the method used to prepare the catalyst.^{70, 73, 80} In many cases, the resulting polymers are characterised by a broad MMD ($M_w : M_n = 3–6$) and can be separated into several fractions by extraction with boiling ether and n-heptane. It is of interest that the differences in molecular masses and stereoisomeric compositions of the fractions prepared in the presence of these catalyst systems are much smaller than those obtained with the use of isospecific heterogeneous catalysts.^{82, 83} Comparison of the data obtained by different researchers^{70, 79, 80} allows the conclusion that the activity of complexes of this type increases with an increase in the Al:Zr ratio (see Table 3, rows 3, 7–9), which is typical of catalyst systems based on metallocenes.

An interesting feature of these catalysts is that the activities of the zirconium and hafnium complexes **16** and **19** are comparable.^{69, 72, 73} As noted above, hafnocenes with C_1 symmetry behave in a similar way.^{56–58} Normally, hafnium metallocenes of other types are much less active than zirconium analogues, all other factors being the same, and give polymers with much higher molecular masses. The 2-phenyl-substituted complexes **16**, **19** have approximately equal activities; in the case of eSBPP prepared on the hafnium complex, the molecular mass is higher and the polydispersity and the degree of isotacticity are much lower than those for eSBPP synthesised under the action of zirconium analogue (see, for example, Table 3, rows 11, 10 and 13, 12). Bruce *et al.*⁷³ believe that the comparable levels of activity of the complexes **16** and **19** are due to the more effective formation of AC in the case of the hafnium catalyst.

A number of publications have been devoted to the analysis of the influence of substituents on the catalytic properties of 2-aryl-substituted complexes and characteristics of the resulting eSBPP. The introduction of methyl substituents at the 3- and 5-positions of the benzene ring (complex **17**) causes some decrease in the catalyst activity and the polymer molecular mass; in addition, the isotacticity of the polymer substantially decreases.^{68, 69} The complex **18** containing trifluoromethyl substituents provides the formation of a crystalline PP (see Table 3, row 14). It is of interest that polymers prepared under the action of the complexes **16**–**18**, even with different contents of isotactic pentads, have rather high melting points (140–150 °C), which implies a small number of regiodefects in isotactic blocks. The introduction of various substituents into the *para*-position of the benzene ring (complexes

20–25) barely affects the activity of the system and the properties of the eISBPP formed.^{72, 78} Both *rac*- and *meso*-forms of the analogue of the complex **16** with the methyl substituent at the 1-position give rise to an amorphous low-molecular-mass PP with very high polydispersity coefficients, $M_w:M_n = 4–15$.⁸⁴ The eISBPP formed under the action of the complex **30** is close in stereochemical composition to the polymer formed with the **16**–MAO catalyst system; however, regarding the melting point and the macrotacticity index, it is close to the eISBPP prepared on catalysts with C_1 symmetry.⁷¹ Complexes **31–35** with mixed ligands and different substituents are less active catalysts than the bisindenyl complexes with identical ligands.⁸⁵

The main channel of chain transfer by the catalyst systems considered is the transfer of the β -hydrogen atom to the metal and the coordinated monomer.⁸⁰ An interesting feature of 2-aryindenyl systems is the clear-cut effect of the co-monomer, which was identified in a study of propylene copolymerisation with ethylene induced by the complexes **16** and **18**.^{79, 86} The activity of the catalyst system increases 2- to 8-fold even at a low ethylene:propylene molar ratio (0.05–0.08) in the monomer mixture. The increase in the activity is accompanied by a substantial (2–3-fold) increase in the molecular mass of the copolymer. The ethylene content in the copolymer varies in the range of 15 mol %–50 mol %. The system activity also increases appreciably upon the introduction of hydrogen. It has been assumed^{86, 87} that the co-monomer effect shows itself as the ability of ethylene to be inserted and to ‘wake up’ the AC after the formation of a regiodeflect of the polymer chain as a result of the monomer 2,1-addition.

Studies of the complexes **16** and **18** showed⁸⁷ that they are more regiospecific than the isospecific $\text{EtInd}_2\text{ZrCl}_2$ catalyst (Ind is indenyl). The non-bridged complex **16** produces PP containing 0.1 mol %–0.3 mol % of 2,1-added units. It is of interest that ‘regioerrors’ are detected only in isotactic sequences of the polymer, *i.e.*, they arise only in those cases where the ‘oscillating’ metallocene occurs in the isospecific state. This is confirmed by the fact that no ‘errors’ are found in the PP synthesised by the polymerisation of propylene in the presence of *meso*- $\text{Me}_2\text{Si}(2\text{-PhInd})_2\text{ZrCl}_2$, whereas the *rac*-analogue of this complex produces PP with ‘errors’ caused by the 3,1-addition.⁸⁸

A specific feature of the ‘oscillating’ catalysts is an increase in the content of the *mmmm* pentads following an increase in the monomer concentration (see, for example, Table 3, rows 15–17). Quantitative analysis of this phenomenon is based on the fact that the rate of polymerisation is proportional to the monomer concentration, while the rate of isomerisation does not depend on it and, since the content of isotactic pentads is determined by the ratio of the rates of these reactions, the regularity of the polymer increases with an increase in the monomer concentration. This has been observed in numerous experiments.^{67–69, 73, 78} As discussed above, an opposite dependence of the content of isotactic pentads on the monomer concentration was found for metallocenes with C_1 symmetry.

A mathematical model has been proposed to describe the oscillation mechanism of polymer chain growth.^{80, 89, 90} Computer generation of PP macromolecules has been carried out with variation of three parameters, namely, the stereoselectivity of the isospecific active centre (α), the selectivity of the aspecific centre (β) and the g/K parameter, which specifies the ratio of the relative reactivity to the stability for iso- and aspecific states ($g = k_{\text{pa}}/k_{\text{pi}}$, $K = k_1/k_2$). Thus $g/K > 1$ corresponds to the predominant existence of the isospecific AC. The dependence on the pentad composition on the monomer concentration for definite α , β and g/K values is determined by the parameter

$$\Delta = \frac{(k_{\text{pi}}/k_1 + k_{\text{pa}}/k_2)[\text{C}_3\text{H}_6]}{2}.$$

The best agreement between experimental and calculated pentad compositions was found for $\alpha = 0.97$, $\beta = 0.56$ and

$g/K = 0.6$. The Δ parameter varies in the 1–10 range as the propylene concentration changes from 1.2 to 11 mol litre^{−1}. However, the authors of the model admit⁸⁰ that the same kinetic dependence of the pentad composition on the monomer concentration can be described qualitatively and quantitatively by the Busico model,^{63, 64, 91} which takes into account the competition between the chain growth and epimerisation processes with the assumption that the AC have two active vacancies accessible for monomer coordination and the polymer chain growth.

Since the model of the ‘oscillating’ complex is widely recognised, several factors deserve attention, both those confirming the proposed mechanism and those conflicting with it. The mechanism in question is supported by the increase in the content of the *mmmm* pentads with an increase in the monomer concentration, which was observed experimentally for these complexes. The mathematical model describing this mechanism provides a quantitative correspondence between the polymer microstructures calculated and found experimentally depending on the polymerisation conditions (monomer concentration, temperatures) for reliable values of model parameters. The X-ray diffraction data for the complexes **16**, **19** are also a forcible argument in favour of the ‘oscillating’ complex. Theoretical studies^{92, 93} demonstrated the presence of two energy minima for the transition state corresponding to the *rac*- and *meso*-forms of the complex **16** and stabilised by the π -interactions between the phenyl substituents and the aromatic system of the indenyl ligands (π -stacking interactions); the two minima are energetically equivalent ($\Delta\Delta H = 0.6$ kcal mol^{−1}). Indeed, on passing to hydrogenated analogues of the complex **16**, (2-CyInd)₂ZrCl₂ (Cy is cyclohexyl), (2-Ph-H₄Ind)(2-PhInd)ZrCl₂ and (2-Cy-H₄Ind)₂ZrCl₂, all other factors being the same, a substantial decrease in the PP isotacticity has been noted: [*mmmm*] = 32%, 15%, 13% and 5%, respectively.⁷⁷

Direct investigation of isomerisation processes for ‘oscillating’ catalysts is of interest. The data of dynamic NMR for (2-PhInd)₂HfBn₂ (see Ref. 73) and structurally related (2-phenylcyclopenta[*l*]phenanthryl)₂ZrCl₂ (see Ref. 94) indicate a very high frequency of rotation of haptic-bonded ligands: 6800 s^{−1} for the former complex and $\sim 1 \times 10^8$ s^{−1} for the latter one. The latter zirconocene activated by MAO ensures (although with a low activity) the formation of a low-molecular-mass PP similar in stereoisomeric composition to the eISBPP prepared under the action of the complex **16**. The frequencies of ligand rotation about the axis passing through the M atom and the centroid of the Cp ring are several orders of magnitude greater than the frequency of olefin insertion estimated from the maximum rate of monomer absorption, which equals 0.1–10.0 insertions of C₃H₆ per second even with allowance for the low efficiency of the formation of AC. Evidently, such a fast rotation should average the stereospecific action of the AC and ensure the formation of PP with a narrow MMD. No data on the rate of isomerisation in real catalyst systems (MAO-activated metallocenes) are available. To explain the observed contradiction, it has been suggested⁹⁴ that the chain growth actually proceeds at a very high rate, which exceeds the rate of rotation of the haptic-bonded ligands but during the period of growth of the macromolecules, the AC pass many times into the ‘dormant’ state, perhaps, due to the formation of a contact ion pair with the counter-ion.

Note that only for the complexes **16** and **19**, was the existence of two energetically equivalent stereoisomers identified. Data from X-ray diffraction analyses of a number of other complexes which catalyse the formation of stereoblock PP indicate the presence of only one stereoisomer, for example, the *meso*-form of the complex **17**,⁶⁸ the *rac*-form of the complex **18**,^{68, 73} and its hafnium analogue⁷³ and the *meso*-form of the complex **21**,⁷⁸ which does not differ from the complex **16** in catalytic properties.

Although ¹³C NMR spectroscopy is a unique tool for analysing the structure of the polymer chain and, correspondingly, the catalytic properties of the AC, which allows one to evaluate its stereo- and regiospecificity, the stereocontrol mechanisms and so

on,^{34–37, 39, 40, 41, 95} this method still does not provide sufficient information for the analysis of the contents of sequences comprising 15–16 monomer units capable of crystallisation.

In the opinion of Gauthier and Collins,^{56, 58} the known data on the microstructure of elSBPP do not allow one to decide unambiguously in favour of one or another statistic model. For example, elSBPP formed under the action of the **19**–MAO catalyst system⁷² has a pentad composition that can be obtained by mathematical generation of the polymer chain in terms of the Bernoullian model with a probability of *m*-addition (*p_m*) equal to 0.58. However, no correspondence was attained between the calculated and experimental compositions for polymers with higher contents of isotactic pentads, which also exhibit elastomeric properties; this indicates that the given model is inapplicable to the description of the real mechanism of formation of stereoblock PP. Nevertheless, the possibility of existence of catalyst systems which form stereoblocks also by this mechanism cannot be ruled out completely.

A finding quite unusual for metallocene catalysis is that PP samples prepared by virtue of 'oscillating' catalyst systems are characterised in some cases by high polydispersity values *M_w* : *M_n* (Tables 3, 4). The correlation between the degree of isotacticity and the polydispersity of PP was first pointed out by Bruce *et al.*⁷³ This can be illustrated by the plots shown in Fig. 8 for the PP samples prepared using the [2-(4-RC₆H₄)Ind]₂MCl₂ and [2-(3,5-R₂C₆H₃)Ind]₂MCl₂ complexes with the MAO cocatalyst (Al : Zr = 1000) at 20–25 °C.^{68, 69, 73, 78} An increase in the polydispersity with an increase in the isotacticity can be followed in Fig. 8 for each type of complex. The hafnium analogues catalyse the formation of PP with a much lower crystallinity and polydispersity. Since the content of isotactic pentads is determined by the isospecific state of complexes of C_{2v} symmetry and can be regarded as a measure of activity, it is reasonable to suggest that this state is realised upon reversible coordination of a component (or components) of the reaction mixture (MAO, AlMe₃, solvent, monomer) by the cationic alkyl metal complex. These interactions might be responsible for broadening of the MMD of the elSBPP samples prepared in the presence of the catalyst systems.

In this connection, the following example is of interest. It has been reported⁸² that the elastomeric PP prepared in the presence of hydrogen (0.044 mmol of H₂ per mole of C₃H₆) in order to decrease the molecular mass differs appreciably from the elSBPP produced in the absence of hydrogen, all other conditions being the same (liquid propylene, 23 °C). The molecular mass of the product decreases and the polymer synthesised in the presence of hydrogen has the following composition: 72% of ether-soluble fraction, 13% of heptane-soluble fraction and 15% of a fraction

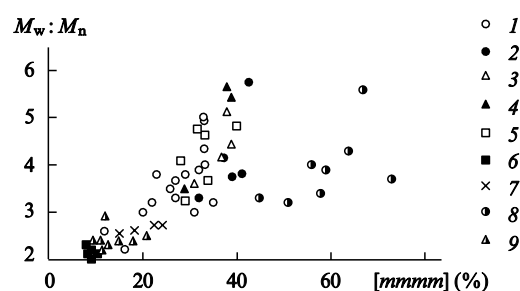


Figure 8. Polydispersity vs. isotacticity for PP samples prepared on 'oscillating' catalysts activated by MAO at 20–25 °C.^{68, 69, 73, 78} Catalyst: (1) **16**; (2) **20**; (3) **21**; (4) **22**; (5) [2-(4-Bu'C₆H₄)Ind]₂ZrCl₂; (6) **19**; (7) **17**; (8) **18**; (9) hafnium analogue of the complex **18**.

insoluble in heptane, whereas the fractional composition of the polymer obtained without hydrogen is completely different: 36%, 43% and 21%, respectively. The microstructures of the fractions are also markedly different, the isotacticity of all fractions being much higher in the case of the polymer prepared in the presence of hydrogen (Table 5, rows 11–14, 15–18).

In a recent study,⁸⁰ it was reported that the synthesis of PP induced by the complex **16** can yield elSBPP with a narrow MMD (*M_w* : *M_n* = 2.1–2.7). However, the polymerisation procedure employed in this study⁸⁰ results, with other conditions remaining the same, the formation of a PP in which the molecular mass is 2–4 times lower than that reported previously. The observed extension of the MMD was attributed⁸⁰ to the increase in the polymerisation rate following an increase in the monomer concentration and by a decrease in the rate of mass transfer and propylene solubility during polymerisation at high rates.

The catalytic properties of 2-alkyl-substituted complexes **26**–**29** in the propylene polymerisation in toluene have been studied.^{81, 96} At a propylene pressure equal to 1 atm, elSBPP with a rather high molecular mass can be formed only at low temperatures (–20, 0 °C). Thus at –20 °C, elSBPP with a molecular mass of 600 000 g mol^{–1} is formed under the action of the complex **26**. When more active catalysts are used, PP with a higher molecular mass is produced. The maximum activity is exhibited by the complexes **26** and **27** (see Table 3, rows 18, 19). The specific activity of the complex **26** is four times lower than that of the complex **16** at 0 °C. The activity of catalysts in propylene polymerisation increases 1.3–2.3-fold as the reaction temperature decreases from 0 to –20 °C. All 2-alkyl-substituted complexes, except for compound **26**, are inactive in ethylene polymerisation at low temperatures. Similar properties are found for complexes **36** and **37** with heterocyclic substituents at the 2-position in the presence of the MAO cocatalyst.⁹⁷ high-molecular-mass elastomeric SBPP is formed on these catalysts only at low temperatures (0, –20 °C); the catalyst activity increases as the reaction temperature decreases; and more active catalysts give rise to elSBPP with a higher molecular mass. Thus the activity of complex **38** at –20 °C equals 59 kg PP (mol Zr)^{–1} h^{–1} atm^{–1}, and the weight-average molecular mass of the resulting PP is 3600 g mol^{–1}. Meanwhile, under similar conditions, complex **36** exhibits an activity comparable to that of the complex **16** and leads to the formation of PP with a molecular mass of 720 000 g mol^{–1}. Dynamic NMR analysis of **36** and **37** identified fast rotation around the axis that passes through the Zr atom and the centroid of the Cp ring and the presence of a conformational equilibrium, fast on the NMR time scale, although an X-ray diffraction investigation of the complex **36** indicated that only *meso*-**36** exists in the solid state,⁹⁷ unlike the situation with the complex **16**. It can be demonstrated in relation to the elSBPP prepared with the complexes **26**, **27**, **29** and **36** that the isotacticity–molecular mass combination of properties is important for the strength and elastomeric characteristics of the polymer (see Table 4).

Table 4. Strain and elastic properties of elSBPP prepared under the action of bis(2-alkylindenyl)zirconium dichlorides in the presence of the MAO cocatalyst (*T_p* = –20 °C, toluene, *p*_{C₃H₆} = 1 atm, Al : Zr = 3500).^{96, 97}

Parameter	26	27	29	36
<i>M_w</i> / g mol ^{–1}	600 000	260 000	90 000	720 000
<i>M_w</i> : <i>M_n</i>	3.5	2.1	2.6	2.8
[<i>mmmm</i>] (%)	10	16	26	19
Tensile strength / MPa	2.4	6.85	0.55	—
Elongation at rupture (%)	1224	1109	1085	839
Modulus of elasticity / MPa	0.98	1.04	0.04	—
Stress at 100% elongation / MPa	0.81	0.86	0.24	0.77
Recovery after 100% elongation (%)	93	95.3	77.3	94
Stress at 300% elongation / MPa	1.07	1.13	0.25	0.76
Recovery after 300% elongation (%)	95.1	95.7	70.2	81

Table 5. Pentad composition of the eSBPP samples prepared using homogeneous catalyst systems.

Row	Catalyst	$T_p / ^\circ\text{C}$	$p_{\text{C}_3\text{H}_6}$ /atm	[mmmm]	[mmmr]	[rmmr]	[mmrr]	[mrmm + +rmrr]	[rmmr]	[rrrr]	[rrrm]	[mrrm]	n_{iso} (see ^a)	Ref.
1	5–MAO	0	1	0.39	0.17	0.03	0.19	0.06	0.02	0.02	0.04	0.09	8.6	58
2	5–MAO	25	1	0.37	0.19	0.03	0.19	0.07	0.02	0.02	0.03	0.09	8.1	58
3	5–MAO	25	3	0.32	0.18	0.03	0.20	0.08	0.02	0.04	0.05	0.09	7.5	58
4	7–MAO	25	1	0.53	0.16	0.02	0.14	0.04	0.02	0.01	0.02	0.06	10.7	56
5	7–MAO	25	4	0.50	0.16	0.03	0.13	0.06	0.03	0.01	0.02	0.06	10.2	58
6	10–MAO	30	2	0.43	0.18	0.02	0.20	0.03	—	0.02	0.03	0.10	8.9	59
7	10–MAO	30	10	0.25	0.17	0.03	0.22	0.09	—	0.06	0.09	0.10	6.9	59
8	10–MAO	50	8	0.49	0.16	0.02	0.18	0.03	—	0.02	0.02	0.09	10.3	59
9	16–MAO	8	see ^b	0.29	0.15	0.05	0.14	0.16	0.08	0.03	0.07	0.03	7.9	70
10	16–MAO	30	see ^b	0.31	0.15	0.06	0.13	0.16	0.08	0.03	0.05	0.04	8.2	70
11	16–MAO ^c	23	see ^b	0.32	0.15	0.04	0.10	0.18	0.09	0.02	0.05	0.05	8.4	82
12	16–MAO ^d	23	see ^b	0.18	0.16	0.06	0.12	0.22	0.11	0.03	0.08	0.05	6.3	82
13	16–MAO ^e	23	see ^b	0.33	0.16	0.05	0.11	0.18	0.08	0.02	0.05	0.04	8.2	82
14	16–MAO ^f	23	see ^b	0.51	0.13	0.03	0.07	0.13	0.06	0.01	0.04	0.04	12.1	82
15	16–MAO ^g	23	see ^b	0.34	0.14	0.04	0.09	0.16	0.08	0.02	0.06	0.06	8.8	82
16	16–MAO ^h	23	see ^b	0.23	0.17	0.05	0.12	0.20	0.09	0.03	0.05	0.06	6.7	82
17	16–MAO ⁱ	23	see ^b	0.53	0.13	0.02	0.09	0.11	0.05	0.01	0.03	0.04	12.5	82
18	16–MAO ^j	23	see ^b	0.81	0.07	0.01	0.04	0.04	0.01		0.01	0.02	28.9	82
19	19–MAO	30	see ^b	0.12	0.15	0.07	0.12	0.25	0.13	0.03	0.08	0.06	5.6	72
20	20–MAO	30	see ^b	0.36	0.14	0.06	0.10	0.16	0.08	0.02	0.05	0.03	9.3	72
21	27–MAO	–20	1	0.16	0.17	0.08	0.12	0.20	0.11	0.04	0.06	0.06	5.9	96
22	R ₂ ZrMe ₂ – AlBu ₃ ⁱ (see ^k)	30	see ^b	0.27	0.14	0.07	0.14	0.16	0.08	0.04	0.08	0.04	7.9	98
23	R ₂ ZrMe ₂ – AlBu ₃ ⁱ (see ^l)	30	4	0.49	0.14	0.03	0.10	0.11	0.05	0.01	0.03	0.03	11.0	98
24	R ₂ ZrMe ₂ – AlBu ₃ ⁱ (see ^m)	30	4	0.18	0.18	0.07	0.15	0.18	0.09	0.04	0.07	0.07	6.0	98
25	(acac) ₂ ZrCl ₂ – MAO ⁿ	0	6	0.28	0.12	—	0.12	0.15	0.08	0.06	0.11	0.09	8.7	99

^a Effective length of isotactic sequences estimated from the content of the corresponding pentads: $n_{\text{iso}} = 4 + 2[\text{mmmm}]/[\text{mmmr}]$ (see Ref. 47).

^b Polymerisation was carried out in the liquid monomer. ^c Non-fractionated eSBPP prepared on the 16–MAO catalyst system (Al:Zr = 1000).

^d Ether-soluble fraction (36%). ^e Heptane-soluble fraction (43%). ^f Fraction insoluble in boiling heptane (21%). ^g Non-fractionated eSBPP prepared on the 16–MAO catalyst system (Al:Zr = 1000) in the presence of hydrogen (0.044 mol H₂ per mol C₃H₆). ^h Ether-soluble fraction (72%). ⁱ Heptane-soluble fraction (13%). ^j Fraction insoluble in boiling heptane (15%). ^k R = 2-PhInd, Al:Zr = 120. ^l Polymerisation was carried out in toluene, $p_{\text{C}_3\text{H}_6} = 4$ atm, R = 2-PhInd, Al:Zr = 100. ^m Polymerisation was carried out in toluene, $p_{\text{C}_3\text{H}_6} = 4$ atm, R = 2-PhInd, Al:Zr = 300. ⁿ Polymerisation was carried out in methylene chloride, $p_{\text{C}_3\text{H}_6} = 6$ atm, Al:Zr = 480.

Analysis of the microstructure of the PP samples prepared with the 26–MAO catalyst system led Naga and Mizunuma¹⁰⁰ to the conclusion that the formation of isotactic sequences during the growth of the polymer chain is dictated by the terminal unit ($4[\text{mm}][\text{rr}][\text{mr}]^{-2} \approx 1$) in the range of polymerisation temperatures of –20 to 40 °C. These results indicate that this stereocontrol mechanism may be involved in the propylene polymerisation under the action of 2-aryl-substituted metallocenes. The synthesis of the high-molecular-mass eSBPP on catalysts with C_2 symmetry,¹⁰¹ namely, *rac*-Me₂C(3-PrⁱInd)₂ZrCl₂ and *rac*-H₂C(3-PrⁱInd)₂ZrCl₂, should also be mentioned. In the presence of MAO, at 50 °C in liquid propylene, these complexes (Al:Zr = 1000–4000) actively $\{A \approx 2.5 \text{ kg PP (mmol Zr)}^{-1} [\text{C}_3\text{H}_6]^{-1} \text{ h}^{-1}\}$ form amorphous polypropylene with a molecular mass of 100 000–160 000 g mol^{–1} and with a content of isotactic pentads of 15.6% for the former catalyst and 25.5% for the latter catalyst. The formation of stereo blocks on these catalysts is determined by the presence of two enantiomers with different isospecificity and a noticeable contribution of the stereocontrolling influence of the terminal unit of the polymer chain to the enantiomeric stereocontrol. An increase in the reaction temperature is accompanied by a decrease in the content of isotactic pentads typical of metallocene complexes of C_2 symmetry (unlike catalysts of C_1 symmetry).^{59, 61, 102}

An increase in the Al:Zr ratio accompanied by an increase in the activity of the 16–MAO system reduces the content of

isotactic pentads in the resulting polymer (see Table 3, rows 3, 7, 9). In this connection, it is of interest to turn to the data of Petoff *et al.*¹⁰³ Analysis of the effect of AlR₃ additives (R = Me, Buⁱ) introduced in MAO demonstrated that aluminium alkyls decrease the activity of the *rac*- and, more appreciably, *meso*-form of Me₂Si(2-PhInd)₂ZrCl₂ but do not change substantially the microstructure of PP prepared on each complex alone. A pronounced increase in the polymer isotacticity upon the introduction of aluminium alkyls, accompanied by a decrease in the activity, was observed in the polymerisation guided by a mixture of *rac*- and *meso*-forms of the complex as the cationic *meso*-form became passive after coordination to TIBA. The addition of aluminium alkyls to the 16–MAO system (Al_{MAO}:Zr = 1000) brought about a decrease in the activity by factors of 1.4 and 1.7 for R = Buⁱ (Al_{AlBu₃}:Zr = 1000) and Me (Al_{AlMe₃}:Zr = 100), respectively, but induced an increase in the content of the *mmmm* pentads from 39% to 47% in the former case and a drop of this value to 19% in the latter case (similarly to polymerisation with a large excess of MAO). Thus, one cannot rule out the possibility of MAO participation in the stereocontrol through chain transfer between aspecific and isospecific sites by the AlMe₃ contained in MAO, as in the case of ‘hybrid’ metallocene catalysts considered below. Apparently, parameters of MAO (degree of oligomerisation, structural characteristics, Lewis acidity), which depend on the temperature and the presence and concentration of AlMe₃, are also important factors influencing the state of the active centre

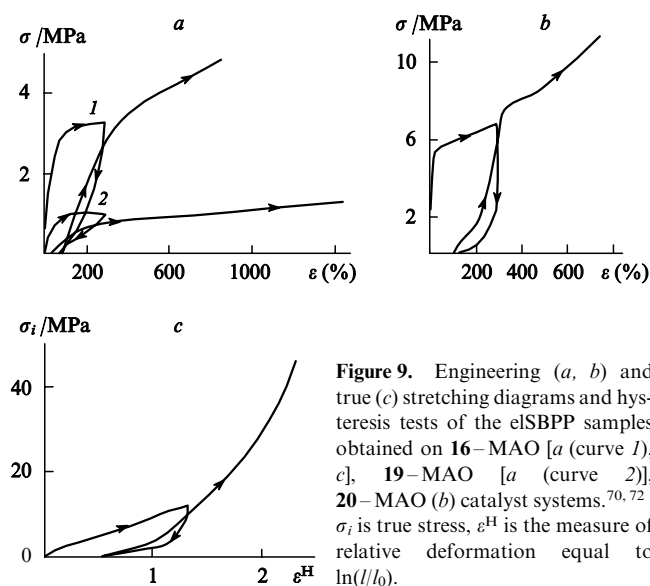


Figure 9. Engineering (*a*, *b*) and true (*c*) stretching diagrams and hysteresis tests of the elSBPP samples obtained on **16**–MAO [*a* (curve 1), *c*], **19**–MAO [*a* (curve 2)], **20**–MAO (*b*) catalyst systems.^{70,72} σ_i is true stress, ε^H is the measure of relative deformation equal to $\ln(l/l_0)$.

(polarisation of the M–C bond, capacity for dissociation upon coordination and insertion of olefin).^{104,105}

The microstructure of stereoblock PP obtained in the presence of ‘oscillating’ catalysts differs from the microstructure of PP formed on catalysts with C_1 symmetry by a much higher content of heterotactic pentads, the average length of isotactic sequences being the same (see Table 5). It is also noteworthy that PP synthesised using ‘oscillating’ catalysts has a stereoblock structure even in samples with low contents of isotactic pentads. Thus a sample of elSBPP with good elastomeric properties formed on the **19**–MAO catalyst system contains only twice as many isotactic *mmmm* pentads as the ideal atactic PP and, correspondingly, half the syndiotactic *rrrr* pentads. In addition, the content of boundary *mmmr* pentads is higher, while that for *rrrm* is lower for stereoblock PP. The proportion of other pentads corresponds to atactic PP.

A lot of data on the strain, strength and elastomeric properties of elSBPP have now been accumulated.^{70,72,80,106–111} Figure 9 *a–c* shows the data on the relaxation dependences for stereoblock PP. It can be seen that polymer samples exhibit good elastomeric properties. The stretching curves follow a pattern typical of classical elastomers,¹¹² i.e., they show uniform deformation

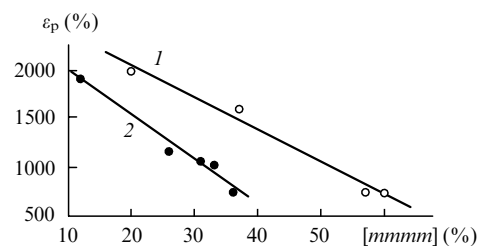


Figure 10. Elongation at rupture (ε_p) vs. content of isotactic pentads in elSBPP samples obtained on metallocenes of C_1 symmetry (1)⁶⁰ and ‘oscillating’ catalysts⁷² (2).

mation upon stretching to great degrees of elongation and high reversibility of deformation.

Some properties of the elSBPP samples obtained on treatment with various types of catalyst are compared in Table 6. The elastomeric SBPP with macromolecules containing more uniform isotactic but also longer atactic sequences have higher melting temperatures but exhibit smaller elongation at rupture, while the molecular masses and the contents of the *mmmm* pentads are the same. Figure 10 illustrates the dependence of the elongation at rupture on the content of isotactic pentads for the PP samples prepared on metallocenes of various types. Figure 11 *a–c* presents the variation of the modulus of elasticity, tensile strength and the residual elongation vs. the molecular mass and the degree of crystallinity for the elSBPP samples synthesised in the presence of the metallocenes **16**, **19** and **20**. As can be seen from the data of Table 6 and Figs 10, 11, an increase in the molecular mass of polymers with invariant stereoregularity and degree of crystallinity results in a higher modulus of elasticity, tensile strength and a smaller residual elongation. A decrease in the stereoregularity for similar molecular masses and crystallinity degrees reduces the modulus of elasticity, the tensile strength and the residual elongation. An increase in the sample degree of crystallinity with invariant molecular masses and stereoregularity brings about an increase in the modulus of elasticity, the strength and the residual elongation. It can be seen that the strength and elastomeric properties are determined by several characteristics including the molecular mass, the degree of crystallinity and the stereoregularity of the polymer.

Presumably, the size and size distribution of the crystallites and the dynamic changes in the structure of the network junctions under the action of load at various temperatures are also signifi-

Table 6. Properties of the elSBPP prepared under the action of various metallocene catalyst systems.

Row	Catalyst	$10^{-3} M_w$ /g mol ⁻¹	[<i>mmmm</i>] (%)	<i>C</i> (%)	T_p /°C	Elongation at rupture (%)	Tensile strength /MPa	Residual elongation (%) (see ^a)	Ref.
1	1	127	40	7	51/66	525	4.0	57 ₃₀₀	51
2	5	30	38	7	47/61	200	3.0	—	56
3	7	49	54	19	54/93	500	16.0	90 ₂₀₀ (see ^c)	56
4	7	140	45	15	50/79	750	16.0	97 ₂₀₀ (see ^c)	58
5	7	380	52	17	53/74	800	39.0	93 ₂₀₀ (see ^c)	58
6	10	171	37	—	—	1700	6.0	—	60
7	16	160	31	4	140	1070	4.8	69 ₃₀₀	72
8	16	145	33	12	150	1015	6.8	101 ₃₀₀	72
9	16	410	26	3	141	1170	7.9	31 ₃₀₀	72
10	20	37	30	11	151	790	2.0	175 ₃₀₀	72
11	20	210	36	14	157	750	11.4	100 ₃₀₀	72
12	20	360	—	10	151	854	14.3	100 ₃₀₀	72
13	19	190	12	—	—	1930	1.5	47 ₃₀₀	72
14	16	455	32	11	138	878	9.3	30–40 ₃₀₀	79
15	16 ^b	257	34	18	140	753	7.0	50–90 ₃₀₀	79

^a The index shows the elongation (in %) after which the load was removed. ^b The sample was prepared in the presence of hydrogen. ^c Recovery.

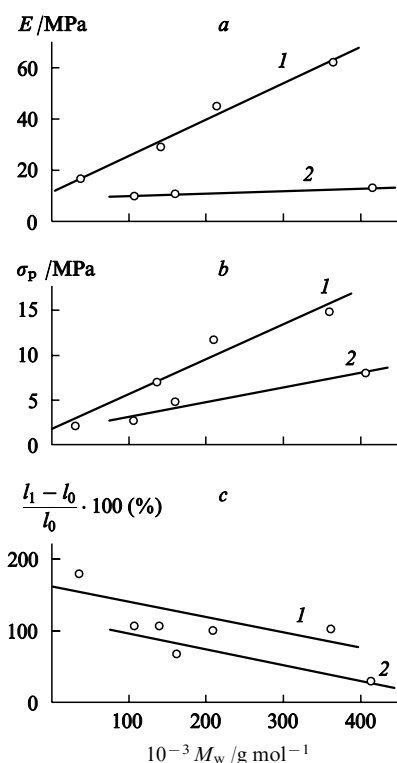


Figure 11. Modulus of elasticity, E (a), tensile strength, σ_p (b), and residual elongation, $(I_1 - I_0)/I_0$ (c) vs. molecular mass of eLSBPP samples with different degrees of crystallinity:^{70,72} (1) 10%–14%, (2) 0%–4%.

cant for strain and elastomeric parameters of eLSBPP. However, at present, it is impossible to perform a comparative analysis of the effects of these factors on the mechanical properties of eLSBPP samples obtained using different catalyst systems as no information needed for this purpose is available.

Thus, by varying the type of the catalyst or polymerisation conditions, one can prepare eLSBPP possessing a required set of properties.

4. Catalyst systems based on metallocenes with activators other than polymethylaluminumoxane

In the preceding sections, we considered metallocene catalysts for the synthesis of elastomeric PP activated by MAO. In these catalyst systems, MAO functions as an alkylating and a cation-generating reagent without being an effective controller of the microstructure or chain transfer agent.⁸⁰ The main factors that control the microstructure of the macromolecule in the catalyst systems considered above are the composition and structure of the initial catalyst and the monomer concentration. The catalyst systems containing MAO as a cocatalyst suffer from some drawbacks. The maximum activity of metallocene catalysts, in particular those considered in this review, is observed at great cocatalyst : catalyst ratios (see, for example, Table 3, rows 4 and 9). Due to the high cost of MAO, the catalysts are expensive. In this section, we give examples of metallocene catalyst systems in which other types of activating additives are used and also catalyst systems that provide additional possibilities of controlling the microstructure of the macromolecules formed.

a. The $(2\text{-PhInd})_2\text{ZrMe}_2$ –TIBA catalyst systems

Recently, we found a new class of homogenous catalyst systems in which TIBA serves as the activating additive. In terms of activity in ethylene and propylene polymerisation, these catalysts are commensurable with systems containing MAO as the cocatalyst; they also retain the stereospecific action.^{98,113} This group of complexes includes the dimethyl derivatives of 2-substituted

Table 7. Polymerisation of propylene in toluene or in the liquid monomer induced by the $(2\text{-PhInd})_2\text{ZrMe}_2$ –TIBA catalyst system.^{98,113}

Row	Al:Zr	$p_{\text{C}_3\text{H}_6}$ /atm	T_p /°C	A	[mmmm] (%)	D_{998}/D_{973}
1	120	see ^a	30	0.10	28	0.26
2	100	6.3	30	0.13	39	0.32
3	200	6.3	30	0.27	—	0.17
4	300	6.3	30	0.42	18	0.18
5	300	2.3	30	0.18	21	0.18
6	120	6.3	10	0.15	—	0.25
7	120	6.3	50	0.76	—	0.17

^a Polymerisation was carried out in the liquid monomer; $M_w = 230\,000\text{ g mol}^{-1}$, $M_w:M_n = 2.8$.

bisindenyl zirconocenes, in particular, the dimethylated analogue of the complex **16**.

Study of the catalytic properties of the $(2\text{-PhInd})_2\text{ZrMe}_2$ –TIBA system in toluene and in liquid monomer showed that its activity is similar to that of **16**–MAO, the molecular mass of the resulting eLSBPP being the same or higher (Table 7). Unlike the **16**–MAO catalyst, for this system, no increase in the content of isotactic pentads following an increase in the monomer concentration was observed (see Table 7, rows 4, 5 and 1, 2). The concentration of TIBA or, with a constant metallocene concentration, the Al_{TIBA}:Zr ratio is the factor which allows variation over broad ranges of the system activity, the kinetic characteristics of the polymerisation process and the properties of the PP formed. Thus an increase in the Al_{TIBA}:Zr molar ratio from 100 to 300 entails a 4-fold increase in the activity, a growth of the molecular mass from 80 000 to 220 000 g mol^{−1} and a decrease in the content of isotactic pentads (Fig. 12). Yet another feature of this catalyst system is the fact that it permits polymerisation to be carried out at relatively high temperatures (see Table 7, row 7). The increase in the activity of the given system with an increase in the reaction temperature is not accompanied by a sharp decrease in the molecular mass, as was observed for the MAO-activated

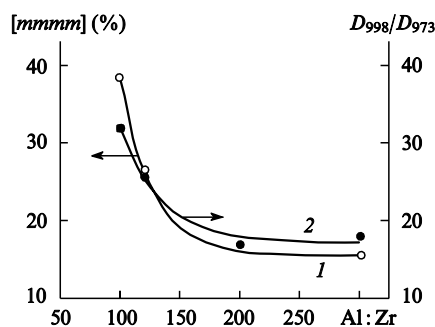


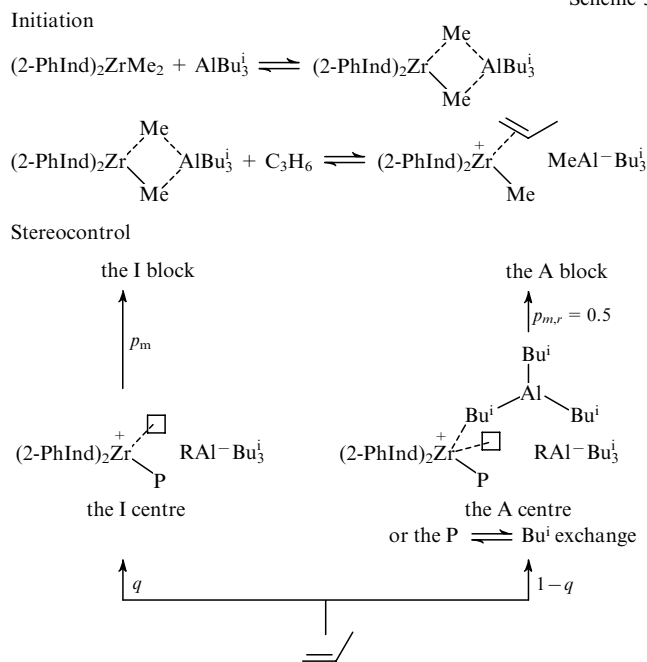
Figure 12. Pentad composition (1) and macro tacticity index (2) of eLSBPP obtained with the $(2\text{-PhInd})_2\text{ZrMe}_2$ –TIBA catalyst system vs. Al:Zr molar ratio ($T_p = 30^\circ\text{C}$).¹¹³

system, and makes it possible to change the isotacticity of eLSBPP (see Table 7, rows 6, 7). Thus, by varying the concentration of the activating agent and the reaction temperature, one can prepare eLSBPP with a specified set of properties.

Panin *et al.*⁹⁸ proposed a model which takes into account the participation of TIBA and the monomer in the formation of the AC (Scheme 3, initiation); this allows one to explain why the rate of polymerisation is first order with respect to TIBA and second order with respect to the monomer.

Another model explains the role of TIBA in the stereocontrolling action of the AC (Scheme 3, stereocontrol).¹¹³ This model

Scheme 3



implies repeated inversion of the AC (fast dynamic equilibrium) from the isospecific to aspecific state during chain growth as a result of coordination of an additional TIBA molecule or the generation of 'errors' due to fast exchange between the alkyl groups of TIBA and the growing polymer chain.

Computer simulation of the growing chain of stereoblock PP (~300 000 units) was carried out with the optimised parameters of probability of monomer addition to the active site in the isospecific (q) or aspecific ($1-q$) state and the probability of monomer addition with a definite orientation in the isospecific centre (p_m). In all model experiments, the last-mentioned value was taken to be unity. The probability of m - or r -addition ($p_{m,r}$) in the aspecific AC was taken to be 0.5. The pentad composition of experimentally obtained eLSBPP samples is consistent with the value calculated in terms of this model; in addition, a logical dependence of the q parameter on the TIBA concentration is observed.

It should be noted that eLSBPP formed under the action of the $(2\text{-PhInd})_2\text{ZrMe}_2$ -TIBA catalyst system is similar in pentad composition to the PP produced by the **16**-MAO system (see Table 5, 6) and exhibits similar elastomeric properties.

The attraction of this catalyst system for the synthesis of eLSBPP is in the use of cheap trialkylaluminium instead of expensive MAO as the activating agent and in the possibility of changing the molecular-mass characteristics and the microstructure of the resulting polymer by varying the Al:Zr ratio and the polymerisation temperature. Apparently, the $(2\text{-PhInd})_2\text{ZrMe}_2$ -TIBA system should be sensitive to the action of hydrogen and ethylene, like the **16**-MAO system described above.^{79, 82, 85, 86} This provides additional opportunities for the control of activity, molecular mass and stereo and fractional composition of the polymer.

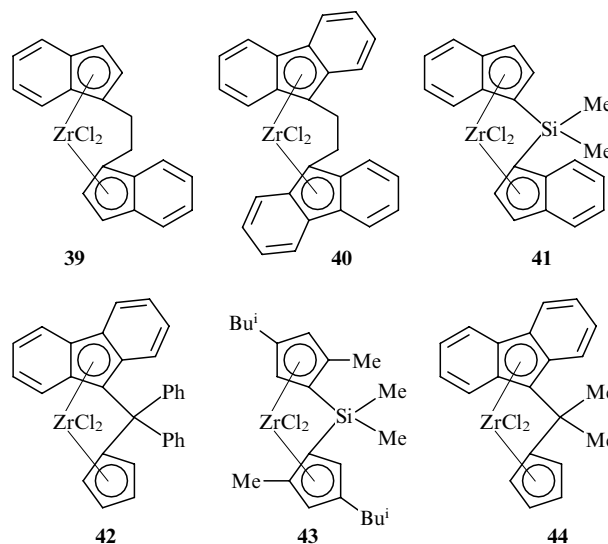
b. 'Hybrid' metallocene catalyst systems

The mechanisms of action of the above-described homogeneous metallocene catalyst systems for the synthesis of eLSBPP have a common feature, *i.e.*, the possibility of the existence of a cationic AC in the isospecific or aspecific state. In recent years, publications appeared on the synthesis of stereoblock PP by polymerisation induced by mixtures of metallocenes with different stereospecificity, 'hybrid' homogeneous^{114–116} or supported¹¹⁷ catalyst systems.

In studies on homogeneous catalyst systems, a combined activator for zirconocene dichlorides, namely,

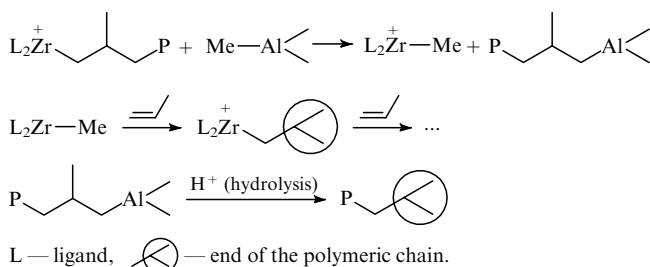
TIBA-CPh₃B(C₆F₅)₄^{114–116} or MAO¹¹⁶ was used. Zirconocene dichlorides on a MAO-treated support were activated by TIBA.¹¹⁷ Presumably, in the homogeneous system, TIBA acts as the alkylating agent in the initiation step, and the subsequent reaction of the alkylated catalyst with the borate gives rise to a cationic alkyl metal AC. The mechanism of activation of metallocene catalyst systems involving trialkylaluminium is currently open to question and its detailed discussion is beyond the scope of this review. Only some facts will be presented. Monoalkylation of a large series of zirconocene dichlorides induced by AlMe₃ has been confirmed experimentally.¹¹⁸ In the case of the Cp₂ZrCl₂-TIBA system (Al:Zr = 10), a ¹³C NMR study showed that the Cp₂Zr(Buⁱ)Cl·TIBA complex is the only identifiable product (19%), whereas in the (Me₅C₅)₂ZrCl₂-TIBA system, the (Me₅C₅)₂Zr⁺Cl...ClAl⁻Buⁱ complex is formed selectively.¹¹⁹ Preliminary reaction of zirconocene dichlorides with MAO at relatively low Al:Zr ratios (~10²) results in complexes that are effectively activated by TIBA in the polymerisation of propylene.^{120–122} The Me₂Si(Me₄C₅)NBuⁱZrCl₂-MAO, Me₂Si(Me₄C₅)NBuⁱZrCl₂-TIBA-CPh₃B(C₆F₅)₄ and Me₂Si.(Me₄C₅)NBuⁱZrMe₂-TIBA-CPh₃B(C₆F₅)₄ systems exhibit different catalytic properties in ethylene polymerisation under identical conditions.^{101, 123–125} Despite the fact that TIBA is widely used as an activator of immobilised metallocene complexes supported on MAO-treated materials,¹²⁶ no data on the mechanism of activation or the role of TIBA have been published. In a number of publications,^{123, 127–130} it is noted that TIBA is not a chain transfer agent in homogeneous catalyst systems for ethylene and propylene polymerisation but functions as an activator.

Propylene polymerisation using a mixture of dichloride metallocene complexes with different stereospecificity, namely, isotactic-atactic complexes **39–40** or **41–40**¹¹⁴ and isotactic-syndiotactic complexes **41–42**¹¹⁵ activated by TIBA-CPh₃B(C₆F₅)₄ gave¹¹⁴ high-molecular-mass products, which were mixtures of homopolymers with the composition corresponding to the stereospecific action of the initial catalysts and a stereoblock fraction. The catalyst systems studied by Chien *et al.*¹¹⁴ exhibit activities of up to 50 kg PP (mol Zr)⁻¹ h⁻¹ [C₃H₆]⁻¹. The content of the stereoblock fraction depends on the molar ratio of the complexes in the hybrid mixture and the TIBA concentration. The stereoblock fraction ensures the compatibility of the resulting polymers. An increase in the concentration of TIBA is accompanied by an increase in the activity of the systems and a decrease in the crystallinity of the polymeric product. At a definite composition, the resulting polymers exhibit good elastomeric properties: the elongation at rupture reaches 900% and the recovery is 97%–98%. The formation of the stereoblock fraction was attributed¹¹⁴ to the fast exchange of growing polymeric chain

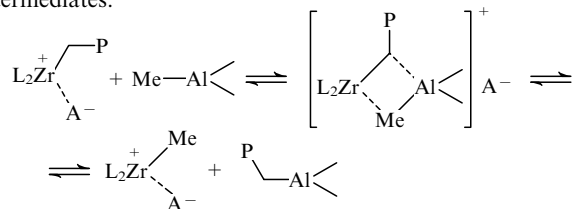


fragments between the AC with different stereospecificities with participation of TIBA.

Recently, experimental data have been published confirming the possible formation of the stereoblock PP fraction by the 'hybrid' mechanism.¹¹⁶ Analysis of the terminal groups of the PP macromolecules formed under the action of zirconocenes with different structures, the isospecific complexes *rac*-Me₂Si.₂(2-MeInd)₂ZrCl₂ (**45**) and **43**, the aspecific complex **40** and the syndiospecific zirconocene **42** activated by MAO or by the TIBA–CPh₃B(C₆F₅)₄ system showed that chain transfer to the organoaluminium compound proceeds efficiently for some catalysts. This is indicated by the high content of the isopropyl groups in the polymer.



The efficiency of chain transfer during propylene polymerisation on MAO (or AlMe₃ present in MAO) is governed by steric parameters of metallocene and is maximum for the sterically most hindered highly stereo- and regiospecific zirconocene **43**. The introduction of an additional amount of AlMe₃ (Al:Zr = 500–5000) results in a considerable increase in the activity and a decrease in the molecular mass of isotactic PP. The efficiency of the chain transfer to the organoaluminium compound reaches 95%; evidently, this process takes place through alkyl–polymer chain reversible exchange reactions in heteronuclear cationic intermediates.¹¹⁶



The aspecific complex **40** is less capable of chain transfer by this mechanism. The introduction of an additional amount of AlMe₃ results in a lower molecular mass of the polymer and a lower system activity, apparently, due to the formation of coordinatively saturated 'dormant' active centres.^{131, 132} The chain transfer during polymerisation is less pronounced in the case of the syndiospecific complex **42** and does not take place when sterically open isospecific zirconocene **45** is used. On none of the zirconocenes studied, was transfer of the polymer chain to TIBA observed in the presence of a combined activator.

By combining complexes with different stereoselectivity (**40**–**43**) exhibiting the maximum capacity for chain transfer to the organoaluminium compound, it was possible to prepare PP with the highest (up to 30%) content of the stereoblock fraction (atactic–isotactic blocks) soluble in boiling hexane.¹¹⁶ The proportion of the stereoblock fraction increases upon an increase in the content of the catalyst more prone to chain transfer to the organoaluminium compound.

Unfortunately, the researchers cited¹¹⁶ did not analyse the dependence of the content of the stereoblock fraction on the concentration of the complexes **40** and **43** and TIBA. A decrease in the concentrations of these components should decrease the probability of exchange reactions and thus reduce the amount of the stereoblock fraction. However, in a recent study,¹³³ doubt is cast upon the widely recognised opinion regarding the nature of the AC (the cationic metal alkyl site stabilised by the counter-ion). Analysis by NMR spectroscopy of anion exchange reactions

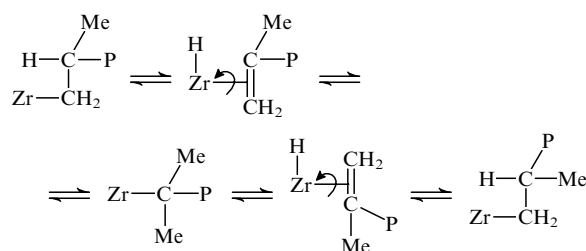
(dynamic symmetrisation of ion pairs of zirconocene) which are accelerated in the presence of Li⁺...MeB[–](C₆F₅)₃ and upon an increase in the zirconocene concentration, mainly due to the entropy factor, provides grounds for belief that quadrupole ion–counter-ion dimers (or polynuclear complexes) act as AC for the ion-coordinate polymerisation of olefins. Proof of the existence of such intermediates would provide a new interpretation of exchange reactions involving zirconocenes with different stereospecificities.

Apparently, stereoblock PP is formed by a chain transfer mechanism between the AC with different specificity through TIBA or the monomer during propylene polymerisation induced by binary supported catalysts which have been reported recently.¹¹⁷ These catalysts were synthesised by co-precipitation of the isospecific zirconocene **41** and the syndiospecific complex **44** from a toluene solution onto silica gel treated with MAO (PQ-SiO₂–MAO). This method of deposition ensures homogeneous distribution of complexes on the surface of the support and creates the possibility for the arrangement of two AC possessing different stereospecific action in the close vicinity of each other. Comparison of the molecular-mass characteristics and the *xxxx/xxxxy* ratios of the pentad contents (*x*, *y* = *m* or *r*) for the PP samples prepared on the PQ-SiO₂–MAO–**41**, PQ-SiO₂–MAO–**44** and PQ-SiO₂–MAO–(**41** + **43**) catalyst systems with all other factors remaining the same showed that the polymer formed under the action of the binary supported catalyst contained a stereoblock fraction in addition to isotactic and syndiotactic fractions. On the basis of the analysis of ¹³C NMR spectra, it was concluded¹¹⁷ that the chain transfer to TIBA or to the monomer takes place, on average, after 75 steps of insertion. Apparently, due to the low activity of the catalyst and relatively low molecular mass of PP samples (40 000–50 000 g mol^{–1}), data on the properties of polymers are not presented in the publication. The melting temperatures of PP formed on the binary supported catalyst at 30–60 °C are close to those of IPP (*[mmmm]* ≈ 90%) prepared using the supported complex **41**. It should be noted that the use of 'hybridisation' with utilisation of procedures giving rise to highly effective immobilised catalysts¹³⁴ after optimisation of the conditions of their synthesis and polymerisation and with appropriate selection of metallocenes, can prove highly promising for the synthesis of eSBPP or polypropylene composites.

5. Catalyst systems of the post-metallocene type

Since the first publications^{135, 136} and to the present day, the interest in the catalyst systems for olefin polymerisation based on chelates formed by Group VIII elements, so called post-metallocene catalyst systems, has continually increased. Most publications are devoted to the study of catalytic activity, the mechanisms of formation and the properties of polyethylene (PE) formed under the action of these systems (see, for example, reviews^{137, 138}). In recent years, approaches to the design of chiral catalyst systems of this type effective for the synthesis of stereoregular PP have taken shape.^{139–143} The chelate complexes of Group IVB metals can also be regarded as post-metallocene catalysts. In a number of publications,^{144–146} high catalytic activity of these complexes activated by MAO in ethylene polymerisation has been reported. A number of publications have been devoted to the catalyst systems based on Group IVB metal chelate complexes efficient in the synthesis of eSBPP.^{99, 147, 148}

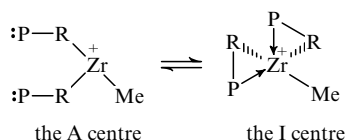
The catalytic activity of MAO-activated zirconium dichloride *rac*-bisacetylacetonate has been studied.⁹⁹ This catalyst system in toluene produces fractions of highly isotactic PP (76%) and eSBPP (24%), while in methylene chloride, eSBPP is formed as the only polymerisation product. It has been suggested⁹⁹ that the cationic metal alkyl complex with a coordinated toluene molecule exhibits an isospecific action. In methylene chloride, which is more polar than toluene, the electrophilicity of the cationic species is manifested as agostic interactions with the growing polymer chain, which result, however, in chain isomerisation rather than chain transfer.



Under certain conditions, this process competes with chain growth and acts a source of 'errors', which deteriorate the growth of isotactic sequences.

Unlike the mechanism realised on C_1 -symmetric catalysts and giving rise to single ...*mrrm*... stereodefects, this mechanism does not rule out the appearance of double 'errors' with the formation of short atactic sequences, which is indicated by the presence of intense signals corresponding to the *mrrm* + *rrmr*, *rmrm* and *rrrm* pentads in the ^{13}C NMR spectrum (see Table 5, row 25). An increase in the reaction temperature promotes more efficient isomerisation. To confirm the proposed mechanism, Shmulinson *et al.*⁹⁹ demonstrated that this system effectively catalyses isomerisation of oct-1-ene to oct-2-, -3- and -4-enes.

High-molecular-mass elastomeric SBPP ($M_w = 120\,000$ – $160\,000\text{ g mol}^{-1}$, $M_w:M_n = 1.7$ – 2.4) is formed on chiral $M(\eta^2\text{-NPhPPPh}_2)_2(\eta^1\text{-NPhPPPh}_2)_2$ complexes ($M = \text{Ti, Zr}$) upon polymerisation in the liquid monomer at 25°C .¹⁴⁷ Apparently, a reason for the formation of alternating isotactic–atactic sequences during polymerisation of propylene induced by these catalysts is reversible coordination of the phosphine ligand resulting in a dynamic equilibrium between the tetrahedral and octahedral isomers. The tetrahedral isomer is aspecific, while the octahedral one is isospecific. The ^{31}P NMR spectra recorded at room temperature point to the predominant formation of the octahedral isomer under the action of MAO, although the tetrahedral complex has also been identified.



The dynamic equilibrium between the tetrahedral and octahedral isomers during polymerisation can result in the formation of isotactic and atactic sequences whose relative lengths are determined by the activity of the complexes. However, in the case of this catalyst system, this is not the only factor deteriorating the growth of isotactic sequences. As in the previous case, Kuhl *et al.*¹⁴⁷ observed isomerisation of alk-1-enes into internal olefins.

The possibility of formation of stereoblock PP as a result of the change in the AC geometry in a dynamic equilibrium during the growth of the polymer chain has been studied¹⁴⁸ in propylene polymerisation in the presence of Ti(III) and Ti(IV) bisallyl chelate complexes, $[(\text{Bu}^t\text{Me}_2\text{SiCH}_2\text{CH}_2)_2\text{Ti}(\mu\text{-Cl})_2\text{Li} \cdot \text{TMEDA}]$ (where TMEDA is N,N,N',N' -tetramethylethylenediamine) and $[(\text{Bu}^t\text{Me}_2\text{SiCH}_2\text{CH}_2)_2\text{TiCl}_2]$. Similar complexes of zirconium induce the formation of isotactic PP under the same conditions. Several allylic complexes of Group IVB metals active in olefin polymerisation have been described.^{149–154} As a rule, these are half-sandwich zwitterion Ti(IV) and Zr(IV) complexes in which the allylic ligand stabilises the electronic state of the active site.^{149–151} The allylic intermediates are described most often as products of deactivation (or temporary deactivation) of the AC.^{152–154}

The Ti(III), Ti(IV) and Zr(III), Zr(IV) bisallylic complexes¹⁴⁸ present unusual examples of comprehensively characterised catalysts active in the polymerisation of ethylene and propylene, in which the M –allyl bond mimicks the type of binding in cene or chelating ligands, and the lability of the allylic bond (σ , η^1 , η^3)^{155–157} determines the stereocontrolling effect. An unusual

finding is that paramagnetic bisallyl Zr(III) ($\mu_{\text{eff}} = 1.5\text{ }\mu_{\text{B}}$) and Ti(III) complexes ($\mu_{\text{eff}} = 1.7\text{ }\mu_{\text{B}}$) are active in the polymerisation of ethylene and propylene upon activation by a slight excess of MAO. Polymers formed in the presence of MAO-activated M(III) complexes possess the same properties as the polymers obtained with M(IV)–MAO catalyst systems (Table 8, rows 4, 5 and 10, 12). It was suggested that, under these conditions, the olefin undergoes oxidative addition to the M(III) bisallyl complex with subsequent formation of the cationic M(IV) alkyl AC upon treatment with MAO. However, participation of the monomer at the active centre initiation step is debatable because the specific activities of M(III)–MAO systems normalised to the monomer concentration are similar (see Table 8, rows 1, 2 and 4, 6).

Table 8. Polymerisation of propylene in toluene induced by the $[(\text{Bu}^t\text{Me}_2\text{SiCH}_2\text{CH}_2)_2\text{M}(\mu\text{-Cl})_2\text{Li} \cdot \text{TMEDA}]$ –MAO catalyst system, where $M = \text{Zr(III), Ti(III)}$, and the $[(\text{Bu}^t\text{Me}_2\text{SiCH}_2\text{CH}_2)_2\text{MCl}_2]$ –MAO catalyst system, where $M = \text{Zr(IV), Ti(IV)}$.¹⁴⁸

Row	Catalyst	Al:M	T_p / $^\circ\text{C}$	$p_{\text{C}_3\text{H}_6}$ /atm	A	$10^{-3}M_w$ /g mol $^{-1}$	$M_w:M_n$ (%)	[mmmm]
1	Zr(III)	400	25	7.2	0.001	16	2.6	61
2	Zr(III)	800	25	7.2	0.003	16	5.3	56
3	Zr(III)	800	50	10.1	0.005	12	2.4	96
4	Zr(III)	1000	25	7.2	0.003	16	2.9	74
5	Zr(IV)	1000	25	7.2	0.002	15	2.9	71
6	Ti(III)	400	0	5.1	0.01	2030	3.6	33
7	Ti(III)	400	25	7.2	0.03	336	2.9	43
8	Ti(III)	400	50	10.1	0.04	78	5.5	45
9	Ti(III)	600	25	7.2	0.04	140	2.5	27
10	Ti(III)	1000	25	7.2	0.03	115	2.7	20
11	Ti(III)	1200	25	7.2	0.03	86	2.8	15
12	Ti(IV)	1000	25	7.2	0.03	115	2.7	22

These catalyst systems induce the formation of polyethylene with a very high molecular mass and a quite substantial polydispersity coefficient, especially in the case of zirconium complexes. Under the action of zirconium complexes, IPP is formed. An increase in the reaction temperature from 25 to 50°C is accompanied by an increase in the isotacticity from 56% to 96% (see Table 8, rows 2, 3). Catalyst systems based on titanium complexes give rise to eSBPP. Ray *et al.*¹⁴⁸ believe that the dynamic change in the geometry of the AC, $C_{2v} \rightleftharpoons C_2$, caused by reversible $\eta^1 \rightleftharpoons \eta^3$ isomerisation of the allylic ligands is responsible for the formation of stereoblocks. Meanwhile, an increase in the Al/Ti ratio is accompanied by a decrease in the molecular mass of the polymer and the content of isotactic pentads and by some decrease in the system activity. Apparently, these facts indicate that the chain transfer by titanium complexes to the organo-aluminium compound and the back reaction can account for the appearance of regular 'errors' in isotactic sequences, similar to the situation observed for the 'hybrid' catalyst systems. Unfortunately, the pentad composition of eSBPP prepared in the presence of Ti(III) and Ti(IV) bisallyl complexes was not reported in the study under discussion.¹⁴⁸

III. Characteristic features of the structure of elastomeric stereoblock polypropylene and the nature of relaxation processes

The possibility of preparing elastomeric materials by homopolymerisation of propylene has triggered considerable interest in these processes. For many elastomers, the influence of the microstructure and the molecular-mass characteristics on the strain, elastic and thermal properties of polymers has been studied. A number of publications have been devoted to the investigation of the rates and mechanisms of the relaxation processes using

differential scanning calorimetry (DSC),^{82, 110, 114} DSC performed in the quasi-isothermal stepwise mode,¹⁵⁸ dynamic mechanical analysis (DMA),^{26, 158, 159} dynamic thermomechanical analysis (DMTA),¹⁰⁷ birefringence,¹⁰⁷ IR polarimetry¹⁰⁸ etc. The structure of the materials has been studied by X-ray diffraction analysis,¹⁰⁷ solid-phase ¹³C NMR spectroscopy, scanning electron microscopy and atomic-force microscopy (AFM).¹⁵⁹ The elSBPP samples subjected to analyses were synthesised using different catalyst systems, both heterogeneous and homogeneous ones based on bridged and non-bridged metallocenes.

The materials prepared using heterogeneous catalysts, namely, non-modified TMC and supported catalysts based on tetraneophylzirconium have been studied.¹¹⁰ The contents of the isotactic pentads in the PP were 60 mass % and 40 mass %, respectively. The samples studied had similar values of melt flow index (0.5 g min⁻¹ at 230 °C under a load of 21.6 kg) and impact strength (280–300 kJ m⁻²). The polymer prepared using TMC was characterised by a higher modulus of elasticity and tensile strength. The DSC curves for homopolymers exhibited clear-cut peaks for melting (from 155 to 140 °C), crystallisation (from 110 to 80 °C) and glass transition (from 4 to -5 °C). The peaks observed at 50 °C correspond, evidently, to relaxation processes in the disordered phase. For the PP samples studied, the DMTA spectra were also measured; they indicated an increase in the material stiffness following an increase in the degree of isotacticity.

The DSC curves for compositionally homogeneous elSBPP samples completely soluble in ether (synthesised using *ansa*-metallocenes) display feebly pronounced melting and crystallisation peaks.^{55, 57, 114}

In a study of the properties of elSBPP produced under the action of homogeneous systems based on non-bridged metallocenes, both the initial samples and separate fractions were analysed, first of all, the fraction soluble in boiling ether, the fraction soluble in boiling n-heptane and that insoluble in boiling n-heptane. For the polymer synthesised using the 16-MAO catalyst system,⁸⁰ two melting peaks were detected (60 and 140 °C), whereas the ether-soluble fraction {36 mass %, [mmmm] = 0.19} showed no peaks in the DSC curves. In the case of the heptane-soluble fraction {43 mass %, [mmmm] = 0.33}, a broadened endothermic peak in the temperature range from 40 to 160 °C was found, pointing to broad size and stability distributions of the crystallites. According to ¹³C NMR spectroscopy, all fractions had a stereoblock structure. For the fraction insoluble in n-heptane {57 mass %, [mmmm] = 0.38}, a melting peak at 150 °C is clearly defined. It can be seen from Fig. 13 that non-fractionated elSBPP exhibits small melting peaks. The pattern of the melting curves depends not only on the method used to prepare the samples but also on their thermal pre-history.

X-Ray diffraction analysis, DSC, and solid-phase ¹³C NMR spectroscopy have been used to compare the structure of the crystallising and amorphous phases of non-fractionated samples and separate fractions of elSBPP prepared by polymerisation under different conditions and differing in the content of mmmm

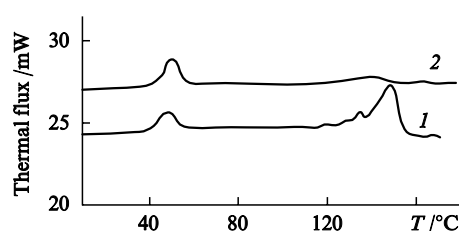


Figure 13. Comparison of the DSC curves of elSBPP samples (16-MAO catalyst system) with different contents of isotactic pentads.⁸⁰ (1) 30% (crystallinity, 11%), (2) 19% (crystallinity, 2%).

pentads and in the molecular mass.¹⁰⁷ Unlike the other smectic fractions, fractions soluble and insoluble in n-heptane crystallise to give α - and γ -forms of PP. It is of interest that only formation of the α -form is noted for the initial polymer. To characterise the degree of ordering of amorphous phases, the influence of the temperature in the range of 20–80 °C on the peak intensity in the ¹³C NMR spectra was studied. The content of the crystalline phase in the elSBPP samples determined from the ¹³C NMR spectra in the solid phase is much higher than the values found by DSC or X-ray diffraction analysis. The results obtained attest to involvement of a synergistic effect in the crystallisation of polymers which contain easily crystallisable chains with high contents of isotactic sequences. The properties of polymers synthesised using the 'oscillating' catalyst and the catalyst containing *rac*- and *meso*-forms of *ansa*-zirconocene were compared as well as those of mixtures of isotactic and atactic PP. The materials were characterised by virtually equal contents of the mmmm pentads. The researchers noted¹⁰⁷ that the thermoplastic elastomers prepared by polymerisation, unlike blend compositions, possess excellent elastic properties even at elevated temperatures. In their opinion, the capacity for relaxation can be regarded as evidence for a multiblock structure of elSBPP. It has been shown by X-ray diffraction analysis, solid-phase NMR spectroscopy and birefringence that samples prepared in the presence of the 16-MAO catalyst behave as elastomers up to a temperature of 80 °C at which they are subject to shear deformation, unlike mixtures of isotactic and atactic PP, which have similar stereoisomer compositions and degrees of crystallinity.

In order to gain a better understanding of the domain structure of elSBPP, Kravchenko *et al.*¹⁵⁸ studied the thermal and morphological properties of PP obtained using the 16-MAO catalyst by the DSC method with temperature fractionation. The PP samples contained 25% and 30% isotactic mmmm pentad; their molecular masses were 240 000–260 000 g mol⁻¹. Preliminarily, the temperature of crystallisation for the studied samples varied from 160 to 50 °C with a step of 10 °C, and the samples were annealed at the appropriate temperatures for 12 h and then heated in the usual way. The resulting curves (Fig. 14) exhibit multiple peaks (Table 9) and differ substantially from the curves observed with fast scanning; this points to the influence of kinetic factors on the processes of crystallisation. Interesting results have been obtained by treating polymeric materials with hot nitric acid:¹⁵⁸ only ~10% of the polymer was insoluble (this corresponds to the content of perfect insoluble crystals). This method is widely used in the investigation of the structures of various polymeric materials. To characterise the domain structure of elSBPP samples, the AFM method was used.¹⁵⁸ Regions consisting of ribbon crystals distributed in the amorphous phase were found in the samples. It was also found¹⁵⁸ that the thickness of the lamellae in elSBPP equals 12 ± 4 nm, which corresponds to 54 monomer units. The elongation at rupture for the material

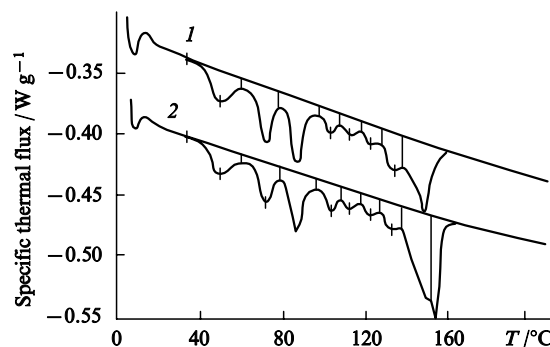


Figure 14. Temperature fractionation of DSC curves for two elSBPP samples with contents of isotactic mmmm pentads of 25% (1) and 30% (2).¹⁵⁸

Table 9. Melting temperatures and heats for eSBPP samples subjected to stepwise annealing.¹⁵⁸

[<i>mmmm</i>] (%)	T_m /°C	ΔH_m /J g ⁻¹
25	46.32	1.059
25	68.71	2.242
25	83.19	3.091
25	100.12	1.274
25	109.11	0.938
25	119.34	0.963
25	129.72	1.399
25	150.07	5.520
25	151.63	2.210
		$\Sigma = 19.39^a$
30	44.07	1.883
30	68.86	2.364
30	93.45	2.860
30	99.98	0.896
30	109.18	0.768
30	119.38	0.635
30	131.21	1.644
30	145.65	3.699
		$\Sigma = 14.93^a$

^a Total heat of melting.

studied reaches 1000% and the tensile strength was 15 MPa. When deformations do not exceed 300%, the hysteresis is high and no destruction of crystals in the samples is observed. In the case of great deformation, the initial lamellar crystallites are destroyed and small blocks are produced, which are mainly contained in fibrils. These processes are similar in mechanism to those taking place in other segmented elastomers such as aromatic polyesters and polyamides. The nanofibrils formed upon drawing contain alternant structures of rigid crystallites and, possibly, initially amorphous segments crystallising under the action of stress with chains oriented in the direction of drawing for both types of segments. The length of these domains is several hundreds of nanometers and the width is ~ 12 nm. After relief of the stress and relaxation, the initial structure of the sample is not restored.

The results obtained in the studies of various samples of eSBPP and their fractions by DSC, DSC with temperature fractionation, by treatment with nitric acid and by AFM point to the cooperative nature of crystallisation processes and to the presence of diffusion and kinetic restrictions.

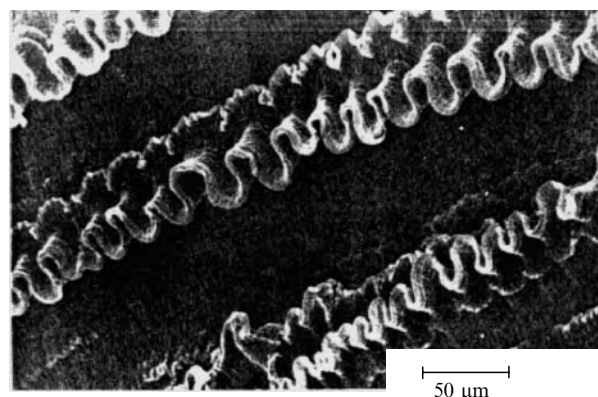
The rates of relaxation processes for compositionally inhomogeneous eSBPP and separate fractions have been studied by the birefringence method.¹⁰⁸ It was shown that the relaxation time and the size of the relaxation plateau depend on the temperature and shear deformation. In the case of 100% deformation, the relaxation time decreases as the temperature rises (2 h at 25 °C, 900 s at 80 °C, and 440 s at 115 °C), and the size of the relaxation plateau changes from 0.62 at 25 °C to 0.43 at 85 °C.¹⁰⁷ The effect of temperature on the rate of the relaxation processes for non-fractionated samples and for separate fractions of PP at different shear deformations (3% to 100%) was studied in detail. In the temperature range of 200–105 °C, complete isotropisation occurs rapidly. At 105 °C and at lower temperatures, the rates and the degrees of isotropisation for the initial samples and for separate fractions are markedly different. It is of interest that repeated application of shear strain resulted under some conditions in an increase in the rate and the degree of relaxation.

The results of studies^{107, 110} indicate that great shear deformations ($\geq 50\%$) are able to destroy the physical junctions at weak points; this gives smaller crystals. An increase in the deformation results in irreversible anisotropy of non-equilibrium crystals. The fractions insoluble in heptane exhibit properties typical of solid elastomers; they are able to induce co-crystallisa-

tion of fractions with lower isotacticity. This results in a higher cross-linking density. It was concluded that the composition and the cooperative role of different fractions determine the elastic properties of materials.

Madkour and Mark^{111, 160} arrived at analogous conclusions. The effect of the molecular mass, MMD and the length and length distribution of isotactic blocks on the moduli of elasticity of the materials have been studied by mathematical modelling. Modelling with allowance for co-crystallisation processes gave the dependences of the modulus of elasticity on the content of isotactic sequences similar to those established experimentally.

The results of an investigation of the fracture mechanism and examination of the fracture surface of eSBPP by scanning electron microscopy are rather interesting.¹¹⁰ The dependence of the fracture energy on the stereochemical composition was elucidated. When the content of the *mmmm* pentads decreases from 60% to 40%, the cohesion energy of fracture for the samples studied changes from 8 to 20.6 kJ m⁻², and the plastic energy, from 53.8 to 9.4 kJ m⁻². In the examination of the fracture surface, the formation of sinusoidal structures parallel to the sample surface and to the load axis has been observed for some samples (Fig. 15). Structures of this type have been described only for some thermoplastic elastomers.

**Figure 15.** Photomicrograph of the fracture surface of the eSBPP sample.¹¹⁰

Thus, it was shown that the regularities observed for eSBPP are similar to those typical of crystalline elastomeric materials. The structure and the properties of the elastomeric PP, as well as of a number of other elastomers are due to the formation of crystallites from thin lamellae or nanofibrils joined by straightened or bent transient chains, which form an amorphous phase in addition to the end chains. The number, volume and the structure of junctions in the physical networks and the degree of ordering of the amorphous phase, the surface free energy of lamellae (end faces), and the values of cohesion and plastic energy determine the sub- and microstructure, the elastomeric properties of these materials, and the patterns of the observed dependences.

IV. Conclusion

The information considered above shows that the discovery of highly effective homogeneous metallocene and post-metallocene catalyst systems has stimulated work on the synthesis of new materials based on polyolefins. Among these, thermoplastic elastomeric stereoblock PP occupies a special place. The interest in its synthesis is great because these polymers can be used as adhesives, binders or elastic films. Numerous catalyst systems and their mixtures have been developed, which allow targeted control of the microstructure and molecular-mass characteristics of elastomeric stereoblock polymers. The mechanism of catalytic

and stereospecific action of these catalysts has been studied. Data on the influence of the microstructure on the mechanical, thermal and relaxation properties of elastomers have been obtained.

This review surveys the state-of-the-art of the research along this line. The necessity of this generalisation is dictated by the vigorous development of the work dealing with the design of new polymeric and structural materials.

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Peptide nucleic acids: structure, properties, applications, strategies and practice of chemical synthesis

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Abstract. The information on the structure and properties of peptide nucleic acids (PNA) is generalised. The use of PNA oligomers in biomolecular studies and biotechnology is exemplified. The published data on the most important methods for the chemical synthesis of PNA oligomers with the main emphasis on the efficiency of condensation reactions are considered. The methods for PNA synthesis are systematised; their advantages and disadvantages are discussed. Some recommendations for optimisation of the condensation procedure and synthesis of PNA are presented. The bibliography includes 153 references.

I. Introduction

Peptide nucleic acids (PNA, **1**) represent analogues of nucleic acids (NA, **2**),^{1–4} but, in contrast to the latter, contain neither carbohydrate nor phosphate residues and have uncharged pseudopeptide backbones.^{1,5–8} The monomeric unit of classical PNA comprises *N*-(2-aminoethyl)glycine and a heterocyclic base (purine or pyrimidine) bound through an acetyl linker. The monomers are linked by amide bonds. The geometry of the achiral backbone and its relative flexibility^{3,9} confer on PNA an ability to mimic, with striking exactness, the spatial structure of carbohydrate–phosphate backbones of NA.⁴

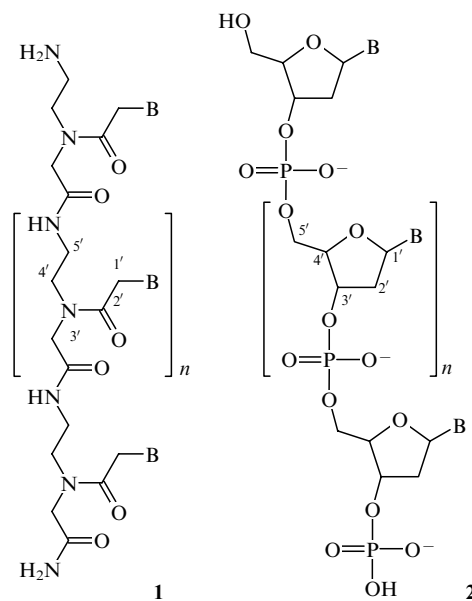
From the chemical standpoint, PNA represent a hybrid of an oligonucleotide wherefrom the nucleases have been adopted and a peptide, the structure of which gave birth to the structural principle of the PNA backbone. Thus, PNA possess properties of both these classes of compounds.^{8, 10} This structural-and-functional duality of PNA determines their unique property.⁴ Indeed, these molecules combine uniquely the strict recognising ability inherent in NA with the flexibility and stability of proteins.

It should be noted that the term 'peptide nucleic acids' is used to point to the structural similarity of these compounds to NA and to reflect the similarity of the PNA oligomeric backbone to that of

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B = Ade, Gua, Thy, Cyt.

peptides, although neither the term ‘acid’ nor ‘peptide’ are applicable to PNA, for in contrast to nucleic acids PNA are not polymeric acids and in contrast to peptides they do not contain amino acids. Nevertheless, the abbreviation ‘PNA’ has now come into general use, although it would be more correct to refer to these compounds as polyamide analogues of oligonucleotides.¹⁰

II. Properties of peptide nucleic acids

Complementary PNA molecules form specific antiparallel PNA–PNA duplexes having helical structures^{4,11} similar to those of DNA and RNA duplexes but, which is even more important, they form highly stable specific (antiparallel and parallel) duplexes with complementary DNA and RNA sequences^{1,5–7,9,12–14} containing Watson–Crick base pairs.^{2,15,16} In all cases, antiparallel PNA–DNA duplexes are more stable than the parallel ones, *viz.*, their melting temperatures differ by ~ 1 °C for each base pair.² The circular dichroism spectra of PNA–DNA and DNA–DNA duplexes are similar,^{2,17} which points to the formation of right-hand helices during the formation of

PNA–DNA duplexes despite the fact that base pairs in PNA–DNA and DNA–DNA duplexes have slightly different geometries.¹⁷ NMR and X-ray crystallography studies of PNA–PNA and PNA–DNA complexes revealed that PNA–PNA duplexes possess broad, deep major grooves and narrow, shallow minor grooves; noteworthy, one complete turn of a helix in PNA–PNA duplexes corresponds to 18 base pairs, whereas that in PNA–DNA duplexes, to 13 base pairs.^{17–20}

PNA–PNA, PNA–DNA and PNA–RNA duplexes are considerably more stable than DNA–DNA, DNA–RNA and RNA–RNA duplexes of the same compositions.^{1, 2, 11–17, 21–23} Even four-membered PNA sequences produce highly stable duplexes with complementary DNAs.¹⁷ In contrast to NA–NA duplexes, the stabilities of PNA–NA duplexes are little dependent on the solution ionic strength.^{2, 24–27} PNA–DNA duplexes are formed faster than the corresponding DNA–DNA duplexes,^{14, 22} but high specificity of hybridisation is preserved.²⁸

The stabilities of PNA–DNA duplexes can be predicted based on a model which takes into account the interactions between only the nearest adjacent bases;^{17, 29, 30} however, this model describes adequately the stabilities of short duplexes comprising no more than eight units.¹⁷

The most essential property of PNA is their unique sensitivity to mismatches in the structure of NA targets.⁷ The difference in melting temperatures of a perfect PNA–DNA complex and a duplex containing one mismatch amounts to 20 °C and even more.³

Peptide nucleic acids form PNA–(DNA)₂ triplexes with double-stranded DNA.^{31–34} These triplexes are less stable than the classical (DNA)₃ triplexes.³⁴ On the other hand, PNA forms stable (PNA)₂–DNA and (PNA)₂–RNA triplexes with single-stranded DNA and RNA targets, respectively.^{5, 12, 14, 16, 33, 35–39} Such triplexes are often formed in the interaction of PNA with double-stranded NA.^{37, 40–44} In the latter case, the formation of triplexes leads to the displacement of one of the DNA strands resulting in complete separation or P-loop formation³⁸ with subsequent incorporation of PNA chains.^{5, 33, 37, 40–44} PNA form Watson–Crick pairs with DNA. The attachment of the second PNA chain is accompanied by the formation of Hoogsteen pairs.^{35, 39} It was found that Watson–Crick chains of PNA are antiparallel to DNA chains, while Hoogsteen strands are parallel to them.^{37, 39}

It is noteworthy that Hoogsteen strands stabilise Watson–Crick PNA–DNA duplexes which are formed first; the latter can be relatively unstable.³⁸

Homopyrimidine PNA molecules and PNA enriched with pyrimidine residues are especially prone to triplex formation.^{9, 35–39} The respective triplexes are extremely stable, *e.g.*, ten-membered (PNA)₂–DNA triplexes have the melting temperatures of ~70 °C.^{9, 39} The ability of cytosine-containing PNA to form triplexes is pH-dependent, since cytosine can form Hoogsteen pairs with guanine residues only in the protonated state.⁹ No triplexes with the composition (PNA)₃ have been found.⁴⁵

Recently, a new type of PNA-containing triplexes has been discovered.³⁷ Both PNA chains in the (PNA)₂–DNA triplex formed upon binding of the PNA oligomer 5′-T₄G₂(TG)₂-3′ to the oligonucleotide 5′-A₄C₂(AC)₂-3′ are in the antiparallel orientation relative to the DNA strand.

The binding potential of PNA with respect to NA is far from being exhausted. Studies of NA-binding properties of PNA aimed at the synthesis of novel PNA possessing improved structures and able to enhance the specific binding of PNA to complementary NA are currently under way.³⁷

The melting of short-chain (PNA)₂–DNA triplexes is a non-equilibrium process, *viz.*, the melting temperature depends on both the concentrations of components and heating velocity.³⁸ Thus, the stabilities of (PNA)₂–DNA complexes were found to be kinetic.³⁸ The dissociation of such triplexes occurs in two steps, *viz.*, the first (limiting) step includes separation of the Hoogsteen

strand of PNA, while the second step includes rapid separation of the Watson–Crick strands of PNA.³⁸

Peptide nucleic acids manifest high chemical and biological stabilities.^{25, 46} They are highly resistant against cell nucleases, proteases and peptidases.^{25, 27, 47} PNA oligomers undergo very slow enzymatic hydrolysis in both cell extracts and *in vivo*.^{25, 46} PNA molecules are distinguished by generally low toxicity and are not prone to non-specific binding to cellular proteins. Being immobilised on solid supports, PNA molecules preserve their hybridisation properties.²⁸

It is known that modifications of NA backbones by replacing phosphodiester or carbohydrate units by non-charged or cationic structures may confer useful properties on NA, *e.g.*, enhanced resistance against nucleases and effective penetration through cell membranes and more specific and stronger binding to complementary target NA.⁴⁸ Attempts are being made to improve the PNA structure in order to increase the ability of PNA for nonspecific binding to NA and their transport across cellular membranes.^{2, 3, 8–10, 36} Thus the addition of certain peptides,^{49–53} *e.g.*, the 16-membered peptide ‘transportan’,^{50, 51} to PNA increases considerably the rate of intracellular transport of PNA.^{9, 23, 49–53} α -Helical PNA (α PNA) have been obtained in which the role of the backbones is played by α -helical peptide structures.^{54–56} Such PNA analogues form highly specific stable Watson–Crick duplexes with complementary NA^{54, 55} and manifest very high biological stabilities.⁵⁶ PNA analogues with chiral backbones with positively and negatively charged groups, PNA–DNA chimeras, *etc.*, have been synthesised.³⁶

Comparative studies of structurally different PNA analogues have shown that classical PNA with *N*-(2-aminoethyl)glycine backbones first synthesised by Peter E Nielsen ten years ago¹ manifest optimum NA-binding properties.⁴ Therefore, the main attention in this review will be given to methods of synthesis of classical PNA molecules based on *N*-(2-aminoethyl)glycine residues.¹

III. Applications of peptide nucleic acids

By virtue of their unique properties,^{13, 37} PNA have found wide use in molecular-biological, biochemical, genetic engineering and clinical investigations.^{2, 3, 14, 26, 27, 36, 57–65} They represent attractive candidates for new-generation genetic therapeutic drugs which interfere selectively with gene expression.^{9, 14, 26, 36, 57, 62–71} The use of PNA oligomers in antisense^{9, 26, 27, 36, 57, 67, 69, 72–74} and antigen^{27, 36, 57, 67, 68, 72, 75, 76} biotechnologies is of considerable promise.

Antisense PNA selectively inhibit the expression of brain proteins.⁴⁷ The design of anticancer and antiviral drugs based on PNA seems to be a very promising approach.^{26, 57, 65} Some PNA derivatives manifest antibacterial³⁶ and antisense activities^{9, 47} towards eukaryotic cells and animal organisms.^{9, 47}

There is evidence that PNA interfere with all the key stages of gene expression.^{9, 46, 57, 77} Used in nanomolar concentrations, PNA cause a practically complete specific arrest of transcription of DNA templates.^{46, 78} The usefulness of PNA oligomers in gene-oriented technologies has been demonstrated with a PNA-dependent arrest of transcription elongation of RNA polymerase as an example.^{27, 46, 67, 68, 72} By virtue of their ability to induce effective blocking of transcription, PNA oligomers represent potential inhibitors of cell growth, which makes them a useful tool in the design of antitumour drugs.⁷⁸

PNA duplexes and especially triplexes with mRNAs, *e.g.*, PNA–RNA and (PNA)₂–RNA, effectively inhibit the translation of mRNA.^{67, 73, 74} Their potent antisense effects *in vitro* are due to high specificities and stabilities of triplex (PNA)₂–RNA.³⁸ The arrest of translation elongation of mRNA occurs even upon addition of six-membered complementary homopyrimidine PNA.⁷³

The antisense efficiencies of duplex-forming PNA are lower than those of triplex-forming ones; in this case, no less than 20-

membered PNA are required for the inhibition of translation elongation of mRNA (however, the translation initiation can be arrested due to formation of even short-chain PNA–RNA duplexes).^{73,74} Nevertheless, RNA molecules in hybrid PNA–RNA duplexes are not cleaved by RNase H.^{67,73,79–81} The antisense effect of duplex-forming PNA is largely due to steric hindrances upon formation of stable PNA–RNA complexes⁹ which hinder the translation of mRNA. PNA-induced degradation of mRNA, which is unrelated to the effect of RNase H, should not be ruled out either.⁹

Duplex-forming PNA can inhibit translation *in vitro*, being specifically directed against the binding sites of ribosomes, whereas triplex-forming PNA are more specific against polypurine sites located ‘below’ the translation initiation point.⁹

Peptide nucleic acids are used for mapping of RNA molecules in molecular biological studies, particularly for detection of RNA domains responsible for binding to other RNAs and peptides.⁸⁰ Their applications open up new possibilities for elaboration of novel approaches to the study of RNA–RNA and RNA–protein interactions and such processes involving non-translatable RNA molecules as splicing. There is evidence that PNA molecules behave as effective ‘traps’ for some DNA-binding proteins.⁸¹ PNA–DNA chimeras are convenient primers for DNA polymerases.⁸² In recent years, PNA have extensively been used as biomolecular tools for the studies of various intracellular processes.^{2,3,8,10,27,57,61–64,80–82}

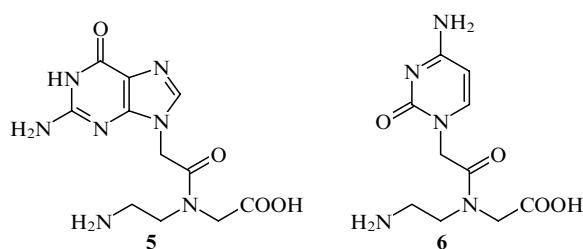
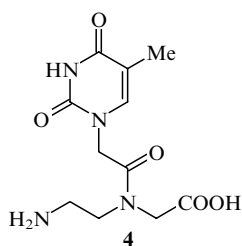
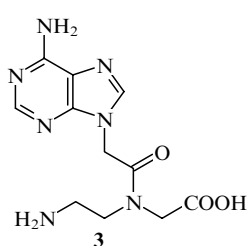
The use of PNA in the design of efficient procedures for the detection of hybridisation, which are extremely sensitive to mismatches in NA targets, is a promising approach.^{28,83} Fluorescently labelled PNA are used as diagnostic probes for detecting specific NA sequences and for the study of penetration of PNA oligomers through cellular membranes and their intracellular distribution.^{84–87} The use of PNA in combination with ion-exchange HPLC (the detection limit is 150 pmol),⁸⁸ MALDI TOF mass spectrometry,⁸⁹ capillary electrophoresis⁹⁰ and other advanced analytical techniques⁸⁸ allows reliable identification of specific genetic sequences in various test samples.

The use of PNA in the design of electrochemical biosensors^{28,91–93} opens up new possibilities for fast screening of primary NA structures and helps overcome many problems of modern biotechnology.^{2–4,8,10,61} These compounds can be used as an outstanding basis for the construction of new generations of highly efficient diagnostic tools, *e.g.*, biochips.⁸³

In this context, the development and optimisation of versatile techniques for the synthesis of PNA oligomers are becoming currently central tasks. The condensation of PNA monomers and oligomers with formation of amide bonds induced by various activating reagents is the key step in PNA synthesis. The combination of protective groups, deprotection and capping conditions as well as post-synthetic work-up of synthetic PNA oligomers strongly depend on the condensation method used.

IV. Basic principles of chemical synthesis of peptide nucleic acids

The chemical synthesis of PNA molecules consists essentially in the oligomerisation of the monomers 3–6 comprising *N*-(2-aminoethyl)glycine backbones and acetic acid residues (acetyl linkers), each containing one of four nucleobases as a substituent.¹⁴ At present, a broad range of methods for the chemical



synthesis of PNA are available; the most efficient of them have become especially popular in the past decade.^{14,94–97}

First of all, a solid-phase methodology is applied for the synthesis of PNA. The synthesis of oligomeric molecules on the surface of polymeric supports was first developed by Merrifield for the synthesis of peptides and proteins in 1962. The strikingly simple idea to immobilise growing oligomeric chains on solid supports has brought biooligomer synthesis to a qualitatively new level. At present, the principle proposed by Merrifield⁹⁸ is widely used in the synthesis of peptides and proteins as well as of DNA and RNA fragments (oligonucleotides). In the overwhelming majority of cases, PNA oligomers are also synthesised on solid polymeric supports. In this review, the main emphasis will be laid on the problems related to the efficiency of solid-phase synthesis of PNA.

Although PNA oligomers can be synthesised by classical methods commonly employed in peptide synthesis,¹⁴ specially designed condensation procedures should be preferred, taking into account peculiarities of chemical structures of PNA monomers. In fact, of the different methods for the activation of carboxy groups based on the use of activated esters, symmetrical anhydrides, acid halides and *in situ* activating reagents, the *in situ* activation has become the most promising approach, which is currently especially popular.

This method envisages the use of reagents based on uronium and phosphonium salts which effect fast (within several seconds) activation of carboxy groups of PNA monomers. Owing to high activation rates, mixing of PNA monomers with an activating reagent can be performed directly in a column with a polymeric support to which the growing oligomeric chain is attached (it is this procedure that represents *in situ* activation) or immediately before the addition of the monomer to the reaction column. This makes it possible to conduct PNA synthesis in an automated regime.

The solid-phase procedure for PNA synthesis involving *in situ* activation will be considered below; its advantages have been corroborated by chemical practice. The data on the efficiencies of other activation techniques can also be useful and proper consideration will be given to them.

V. Factors determining the efficiency of condensation in the synthesis of peptide nucleic acids

The yields of condensation products in the synthesis of PNA using the *in situ* activation procedures depend critically on a number of factors. The most essential of them are as follows:

- the nature and concentration of the activating reagent;
- the nature and concentration of the PNA monomer;
- the nature of a nucleobase component of the PNA monomer and the nature of the nucleobase incorporated into the PNA oligomer in the preceding step;
- the nature and the concentration of a base (as a rule, tertiary amines);
- the nature of the solvent(s);
- the presence or absence of catalysts, *e.g.*, 1-hydroxybenzotriazole;
- the experimental procedure (*e.g.*, preactivation of the PNA monomer or mixing of the PNA monomer with the condensation reagent *in situ*);

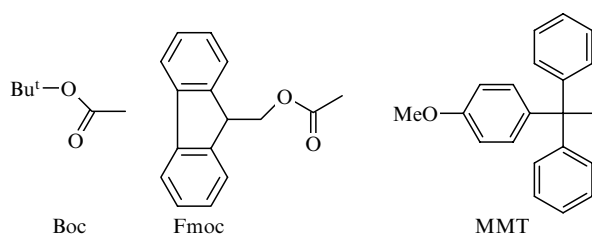
— condensation conditions (reaction time and temperature);
 — other conditions (*e.g.*, the quality of reagents, dryness of solvents, inertness of the reaction atmosphere, *etc.*).

It should be noted that information concerning the dependence of the yields of the condensation products on the nature of the heterocyclic bases of PNA monomers is practically absent. This problem demands special investigation. The majority of literature sources cite average yields of PNA condensation products calculated per coupling cycle of a hypothetical monomeric fragment (irrespective of the nature of the monomer) or the total yields of the PNA oligomer.

It seems reasonable to consider all the factors mentioned above. Hence, it is expedient to discuss in detail the main aspects related to the efficiencies of PNA condensations inherent in particular synthetic strategies.

VI. The main strategies of peptide nucleic acid synthesis

Usually, PNA synthesis utilises conventional solid-phase peptide synthesis protocols.¹⁴ Three synthetic strategies are currently especially popular which produce PNA in high yields and purity. These strategies differ in the nature of protective groups blocking 5'-terminal primary aliphatic amino groups in PNA monomers. *tert*-Butoxycarbonyl (*t*Boc or Boc), 9-fluorenylmethoxycarbonyl (Fmoc) and 4-methoxyphenyldiphenylmethyl (monomethoxytrityl, MMT) groups are generally used as protective groups, and Boc,^{12, 94, 99, 100} Fmoc,^{77, 97, 101–106} and MMT strategies^{96, 107–112} of PNA synthesis are distinguished, correspondingly.



The chemical nature of these groups and the differences in the conditions for their removal determine the choice of optimum condensation reagents and condensation conditions for each particular strategy, although the main principles of PNA synthesis are the same.

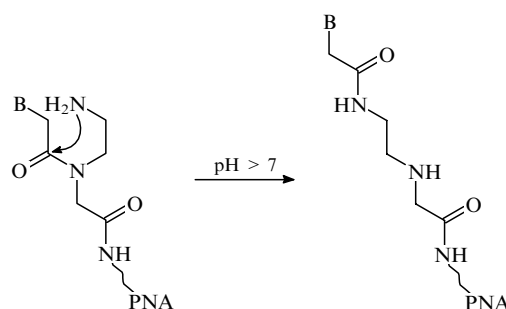
The Boc strategy^{12, 94, 99, 100} was the first to be used for the PNA synthesis. In this case, exocyclic amino groups of heterocyclic bases are usually protected by the benzyloxycarbonyl (Z, Cbz) group (the Boc/Z version),⁹⁴ and *O*-benzyl groups are sometimes used as additional protective groups for guanine.¹¹³ The Boc/acyl version of the Boc strategy, where exocyclic amino groups of nucleobases are protected by acyl groups, has also been described.⁹⁵ One of the well-known disadvantages of the Boc strategy is the necessity to use strong acids for the removal of Boc groups (trifluoroacetic acid) and the cleavage of PNA oligomers from the polymeric supports (hydrofluoric acid, trifluoromethanesulfonic acid, *etc.*). Such drastic conditions limit the range of PNA synthesised according to the Boc protocol.

A search for milder conditions has led to the development of the Fmoc strategy of PNA synthesis.^{14, 77, 96, 97, 101–106, 114} Here, the Fmoc groups are removed by mild treatment with piperidine.¹⁴ The benzyloxycarbonyl (Z),⁹⁷ benzhydryloxycarbonyl (Bhoc)¹⁰⁶ or MMT groups^{12, 96, 114} are used to protect amino groups of nucleobases. The advantage of a Fmoc/acyl version of this strategy^{77, 102–105} is the possibility of selective removal of the Fmoc groups without affecting the acyl protective groups of the heterocyclic bases.^{102, 103} The use of this strategy ensures higher yields of PNA in comparison with the Fmoc/Z strategy, while the

conditions for PNA synthesis are compatible with those of peptide and oligonucleotide syntheses.^{104, 115} This opens up new opportunities for the synthesis of hybrid PNA–DNA and PNA–peptide molecules.

In addition to Boc and Fmoc protection, it was proposed to use MMT groups for protection of 5'-terminal primary amino groups.^{96, 107–112, 116} Although the MMT group, like the Boc group, is acid-labile, this can be cleaved under considerably milder conditions than the Boc groups (the MMT groups are split off by treatment with 3% trichloroacetic acid).¹⁰⁷ In the MMT strategy, the amino groups of heterocyclic bases of the PNA monomers are usually protected by acyl groups (*e.g.*, acetyl, isobutyryl, anisoyl, benzoyl, *tert*-butylbenzoyl) (MMT/acyl version of the MMT strategy).^{96, 107, 110, 116} The reaction conditions are mild, which makes it possible to perform automated synthesis of PNA oligomers using the oligonucleotide synthesisers, while their compatibility with oligonucleotide synthesis protocols allows one to obtain PNA–DNA chimeras.^{107–109}

The efficient condensation requires that the 5'-terminal amino groups were not protonated, since in the form of cations they do not manifest nucleophilic properties. However, under basic conditions where the amino group is not protonated and hence is active, the undesirable transfer of the *N*-terminal acetyl group with the attached heterocyclic base to 5'-terminal primary aliphatic amino group may take place.^{94, 97, 115, 117}

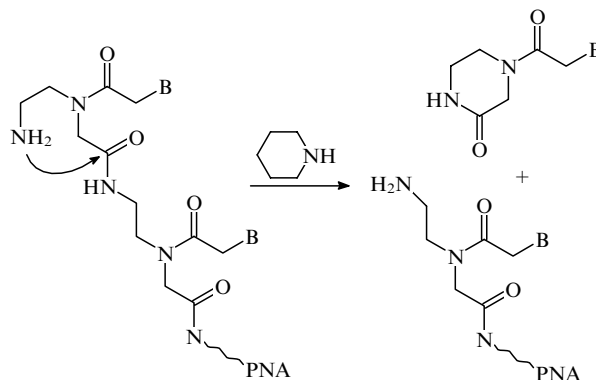


PNA — C-terminal fragment of the PNA oligomer.

This reaction can also occur under neutral conditions⁹⁴ resulting in the break of growing PNA chains and accumulation of short-chain oligomers. This affords a mixture of products and the isolation of target PNA presents a serious problem.

The formation of isomeric structures can be avoided provided the condensation is very fast. In this case, side products cannot be formed, since the *N*-acyl transfer is a rather slow process.^{94, 97, 100, 117} In the presence of reagents based on uronium and phosphonium salts, the condensation occurs so fast that even *in situ* activation of carboxy groups of PNA monomers is possible.

Splitting of the *N*-terminal monomeric unit¹² under the action of piperidine used for removal of Fmoc groups is yet another side reaction.



It should be stressed that the problem of side reactions and the efficiency of PNA synthesis on the whole depend critically on the combination of protective groups used. Indeed, the Boc and Fmoc strategies differ essentially in the conditions of deprotection of 5'-amino groups of the last added monomer. As mentioned above, the removal of Boc groups requires rather drastic acidic treatment, which leads to the protonation of 5'-amino groups. Therefore, this group should be neutralised before the addition of the next monomeric fragment, which is not required in the case of the Fmoc strategy.

On the other hand, the removal of Boc groups is always quantitative and rather fast, whereas splitting of Fmoc groups by basic treatment proceeds slowly and not always completely,^{118, 119} which negatively affects the efficiency of condensation.

Aggregation of growing oligomeric chains is an additional obstacle to efficient condensation. Interchain aggregation makes the deprotected terminal amino group only partly accessible for subsequent condensation, which decreases the efficiency of the process on the whole.^{120, 121} It should be noted that aggregation is only possible in the case of the non-protonated amino group.^{120, 121} Apparently, repulsion of positively charged amino groups prevents the aggregation of oligomers. Thus, the interchain aggregation never takes place in acidic media and terminal amino groups are more accessible to condensation. However, the amino group cannot efficiently react with the activated monomer, since its nucleophilicity is suppressed.

Deprotonation of terminal amino groups of PNA with simultaneous condensation (neutralisation *in situ*) is the most elegant approach to solving this problem. This methodology was first employed for peptide synthesis in 1987.¹²² The use of neutralisation *in situ* in the synthesis of peptides using Boc and Fmoc protocols results in a significant increase in the condensation rate.^{123–125} This effect was especially spectacular in the synthesis of 'problematic' sequences which are especially prone to undergo interchain aggregation. Their syntheses by conventional methods involving preliminary neutralisation of terminal amino groups face the most serious problems.^{126, 127}

At present, neutralisation *in situ* has become very popular for the synthesis of PNA along with conventional methods where deprotonation of 5'-amino groups of PNA oligomers precedes condensation. In some cases, the use of neutralisation *in situ* helps solve the problem of side reactions of PNA isomerisation and increases the yields of condensation products.

VII. Some regularities of condensation reactions in the synthesis of peptide nucleic acids

A detailed knowledge of condensation reactions associated with PNA synthesis and a search for efficient procedures for its optimisation demand that the data available should be interpreted with due regard to the nature of reagents used for the activation of PNA monomers. The methods for the synthesis of PNA–DNA chimeras are described separately, since in this case condensation has a number of specific features.

1. Activated esters and carbodiimide activation

For the first time, the method of activated esters has been successfully employed for the synthesis of thymidine PNA oligomers.^{1, 5} The synthesis of thymidine PNA using Boc-protected pentafluorophenyl (PFP) ester of a thymidine PNA monomer as a monomer was carried out in 1992.⁵ When the monomer concentration was 0.1 mol litre⁻¹, the yield of the condensation product was > 99%. However, an attempt to apply this method to the synthesis of cytidine PNA oligomers was without success: the yield of the target product did not exceed 50% under identical conditions.⁶

There are some examples of successful applications of the method of activated esters for the synthesis of heterogeneous PNA. Thus the synthesis of PNA oligomers from Fmoc/Z-protected monomers by ester activation has been described.⁹⁷

This was one of the first examples of the implementation of the Fmoc protocol to the synthesis of PNA. In this case, the use of the activated esters strategy ensured high efficiency of condensation.

The yields of condensation products in the synthesis of PNA oligomers with the chain lengths of up to 20 residues varied from 95% to 99%.⁹⁷ The average yields in the synthesis of PNA containing all the four types of nucleobases were 97% over each step, which corresponds to the 70% yield of target oligomers. With allowance for subsequent isolation, the yield of PNA oligomers was 43%.

It is of note that the choice of strategies for the synthesis of PNA is often determined by the necessity to obtain high yields of condensation products at low expenditures of expensive PNA monomers where the use of manyfold (fourfold and higher) monomer excess is undesirable. A combined use of the Fmoc protocol and PFP activation allows the use of as little as a twofold excess of PNA in a single condensation.⁹⁷ The use of threefold (or greater) excesses of PNA monomers did not result in further increase in the yields of condensation products. The dimethyl sulfoxide (DMSO)–*N*-methyl-2-pyrrolidinone (MP) mixture (1 : 4) appeared to be the solvent system of choice.⁹⁷ Apparently, this system favours rapid access of the reagents to the growing PNA oligomers.¹²⁸ However, for other activation procedures, other solvent systems were more efficient.

The use of the activated esters approach to PNA synthesis sometimes gives reasonable results;¹² however, in the majority of cases, higher (94%–99%) yields of condensation products were obtained using the *in situ* activating reagents.^{1, 5} In principle, the PNA synthesis can successfully be performed using the so-called carbodiimide activation involving, e.g., dicyclohexylcarbodiimide (DCC) or *N,N'*-diisopropylcarbodiimide,¹² which sometimes affords high (up to 98%–99%) yields of condensation products.^{6, 7} Low rates of PNA condensation is the main disadvantage of this activation procedure.⁹⁹

Carbodiimide activation by DCC made it possible to obtain addition products of thymidine and cytidine PNA monomers in quantitative yields. Purine monomers are only partly incorporated into PNA oligomers; repeated condensation does not result in quantitative yields of the addition products.

The use of *N,N'*-diisopropylcarbodiimide as the activating reagent has made it possible to obtain nearly quantitative yields even for purine monomers.⁹⁹ However, this required the use of a fourfold excess of the monomers and the activating reagent, and the condensation lasted no less than 60 min.⁹⁹ In addition, the introduction of the adenine and the guanine monomers into PNA oligomers required two and three condensation cycles, respectively.

The carbodiimide activation is a convenient procedure for obtaining PNA adducts with other molecules. Thus the synthesis of hybrid PNA peptides containing biotin residues, which confer on PNA the ability to penetrate cell membranes efficiently, has been described.¹²⁹ The peptide fragment of the chimeric molecule was prepared using a standard peptide synthesis protocol,¹³⁰ while the synthesis of the PNA fragment was carried out manually, using the Boc strategy based on the methods described in the classical work by Nielsen.⁹⁴ The activation with DCC was performed in the presence of 1-hydroxybenzotriazole, using a fivefold excess of a PNA monomer. The condensation was performed at an elevated (37 °C) temperature to increase the yield of the target product.¹²⁹

In other examples of the synthesis of hybrid PNA–peptide molecules,⁴⁹ the Boc protocol was combined with carbodiimide activation.^{94, 129} Such an approach to the preparation of chimeras is justified, since it ensures complete compatibility of syntheses of both the peptide and PNA fragments of the hybrid molecules⁴⁹ and overall yields of target products of no less than 50%.⁴⁹

A combined use of carbodiimide activation with the Boc/acyl protocol common in peptide synthesis,¹³⁰ allows one to obtain both classical PNA molecules with *N*-(2-aminoethyl)glycine backbones and molecules with non-canonical backbones containing

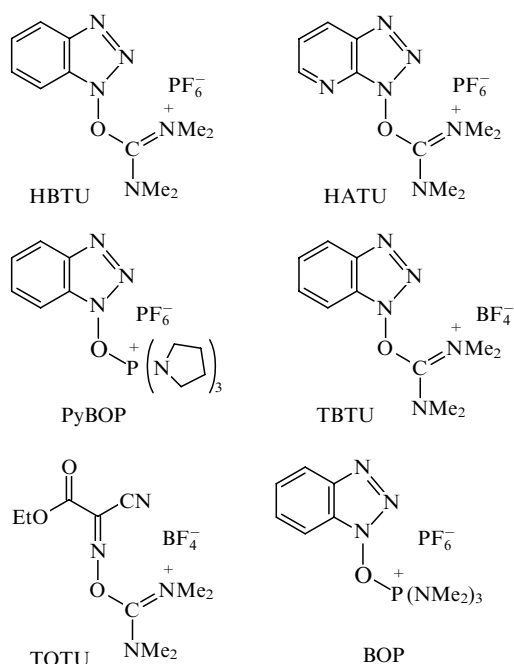
optically active monomeric fragments where the glycine residues are substituted by other amino acids, *e.g.*, lysine, serine, isoleucine and glutamic acid.¹³¹ Incorporation of D-lysine-based monomers into PNA oligomers increases the stabilities of PNA–DNA and PNA–RNA duplexes. With other amino acids, the stabilities of these types of duplexes are usually low.¹³¹

In some cases, such as in the synthesis of PNA–peptide chimeras and thymidine PNA oligomers, the activated esters and carbodiimide methodologies are employed. Sometimes, the yields of condensation products prepared by the activated esters (PFP) method even exceed those obtained by *in situ* activation.⁹⁷

Nonetheless, it is generally acknowledged¹² that PNA synthesis based on the use of *in situ* activation reagents, *viz.*, uronium and phosphonium salts, is the most reliable approach, since it ensures higher yields of the condensation products. This approach has considerably been developed in the recent years and it is this procedure that offers the broadest opportunities for the synthesis of PNA and their derivatives.

2. *In situ* activation by reagents based on uronium and phosphonium salts

The most popular activating reagents for PNA synthesis are *O*-(benzotriazol-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (HBTU), *O*-(7-azabenzotriazol-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (HATU), (benzotriazol-1-yloxy)tris(pyrrolidino)phosphonium hexafluorophosphate (PyBOP), *O*-(benzotriazol-1-yl)-1,1,3,3-tetramethyluronium tetrafluoroborate (TBTU), *O*-[(ethoxycarbonyl)cyanomethylideneamino]-1,1,3,3-tetramethyluronium tetrafluoroborate (TOTU) and (benzotriazol-1-yloxy)-tris(dimethylamino)phosphonium hexafluorophosphate (BOP), although other reagents are also known.



Since condensation strongly depends on the strategy used for PNA synthesis, in the first place, on the combination of protective groups, it seems expedient to classify the data on the *in situ* activation into three groups corresponding to Boc, Fmoc and MMT strategies.

a. The Boc strategy

The Boc/Z-modification of the Boc strategy is a classical approach to PNA synthesis. The dependence of the condensation efficiency of the Boc/Z strategy on different factors has been studied in sufficiently great detail.⁹⁴ This strategy makes it possible to obtain high yields of PNA containing > 15 units with all the four types of

heterocyclic bases. The use of the carbodiimide activation procedure for the synthesis of such oligomers is usually less efficient.⁹⁴

Studies of the effects of various factors, such as the nature of activating reagents, solvents, monomer concentrations, the nature of the organic base (tertiary amine), catalysts, *etc.*, on the efficiency of condensation in the *in situ* activation revealed that all of them are important for the optimisation of condensation conditions.⁹⁴

Comparison of the efficiency of condensations under the action of some uronium activating reagents, *viz.*, the most popular reagents HBTU and TBTU and the relatively new reagents HATU and *O*-(1,2-dihydro-2-oxo-1-pyridyl)-*N,N,N',N'*-bis-(tetramethylene)uronium hexafluorophosphate (HDPU), revealed that the condensation was efficient in all the cases under study, but the yields of addition products were the highest with HBTU.^{94, 100}

It should be noted that these results are valid exclusively for a DMF–pyridine solvent system and for the concentrations of the PNA monomer and the base [diethyl(cyclohexyl)amine, DECHA] of 0.05 and 0.1 mol litre⁻¹, respectively. Under these conditions, the average yields of the condensation products were 92.2%–97.1% irrespective of the nature of PNA monomers. However, conditions can be selected where other activating reagents will be more efficient than HBTU, *e.g.*, in other solvent systems or in the presence of other bases. This suggests that condensation conditions are to be chosen for each activating reagent.

Comparison of the efficiencies of HBTU and PyBOP has demonstrated the former to be superior under identical conditions. The overall yields of PNA oligomers using HBTU and PyBOP activation were 61% and 40%, respectively, which corresponds to average yields of 97.1% and 94.7% in each step.^{94, 100} It is of note that this comparative study was carried out under conditions optimum for HBTU.

An important role in efficient condensation is played by the solvent system used. Thus in a DMF–pyridine mixture, the overall yield of the condensation product was 61%, whereas those in DMF or DMF–DMSO were 55% and 22%, respectively.⁹⁴ However, it was not indicated which monomers determined the lowest yields of PNA. Noteworthy, virtually none of the works cited in this review provide these data.

Studies of the dependence of the yield of a PNA oligomer on the nature of an organic base (tertiary amine) have shown that 4-dimethylaminopyridine (DMAP), DECHA, (dicyclohexyl)methylamine and (dicyclohexyl) ethylamine were as efficient as (diisopropyl)ethylamine (DIPEA) which is widely used in peptide synthesis.⁹⁴

The nature of the tertiary amine only slightly affected the yields of the condensation product (93.7%–95.3%). The condensation in the presence of DIPEA in the DMF–pyridine system is not optimum, since this amine reacts with the monomers to give insoluble salts. Better conditions for this reaction can be found. The condensation in the presence of DIPEA is efficient in MP–DMSO.

Studies of relationships between the yields of condensation products and concentrations of PNA monomers revealed that acceptable yields can be obtained when the monomers are used at concentrations no less than 0.1 mol litre⁻¹. At lower concentrations (0.05 mol litre⁻¹), the condensation proceeds as a rule too slowly resulting in the accumulation of side products from competing reactions.⁹⁴

Addition of catalytic amounts of DMAP and 1-hydroxybenzotriazole to the reaction mixture may have a negative effect on the efficiency of condensation, although it is known that their addition sometimes favours the formation of amide bonds.⁹⁴

The loading[†] of the polymeric support should not exceed 0.1–0.2 mol-equiv. g⁻¹, which is essential for the maximum yield

[†] Here, loading is expressed as the number of functional groups per unit surface area.

of the PNA oligomer. With a higher degree of loading, the efficiency of PNA synthesis is lower.^{94, 100}

The use of the Boc/Z strategy ensures high (99.4%) yields of target products with *in situ* activation (HATU) in the presence of DIPEA.⁹⁵ In this case, the reaction mixture must contain a large (e.g., sevenfold) excess of the PNA monomer with respect to loading of the polymeric carrier.⁹⁵ The amount of the activating reagent is usually reduced by 10%, while the tertiary amine is taken in a twofold excess with respect to the PNA monomer.⁸⁸

Acceptable yields are obtained with a fourfold excess of the PNA monomer and by activation with HATU (the amount of HATU is 0.9 mol-equiv. with respect to a monomer) in the presence of DIPEA and lutidine.⁴⁷ The use of a fivefold excess of PNA monomers and a tenfold excess of DIPEA makes it possible to increase the overall yields of PNA oligomers to 92%.¹⁷

Very often, the yields can be increased upon preactivation of PNA monomers. To this end, the PNA monomer is mixed and incubated with the activating reagent for several seconds before being loaded onto the column.^{95, 96, 109, 110, 113, 115, 116} Strictly speaking, here we do not deal with the *in situ* activation, however, the term '*in situ* activation' is conventionally related to the nature of the activating reagent rather than to the order of mixing of the reagents. It is of note that the methodology of preactivation does not imply the isolation of activated monomers. Usually, the amount of the activating reagent is 5%–10% smaller than that of the monomer.

Preactivation of PNA monomers by incubating them with the activating reagent for 2 min and condensation in an MP–pyridine mixture make it possible to obtain PNA oligomers in overall yields of 90%. Depending on the length and composition of sequences, the yields of PNA vary from 68% to 90%.⁸⁸

In a search for the most rational technique for PNA synthesis, an investigator has to select between a rapid and cheap synthesis with the use of a small excess of PNA monomers and low (but acceptable) yields and lengthy syntheses with large expenditures of expensive monomers and activating reagents, but giving nearly quantitative yields.

Attempts to specify the conditions for effective synthesis of PNA have been undertaken time and again.⁹⁵ Primary attention in the optimisation of PNA synthesis is usually given to such factors as the low cost and ease of synthesis of PNA monomers, nearly quantitative yields of condensation products, the simplicity and efficiency of the procedure for isolation of PNA oligomers from the reaction mixture after completion of the synthesis and the possibility to obtain chimeric DNA–PNA duplexes and ligand-containing PNA molecules.

Such a choice of optimisation parameters seems to be justified, however, other factors, such as reaction rate and economy, are no less important. Thus the rate of condensation should be high enough to minimise side reactions. The synthetic strategy should first of all be efficient and allow for economic expenditure of expensive PNA monomers and activating reagents. The latter factor is of crucial importance in large-scale syntheses of PNA.

While comparing the Boc/Z and the Boc/acyl strategies of PNA synthesis, preference is given to the latter, since it is thought to be more promising. Although the average yields of oligomers calculated per one condensation cycle are high in both cases, *viz.*, no less than 98% (Boc/acyl) and about 99% (Boc/Z), the yields of PNA oligomers in the case of the Boc/acyl synthetic strategy and conventional isolation procedure do not exceed 65% (relative to the support loading), and are as low as 20% according to the Boc/Z protocol.⁹⁵ In addition, the Boc/acyl strategy allows one to synthesise PNA–DNA chimeras and to prepare addition products of acid-labile ligands to PNA, which is inattainable in the case of the Boc/Z strategy.⁹⁵

The synthesis of thymidine PNA oligomers makes use exclusively of Boc-protection of 5'-terminal amino groups, since the thymidine PNA monomer does not require protection of the heterocyclic base.^{77, 79} Such oligomers are conveniently synthesised by manual techniques.⁷⁹ In this case, by analogy with

previously developed procedures,^{94, 131, 132} the Boc strategy is combined with HBTU activation in the presence of DECHA. This approach affords high yields of condensation products, but requires the use of a fourfold excess of PNA monomers.⁷⁹

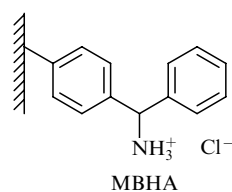
The Boc strategy is also used in the synthesis of PNA oligomers containing modified units.^{131, 133–135} Thus PNA molecules may incorporate units containing anthraquinone and acridine residues.¹³³ Such oligomers are used to study the melting behaviour of hairpin-shaped PNA of high-molecular-mass PNA–PNA duplexes by fluorescence quenching (the so-called 'molecular beacon' method). High yields of condensation products are obtained. Its repeated condensation is used for the attachment of a modified PNA monomer followed by a non-modified monomer to PNA oligomers.¹³³

The Boc/Z method combined with HBTU activation^{94, 134} allows synthesis of PNA molecules with fluorescent labels at their N-termini.¹³⁴ Such PNA derivatives can be used for detecting specific NA sequences. The fluorescence of the label may increase more than 50-fold upon hybridisation of PNA with the complementary NA target in comparison with that of the free PNA.¹³⁴

The classical Boc/Z strategy is also used for the synthesis of PNA chimeras containing clusters of modified fragments, *e.g.*, those with positively charged, chiral backbones built up of D-lysine residues.¹³⁵ The presence of such fragments in PNA confers useful properties on the latter.^{131, 135} In contrast with ordinary PNA, chimeric PNA form exclusively antiparallel duplexes with DNA; their stability depends critically on the presence of mismatches. Even one mismatch decreases sharply the stability of hybrid duplexes. If a mismatch is located in the middle of clusters containing three modified residues, ten-membered PNA–DNA duplexes are unstable even at 15 °C ($\Delta T_m = 28$ °C). Such PNA can serve as the basis for the development of genetic diagnostic tools, particularly, for the detection of point mutations.

Synthesis of these PNA derivatives by the Boc strategy combined with HBTU activation in the presence of DECHA,^{131, 136} affords chiral oligomers in overall yields of 80%–90%,¹³⁵ and optical purity of no less than 90%.

In the majority of cases, the Boc protocol includes the use of standard polymeric supports containing (4-methylbenzhydryl)-amino groups (MBHA).^{11, 131, 132, 135, 136}



PNA oligomers are cleaved from the solid phase by treatment with $\text{CF}_3\text{COOH} - \text{CF}_3\text{SO}_3\text{H}$.^{11, 131, 136}

The Boc strategy allows the use of various activating reagents including BOP.¹³⁷ The use of BOP and DIPEA as a base affords high yields of condensation products in various solvent systems, *e.g.*, DMF– CH_2Cl_2 and DMF–DMSO. In this case, the use of a twofold excess of PNA monomers is sufficient, but each condensation reaction should be repeated in order to provide more efficient binding of the monomers.¹³⁷

PNA can also be synthesised using the Boc/Z strategy combined with the *in situ* activation with TBTU in DMF–pyridine¹¹³ as described in the classical work of Nielsen.⁹⁴ However, it is more expedient to carry out the condensation in DMF in the presence of a twofold excess of DECHA as a base with respect to the monomer. This is associated with the good solubility of PNA monomer salts formed in DMF.¹¹³ The use of a threefold excess of PNA monomers is optimum. This approach allows one to use 2-amino-6-benzoyloxypurine with the non-protected amino group as a guanine precursor.¹¹³ The side reaction (capping) of the oligomeric chain can be avoided if the amount of TBTU is 10%

less than that of the PNA monomer¹¹³ or if the PNA monomer is subjected to 5-min preactivation.⁹⁶

Capping of oligomeric chains occurs both in PNA and peptide synthesis¹²³ provided the free activating reagent is present in the reaction mixture. This is possible owing to the fact that the terminal amino group of the peptide following deprotection reacts with both the activated amino acid derivative and the activating reagent.¹²³ Thus in the presence of an excess of HBTU, the tetramethylguanidine derivative was formed, which did not undergo subsequent elongation of the peptide chain.¹³⁸ This side reaction can be avoided if the amount of the activating reagent is smaller (by 5%–20%) with respect to the monomer.¹¹³

With TBTU as the activating reagent, another side reaction, *viz.*, the *N*-acyl transfer, can take place.^{94, 113, 123} To avoid this, neutralisation *in situ* is used.¹²³ In this case, condensation is carried out in the presence of a base without preliminary neutralisation of the 5'-terminal primary amino group of the oligomer.¹¹³ The efficiency of condensation is monitored by HPLC analysis of aliquots obtained by appropriate treatment of a small portion of a polymeric carrier (3–5 mg) following attachment of the next monomeric unit.¹¹³

In the synthesis of thymidine PNA oligomers based on the use of the Boc strategy and TBTU activation, a decrease in the yields of condensation products is observed sometimes after addition of the first 3–4 monomeric fragments.¹¹³ This leads to the accumulation of short chains, whereas the overall yield of PNA does not exceed 30% (in the case of a 10-membered oligomer). The same problem sometimes arises with HATU activation, presumably, due to aggregation of growing thymidine PNA oligomers. This can partly be overcome through the attachment of lysine residues at the C-ends of PNA chains, which prevents the interchain aggregation of the oligomers formed.

It is noteworthy that the synthesis of heterogeneous PNA oligomers containing monomeric fragments of all the four types is not accompanied by significant reduction of product yields in the PNA synthesis.¹¹³ In this case, the yield over each condensation step reaches 97%, which corresponds to 66% overall yield of the target 16-membered oligomer.

Similar problems, *viz.*, aggregation of PNA chains, may arise during the removal of protective Z groups after completion of PNA synthesis resulting in a significant decrease in the yields of PNA.^{11, 113} A crucial role in this process belongs to complementary interchain and intramolecular coupling of PNA oligomers. Even four-membered PNA–PNA duplexes significantly hinder post-synthetic work-up of PNA oligomers.¹¹³ Therefore, oligomeric PNA sequences should be analysed for the possibility of intramolecular hairpin and intermolecular cluster formation prior to the synthesis. It was found that the overall yields of PNA can be increased to 75% and even more through incorporation of a lysine residue into PNA heterooligomer, since the charged ϵ -amino group of lysine partly prevents the aggregation of PNA chains.

These data suggest that the efficiency of synthesis of PNA oligomers strongly depends on the properties of PNA sequences to be prepared irrespective of the synthetic procedure used.¹³⁹ Theoretically, PNA may contain any combination of monomers, while the synthesis of certain sequences in quantitative yields faces difficulties. Thus the attachment of a purine monomer to an oligomeric PNA sequence containing a 5'-terminal purine base is problematic. Therefore, if PNA containing purine clusters are to be synthesised, the synthetic protocol should include repeated condensations.¹³⁹ The lowest yields were obtained in the synthesis of PNA oligomers containing several consecutive guanine residues.

In conclusion, it may be said that the Boc strategy can be implemented in both manual and automated variants.¹³⁹ Although the former seems to be rather efficient and inexpensive,¹⁴⁰ automated synthesis using peptide and oligonucleotide synthesisers holds especially great promise.¹⁴¹ The reason is that the manual synthesis of PNA is not only lengthy and laborious, but also needs large-scale synthesis (not less than 5 mmol) in order to obtain acceptable yields of condensation products.

b. The Fmoc strategy

It is generally recognised that the Fmoc strategy of PNA synthesis^{14, 77, 96, 100–106, 114} requires milder conditions than the Boc strategy.¹² In particular, no treatment of PNA oligomers with strong acids before and after synthesis is necessary. This allows the use of other protective groups for exocyclic amino groups of heterocyclic bases of the PNA monomers. Correspondingly, the Fmoc strategy affords higher degrees of purity of reaction mixtures and higher overall yields of PNA oligomers. The Fmoc/acyl strategy of PNA synthesis is especially promising,^{77, 104, 105} since it can also be used for the synthesis of PNA–DNA and PNA–peptide chimeras.

Various versions of the Fmoc strategy are currently known. Thus Bhoc protection of heterocyclic bases of the PNA monomers and HATU activation allows automated synthesis on oligonucleotide synthesisers.¹⁰⁶ The use of a DIPEA–lutidine mixture seems to be more effective than the use of only one base, since it affords higher yields of the condensation products.¹⁰⁶

DMF is a suitable solvent for the Fmoc condensation, and HATU is one of the most potent activating reagents.¹⁴¹ However, in this case, too, the synthesis of individual PNA oligomers may face problems related to non-efficient condensation.¹⁴¹ Thus the synthesis of PNA oligomers with sequences containing several identical consecutive heterocyclic bases (not necessarily purines) yields short-chain products. This problem can partly be overcome through the use of repeated condensations.¹⁴¹

Two condensation cycles are carried out in the following cases: in the synthesis of sequences containing four or more identical consecutive residues after attachment of two or three identical PNA monomers to the oligomer, in the synthesis of PNA oligomers containing purine clusters and in the synthesis of 18-membered and more extended PNA oligomers independent of the composition of the sequence after the attachment of the 17th residue.¹⁴¹

The yields of PNA obtained using the Fmoc strategy and HATU activation vary from 26% to 38%.¹⁴¹ In some cases, the overall yields of PNA oligomers do not depend on the sequence lengths but are determined by the efficiency of the attachment of the first PNA monomer to the polymeric support, since the yield of the first condensation product can be lower than the yields of the products obtained in subsequent condensations.¹⁴¹

In the majority of cases, reversed phase HPLC is used for the analysis of reaction mixtures and isolation of target products under conditions for the separation of peptides rather than oligonucleotides.¹⁴¹ The condensation efficiency of the Fmoc strategy can also be estimated spectrophotometrically by measuring UV absorption of a product formed upon removal of Fmoc groups by piperidine in the range of 256–301 nm. This method is especially convenient for stepwise monitoring of PNA oligomerisation.⁹⁷

Thus, the Fmoc strategy can be used for the synthesis of PNA oligomers unattainable by other methods. This procedure allows modifications to the synthetic protocol aimed at increasing the yields of condensation products in separate synthetic cycles.¹⁴¹

The low efficiency of the condensation encountered in the Fmoc strategy of PNA synthesis seems to have the same reasons and solutions as those in peptide synthesis.¹⁴² It is known that many problems of automated solid-phase peptide synthesis are related to the nature of the sequence to be synthesised.¹⁴² Low condensation yields are due to the formation of bulky spatial peptide structures, which may interfere with the formation of amide bonds.

Those peptide chain fragments which are susceptible to interchain aggregation, can also decrease the accessibility of the amino group and thus prevent further elongation of the chain.¹²⁰

Spatial hindrances appear in the course of PNA synthesis which decelerate the removal of protective Fmoc groups from the 5'-termini of PNA oligomers and decrease the efficiency of subsequent condensation.¹⁴³

The synthesis of purine-rich PNA presents a special problem. If a PNA sequence contains more than two consecutive purine residues, the efficient attachment of the next purine monomer requires a longer reaction time and repetition of the condensation procedure three or four times. The attachment of the guanine monomer to the 5'-terminal guanine unit proceeds at a very slow rate.

Aggregation of PNA chains is the main reason for low condensation efficiency inherent in both Fmoc and Boc strategies. The synthesis of partly or fully self-complementary sequences may produce problems relevant to intrachain association of PNA oligomers. In addition, the solid-phase synthesis conditions favour intermolecular aggregation of growing oligomers. Thus purine-rich PNA and thymidine PNA oligomers (both four-membered and more extended ones) are prone to aggregation.

The condensation efficiency strongly depends on such factors as the loading of the polymeric support and the composition of the solvents. Thus, low densities of oligomers 'growing' on solid supports favour solution of the problem of intermolecular aggregation of PNA chains, whereas certain solvents prevent inter- and intramolecular aggregation of PNA molecules (*e.g.*, the formation of hairpin structures) and ensure effective diffusion of reagents to the N-termini of the growing PNA chains.

Studies aimed at optimisation of conditions for PNA synthesis are currently under way, since no ideal method for PNA synthesis has been developed so far. The Fmoc/acyl strategy of PNA synthesis seems to be the most advanced one, since it permits one to obtain oligomers of virtually any composition in high yields.^{104, 115}

Thus the synthesis of thymidine PNA oligomers by the Fmoc/acyl method combined with HATU activation requires only small (twofold) excess of the monomer¹¹⁵ and a 20% deficiency of the activating reagent. It is more expedient to use MP as a solvent and the DIPEA–lutidine mixture as a base. Preactivation of PNA monomers for 2 min is yet beneficial. The yield of the condensation product in each step is 85%–90%, the condensation time is 30 min and the overall yields of the 7-membered oligomer is no less than 50%.¹¹⁵ The efficiency of the reaction is most conveniently monitored spectrophotometrically.

Attempts have been made to optimise condensation conditions in solution using mixtures of PNA monomers and amino acid esters as model systems.¹¹⁵ Direct application of the data obtained in these model systems to solid-phase PNA synthesis is questionable, since the optimum conditions for the synthesis in solution and on polymeric supports may differ in principle. This circumstance should be taken into consideration when selecting model systems. On the other hand, these studies sometimes give valuable results.

The yields of condensation products in the reaction of PNA monomers with L-phenylalanine *tert*-butyl ester were not lower than 95% irrespective of the nature of the activating reagent (HATU or HBTU in the presence of 1-hydroxybenzotriazole), of the tertiary amine (*N*-methylmorpholine, lutidine or the DIPEA–lutidine mixture) and of the solvent (DMF or MP). The nature of the base and the activating reagent did not influence the efficiency of the reaction. The best result was obtained in the case of HATU activation in the presence of lutidine in DMF.¹¹⁵

As mentioned above, the overall yields of PNA oligomers may depend on the efficiency of attachment of the first monomer to the polymeric support. Thus the yield of the attachment product of the first cytosine monomer to the polymeric support (Tentagel) in the synthesis of heterogeneous PNA by the Fmoc/acyl strategy combined with conventional HBTU activation in the presence of 1-hydroxybenzotriazole and lutidine did not exceed 50%,¹¹⁵ whereas those obtained in subsequent condensation steps were no less than 80%. The efficiency of attachment of the first PNA monomer can be increased to 80% and even higher using repeated condensation. In this case, the time for each condensation can be reduced.¹¹⁵ Low yields of the attachment products of the first

monomeric unit to a polymeric support have also been reported.¹⁴¹

The best conditions for the PNA synthesis by the Fmoc/acyl strategy include the use of a twofold monomer excess (0.125 mol litre⁻¹), preactivation with HATU (0.8 mol-equiv.), DIPEA and lutidine (1–2 min), condensation (20 min) and repetition of the condensation procedure in each (with the exception of the first) reaction cycle. This provides an overall yield of heterogeneous PNA of 43% (for 16-membered oligomers), which corresponds to the average yield of the condensation product of 95% (in this case, the attachment of the first monomeric fragment occurs with high yield). The main disadvantage of this method is the necessity to repeat the condensation procedure in each cycle.¹¹⁵ The expedience of this approach is doubtful despite its obvious advantages, *viz.*, good reproducibility of experimental results.

c. The MMT strategy

This strategy of PNA synthesis is rather promising^{38, 96, 107–112, 116, 144, 145} particularly its MMT/acyl version,^{96, 107, 110, 116} which is fully compatible with oligonucleotide synthesis protocols. It allows the use of automatic DNA synthesisers without modification of their design or software, which is especially convenient for conducting the syntheses of PNA–DNA chimeras.

The MMT strategy allows the use of a broad range of activating reagents,^{38, 112, 144, 145} including mesitylenesulfonyloxybenzotriazole (TMSOBT)¹¹² and 3,4,6-triisopropylbenzenesulfonyloxybenzotriazole (TPSOBT).¹⁴⁴ The latter gives higher yields of the condensation products (the average yield in one cycle reaches 96%) than the commercially available activating reagent PyBOP.^{112, 144} Depending on the nature of the PNA monomer and the 5'-terminal oligomeric fragment, the yield in each condensation step varies from 91% to 99%.¹⁴⁴

The efficiency of condensation carried out by the MMT strategy can be estimated spectrophotometrically by measuring UV absorption spectra of the MMT⁺ cation formed upon removal of the protective MMT group from the 5'-terminal amino group of a PNA oligomer. The MMT strategy combined with TPSOBT activation is compatible with oligonucleotide synthesisers.¹¹² This approach was first used in the synthesis of PNA molecules containing uracil residues.¹¹² The 'manual' variant of the MMT strategy is also effective, *e.g.*, in the synthesis of thymidine PNA oligomers.³⁸

The use of PyBOP as an activating reagent allows one to reach 95%–99% yields in each step of the monomeric fragment coupling.⁹⁶ However, in this case, the use of concentrated (0.3 M) solutions of PNA monomers and PyBOP is necessary. It is more expedient to use *N*-ethylmorpholine as a base and to perform preactivation of PNA monomers.⁹⁶

The MMT strategy is used for the synthesis of phosphonate analogues of PNA (pPNA).^{110, 116, 146, 147} The presence of negatively charged groups in the pPNA backbone makes PNA analogues readily soluble in aqueous solutions in comparison with classical PNA oligomers. These molecules bind specifically to complementary fragments in DNA and RNA, although the melting temperatures of pPNA–NA complexes are somewhat lower than those of the corresponding PNA–NA complexes.

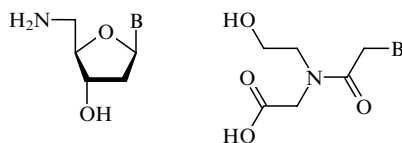
A combination of the MMT/acyl protocol with triisopropylbenzenesulfonylnitrotriazole activation is efficient in the synthesis of pPNA.^{110, 116, 146, 147} The condensation in the presence of *N*-methylimidazole as a nucleophilic catalyst permits one to obtain the average yields of 95% in the condensation step with a reaction time of 10 min.^{110, 116} However, the quantitative overall yields of condensation products are not achieved, although the use of dilute solutions of PNA monomers (0.05 M) and the activating reagent (0.06 M) together with preactivation (mixing of the PNA monomer with the activating reagent and *N*-methylimidazole), makes this procedure attractive.^{110, 116}

3. Some peculiarities of the synthesis of PNA–DNA chimeras

The interest in PNA–DNA chimeras has arisen in the past decade, which gave a strong impetus to the development of methods for their synthesis.^{77, 109, 111, 144, 148–150} The use of classical PNA in biochemical studies is limited due to their poor solubilities in aqueous solutions, proneness to self-aggregation^{4, 12, 34} and low penetrability through cell membranes.^{4, 9, 84, 151} The latter is the main obstacle for the use of canonical PNA oligomers as antisense agents *in vivo*.⁹

Chimeric PNA–DNA molecules are devoid of most of these drawbacks. They possess all the advantages of PNA together with valuable properties inherent in NA. Indeed, the PNA–DNA chimeras synthesised so far combine high biological stabilities, high affinities and selectivities of binding to NA targets typical of PNA with perfect solubilities and the ability to activate hydrolysis of RNA targets by RNase H, which are characteristic of DNA.^{9, 34} Chimeric PNA–NA molecules have various applications, *viz.*, they are promising therapeutic (including antisense) drugs⁹ and can be used as a basis for highly effective diagnostic tools and highly sensitive biomolecular probes.^{77, 96, 107–109, 144, 148, 149} Synthesis of hybrid PNA–NA molecules manifests specific features, which necessitates a consideration in a separate section.

The correct choice of linkers between PNA and DNA fragments of the chimeric molecules is one of the most important problems. Depending on whether the 5'-terminal fragment of the hybrid molecule belongs to PNA or DNA, the linker used is represented either by modified nucleosides (*e.g.*, 5'-amino-2',5'-dideoxynucleosides^{77, 149}) or modified PNA monomers [*e.g.*, *N*-(2-hydroxyethyl)glycine derivatives].¹⁴⁸



Syntheses of both types of PNA–DNA hybrids, *viz.*, 5'-PNA–DNA-3' and 5'-DNA–PNA-3', have been described. Owing to the charged backbones of their DNA fragments, PNA–DNA chimeras are perfectly soluble in aqueous solutions, which makes possible their isolation and analysis by standard methods, such as polyacrylamide gel electrophoresis and ion-exchange reversed phase HPLC.¹⁰⁸

In the case of 5'-terminal PNA fragments, PNA and DNA fragments are linked by the amide bond and 5'-amino-2',5'-dideoxynucleosides are used as linkers.⁷⁷ Such hybrid molecules are synthesised by various methods. Thus 5'-PNA–DNA-3' hybrids are prepared according to Boc/Z protocols commonly used in the synthesis of PNA-peptide conjugates.¹⁵² However, the use of this technique for the synthesis of PNA–DNA chimeras containing purine nucleotide residues may result in acid-catalysed apurination of the DNA fragment during deprotection of heterocyclic bases of PNA.⁷⁷ Therefore, this approach is used exclusively for the synthesis of PNA–DNA hybrids the DNA fragments of which contain more stable pyrimidine nucleotides, whereas 5'-PNA–DNA-3' chimeras are more efficiently synthesised using the Fmoc/acyl strategy.⁷⁷

If hybrid molecules contain 5'-terminal DNA fragments, the PNA and DNA parts can be linked by phosphoramidate bonds without any linkers. In this case, the synthesis of PNA fragments is carried out using the Fmoc/acyl protocol. With the thymidine monomer, Boc-protection of the 5'-terminal amino group is possible. The activation is performed with HATU in the presence of DIPEA and DMAP; the condensation is carried out in DMF. In this case, the use of acid-labile groups for protection of heterocyclic bases of PNA monomers is inadmissible because of easy acid hydrolysis of phosphoramidate bonds.⁷⁷

The synthesis of PNA fragments of such chimeric oligomers usually employs the MMT/acyl strategy. In this case, the conditions of PNA synthesis are compatible with those of oligonucleotide synthesis;^{36, 149} PNA fragments can be synthesised by manual techniques. The condensation is performed in the DMF–pyridine mixture with 2-[2-oxo-1(2*H*)-pyridyl]-1,1,3,3-bis(pentamethylene)uronium tetrafluoroborate (TOPPipU) as the activating reagent and DECHA as the base.¹⁵³ Under these conditions, the condensation of thymidine and cytidine PNA monomers proceeds smoothly, purine monomers are attached inefficiently to the growing PNA chain.¹⁴⁹ If HATU is used as the activating reagent, DIPEA as the base and acetonitrile as the solvent in the presence of a fivefold excess of PNA monomers (necessary to attain high yields of condensation products), the reaction time is no less than 15 min.³⁴ This method was used for the synthesis of chimeric molecules containing 5-bromouracil and 5-methylcytosine residues.³⁴ The incorporation of 5-methylcytosine residues into the PNA chains of chimeric molecules increases the stabilities of their duplexes and triplexes with complementary DNA.³⁴

The modified thymidine PNA monomer based on *N*-(2-hydroxyethyl)glycine^{34, 107, 148} is often used as a linker between DNA and PNA fragments of chimeric molecules of the 5'-DNA–PNA-3' type; the latter can be synthesised using both Boc¹⁴⁸ and MMT strategies.^{34, 107} If the Boc/Z strategy is used, the PNA synthesis is carried out on a solid phase; the linkers are attached under the same conditions.¹⁴⁸ Subsequent synthesis of DNA fragments of hybrid molecules should also be performed on the solid phase. It is inadmissible to perform the synthesis of DNA fragments in solution, since the solubility of PNA oligomers devoid of protective groups in organic solvents is insufficient to provide efficient condensation with phosphoroamidite derivatives of nucleosides.¹⁴⁸

The solid-phase MMT method is more suitable for the synthesis of the 3'-PNA fragments; after completion of PNA synthesis, solid-phase synthesis of the DNA fragment is continued without detachment of the oligomer from the support. This prevents the use of PNA monomers the heterocyclic bases of which are protected by acid-labile groups, since the DNA fragments will not withstand acid treatment used to remove protective groups. This synthetic procedure is inapplicable to chimeric molecules containing PNA monomers of all the four types, but can be used for the synthesis of hybrid molecules with the pyrimidine monomers constituting the PNA fragments.¹⁴⁸

The MMT/acyl modification of this method is devoid of these disadvantages and allows the synthesis of PNA–DNA hybrids containing all the four types of nucleobases in both DNA and PNA fragments.^{108, 109, 150}

The MMT/acyl strategy allows the application of the fully automated protocol on oligonucleotide synthesisers. The DNA fragments of hybrid molecules are usually synthesised according to a conventional phosphoroamidite protocol, which makes use of commercial 2'-deoxynucleoside phosphoroamidites.¹⁰⁸ This method of synthesis of PNA–DNA chimeras has practically no drawbacks.^{108, 150}

The synthesis of PNA fragments of 5'-PNA–DNA-3' oligomers may involve HBTU activation in the presence of DIPEA in DMF–acetonitrile.¹⁵⁰ Solutions of PNA monomers and activating reagents should be used at concentrations of no less than 0.1 M (preferably, 0.2 M); preactivation is also desirable. A commercially available aminohexanol phosphoroamidite derivative can be used as a linker between the PNA and DNA fragments; this is attached to the 5'-end of a DNA fragment by a standard oligonucleotide synthesis protocol. Then the synthesis of a 5'-terminal PNA fragment of a chimeric molecule is followed.¹⁵⁰

The MMT/acyl strategy is used in the synthesis of chimeric molecules with the composition 5'-PNA–DNA–PNA-3'.¹⁰⁹ In this case, both PNA fragments are synthesised in an automated regime using HBTU activation in the presence of DIPEA in DMF–acetonitrile mixture; this may require an eightfold excess

of the reagents with respect to the carrier loading. Preactivation of PNA monomers makes it possible to increase the condensation efficiency and the average yields in the attachment of monomeric fragments up to 96%.¹⁰⁹

Obviously, the problem of efficiency of each individual approach to the synthesis of PNA molecules has no unambiguous solution. The choice of the most adequate strategy for the PNA synthesis depends on the goal and facilities as well as on the number of PNA oligomers to be synthesised, the scale of synthesis, composition and purity of PNA oligomers.

VIII. Conclusion

The design of the most efficient method for the synthesis of PNA oligomers requires that a rational compromise between the efficiency and economy of the synthetic process be found.

On the one hand, one has to reach the maximum yields of condensation products and the choice of synthetic strategy must take into account both the nature of the activating reagent and other factors discussed in this review.

On the other hand, the synthesis of PNA should be rational. This implies that the synthetic procedure should not only be efficient, but also fast and as cheap as possible. Examples of both the approaches to PNA synthesis have been presented in this review.

In low-budget laboratories, where the primary goal is economic PNA synthesis, it is the 'slow' synthesis that is most commonly used. Although this procedure is rather laborious, it gives excellent yields in the condensation step.

'Fast' processes are utilised in the majority of large biotechnological companies which manufacture PNA oligomers for commercial purposes. Here, large excesses of PNA monomers and the most potent activating reagents are employed in order to ensure high yields of the condensation products. However, quantitative yields cannot be attained due to a reduction of the condensation time; therefore, pure PNA oligomers can be obtained by virtue of complex isolation procedures.

The most rational synthetic strategies combine the best features of both approaches, viz., the 'fast' and the 'slow' syntheses of PNA.

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Oxygen compounds of halogens X_2O_2 (X is a halogen atom)

I V Nikitin

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Abstract. The results of studies on the structure and properties of the O_2F_2 , Cl_2O_2 , Br_2O_2 and I_2O_2 molecules and the FOO , $ClOO$ and $BrOO$ radicals obtained mainly in the past decade are surveyed. The bibliography includes 173 references.

I. Introduction

Compounds of the general formula X_2O_2 pertain to the class of high-energy compounds. Representatives of this class are thermally unstable and are characterised by low binding energies. Some of them are the most potent inorganic oxidants.

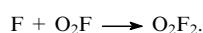
In my book¹ published in 1986 and devoted to the oxygen compounds of halogens, compounds with the general formula X_2O_2 were represented by only dioxygen difluoride O_2F_2 . Moreover, it was mentioned that this compound has no Cl -, Br - and I -analogues. Such a conclusion was drawn based on the fact that in the mid-80's, the works which admitted the existence of Cl_2O_2 were few, and virtually none dealt with Br_2O_2 and I_2O_2 . However, in recent studies on atmospheric chemistry it was reported that halogen oxides X_2O_2 (and halogen atoms, particularly, those of chlorine and bromine) are involved in depletion of stratospheric ozone. This fact has attracted the attention of researchers to these compounds, and new information appeared on this class of compounds, which allowed the X_2O_2 oxides to be characterised in more detail. Thus, this review supplements the book.¹

It should be noted that, as for other halogen–oxygen compounds, the distinctions between the structures and properties of X_2O_2 oxides override their similarities.

II. Dioxygen difluoride and related compounds

1. Dioxygen difluoride

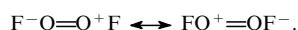
Dioxygen difluoride exists only at low temperatures (m.p. = 119 K, b.p. = 216 K). It was obtained for the first time in 1933 by Ruff and Menzel² upon action of an electric discharge on a fluorine–oxygen mixture. The most probable mechanism of O_2F_2 formation is as follows:



Inasmuch as the synthesis of O_2F_2 was described in detail in the book,¹ this issue will not be discussed here.

Jackson³ established the structure of the O_2F_2 molecule in 1962 by using the method of microwave spectroscopy (MW). The dioxygen difluoride molecule was shown to represent spatially skewed chains of atoms $F-O-O-F$ with C_2 symmetry. This structure was confirmed later by electron diffraction (ED).⁴ Table 1 shows the bond lengths (r) and bond and torsion angles in the O_2F_2 molecule.

Being formally close to the hydrogen peroxide structure, the molecular structure of dioxygen difluoride, however, differs substantially in its details. For instance, the $O-O$ bond length in the H_2O_2 molecule is 1.48 Å, which is close to that of a single bond, whereas the bond length in the O_2F_2 molecule suggests a double-bond nature, being similar to the bond length in the O_2 molecule and the O_2^+ cation (1.208 and 1.12 Å, respectively, according to the data from Ref. 7). Thus, the following resonance structure was proposed for the O_2F_2 molecule:



Calculations of the structure of O_2F_2 molecules by the local density functional (LDF)⁵ method provided good agreement with the experimental⁵ data: the calculated $O-O$ and $O-F$ bond lengths differed from those found experimentally by no more than 0.01 and 0.015 Å, respectively (see Table 1). The geometrical parameters of the $FOOF$ molecule calculated using the Becke–Perdew–Wang B3PW91 functional⁶ fit less the experimental data, and the Hartree–Fock theory usually applied in calcula-

Table 1. Geometrical parameters of the O_2F_2 molecule.

Parameter	Experimental data		Quantum-chemical calculations	
	MW ³	ED ⁴	LDF ⁵	B3PW91 ⁶
$r(O-O)/\text{\AA}$	1.217(3)	1.216	1.215 ^a	1.222
$r(O-F)/\text{\AA}$	1.575(3)	1.586	1.562 ^a	1.523
$F-O-O/\text{deg.}$	109.5	109.2	110.5 ^a	109.2
$FOO/OOF/\text{deg.}$	87.5	88.1	88.4 ^a	88.1
Rotation barriers /kcal mol ⁻¹	30		36–42	

^a A mean value is given (averaged from nine values calculated using different Gaussians).

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tions of geometrical parameters of molecules gave unsatisfactory results for dioxygen difluoride (see Ref. 5).

According to calculations,⁵ the internal rotation barrier in the O_2F_2 molecule is $\sim 36\text{--}42\text{ kcal mol}^{-1}$, which exceeds substantially the value of 30 kcal mol^{-1} suggested by Jackson³, the value of $20.83\text{ kcal mol}^{-1}$ determined by the CNDO/2 method¹ and the energy of the $\text{O}-\text{F}$ bond dissociation equal to 20 kcal mol^{-1} (see Ref. 8).

Vibrational spectra (IR and Raman) of dioxygen difluoride samples in both solid state and solution are described in the book,¹ and the IR spectrum of gaseous O_2F_2 was measured with an IR Fourier spectrometer in a multipass cell at 175 K (Ref. 9). The O_2F_2 molecule is characterised by six normal vibrational modes active in the IR spectrum, *viz.*, $\text{O}-\text{O}$ stretching (ν_1), $\text{O}-\text{F}$ stretching symmetrical (ν_2) and antisymmetrical (ν_3), $\text{O}-\text{O}-\text{F}$ bending symmetrical (ν_4) and antisymmetrical (ν_5) and also torsion (ν_6) modes. The most intense absorption bands were obtained at 1210 cm^{-1} (ν_1) and 615 cm^{-1} ($\nu_2 + \nu_3$ combination). The ν_1 frequency in the spectrum of gaseous O_2F_2 is 100 cm^{-1} lower as compared with the spectrum of matrix-isolated O_2F_2 . The IR spectral band of gaseous O_2F_2 observed at 1490 cm^{-1} was attributed to $\text{O}-\text{O}$ stretches of the O_2F radicals present in equilibrium with O_2F_2 . It was noted⁹ that the half-life of O_2F_2 at a temperature below 180 K exceeds 2 h .

An experimental value for the enthalpy of formation of dioxygen difluoride $\Delta H_{298}^\circ(\text{O}_2\text{F}_2) = 4.73 \pm 0.30\text{ kcal mol}^{-1}$ first determined in 1959¹⁰ was never refined. It should be noted that this quantity was calculated by different methods (Table 2) in quite a number of studies (see, *e.g.*, Refs 6, 11–15). In 1996, Chase¹¹ tabulated the recommended thermodynamic constants for oxygen halides (NIST–JANAF) based on spectroscopic and thermodynamic data published up to 1994 inclusive, and the value of $4.6 \pm 0.2\text{ kcal mol}^{-1}$ was proposed for the enthalpy of formation of dioxygen difluoride. Later, this value was argued against by Kieninger *et al.*⁶ who calculated the thermodynamic characteristics of oxygen fluorides by the density functional method. Using the B3PW91 functional, they have obtained good agreement between experimental and calculated enthalpies of formation of the OF , O_2F and OF_2 molecules (the largest deviation was observed for the OF molecule and amounted to $\sim 0.6\text{ kcal mol}^{-1}$ at 0 K). However, the same calculation method gave overestimated values for the enthalpies of formation of O_2F_2 , namely, 7.3 kcal mol^{-1} (at 298 K) and 9.0 kcal mol^{-1} (at 0 K).⁶ The value for 298 K exceeded the recommended one¹¹ by 64%. At the same time, the high value of 9.0 kcal mol^{-1} did not differ dramatically from the values $\Delta H_0^\circ(\text{O}_2\text{F}_2) = 8.2\text{ kcal mol}^{-1}$ estimated¹⁴ by using the B3LYP functional and $\Delta H_0^\circ(\text{O}_2\text{F}_2) = 8.7 \pm 0.2\text{ kcal mol}^{-1}$ calculated in Ref. 15. Although the difference in experimental and calculated enthalpies of formation of the FOOF molecules cannot be called a dramatic one, however, further studies should be performed in order to refine the experimental value for the enthalpy of formation of FOOF.

Table 2. The enthalpy of formation of the FOOF molecule calculated by different methods.

T/K	$\Delta H^\circ/\text{kcal mol}^{-1}$	Ref.
298.15	4.6 ^a	11
	4.5	12
	5.0	13
	7.3	6
0	9.0	6
	8.2	14
	8.7	15

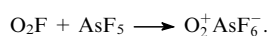
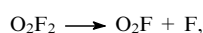
^a This value is included in the recommended NIST–JANAF Thermochemical Table.

Dioxygen difluoride is a strong oxidative-fluorinating agent, which reacts over a wide range of low temperatures.

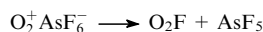
Thus, fluorination of ClF_3 by O_2F_2 occurs at 195 K to give chlorine pentafluoride in a quantitative yield.¹⁶ All the other methods of ClF_3 synthesis require much higher temperatures and pressures.¹⁷ Xenon is fluorinated by an excess of O_2F_2 to give a mixture of XeF_2 and XeF_4 at $153\text{--}195\text{ K}$, repeated treatment producing pure xenon tetrafluoride.¹⁸ Fluorination of actinides by O_2F_2 can be carried out at ambient and lower temperatures.¹⁹

Due to low $\text{O}-\text{F}$ binding energy, the dioxygen difluoride molecules and O_2F radicals behave as more efficient sources of the fluorine atoms as compared with molecular fluorine and rank below krypton difluoride only.²⁰

Synthesis of dioxygenyl salts in the reaction of O_2F_2 with fluorine-containing Lewis acids is among the most important preparative reactions of dioxygen difluoride.¹ Here, dioxygen difluoride is a source of O_2F radicals, which react with Lewis acids to give salts, *e.g.*, $\text{O}_2^+\text{AsF}_6^-$.



The radicals O_2F can be obtained from this salt by thermolysis

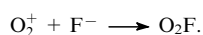


and used, *e.g.*, for the preparation of electronically excited and vibrationally excited ClF , BrF and IF molecules in their ground electronic states, which are employed in various spectroscopic studies (see Ref. 17 and references cited therein).

2. The O_2F radicals

The O_2F radicals are formed upon a low-temperature impact (photolysis, radiolysis, *etc.*) on systems containing fluorine and oxygen. Following stabilisation in low-temperature matrices, they can be studied by various spectral techniques.

Recently, Bartlett and co-authors²⁰ reported the possibility of regenerating O_2F radicals from dioxygenyl salts at low temperature. Solvated O_2F radicals were formed from the salts ($\text{O}_2^+\text{AsF}_6^-$, $\text{O}_2^+\text{SbF}_6^-$) dissolved in anhydrous HF in the presence of an alkali-metal fluoride by the reaction



A nonlinear O_2F radical represents a prolate asymmetrical rotor^{21,22} with the rotational constants $A = 78.4301$, $B = 10.013935$ and $C = 8.855247\text{ GHz}$. The ground state of the O_2F radical is X^2A'' ; the energy of the $^2A'$ state exceeds that of the ground state by $\sim 1.07\text{ V}$ (8630 cm^{-1}).²³ The asymmetrical OOF isomer is by 100 kcal mol^{-1} (according to Ref. 23) or 85 kcal mol^{-1} (according to Ref. 24) more stable than the symmetrical OFO isomer. In contrast to OOF, the OFO radical has never been observed experimentally.^{23,25} In addition, as compared with the OFO^+ cation, the FOO^+ cation is more energetically favourable. The FOO^+ ion represents a charge-transfer complex $\text{F}(\text{P})-\text{O}_2^+(\text{P})$, which dissociates readily to F and O_2^+ (see Ref. 26).

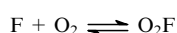
Internuclear distances $r(\text{O}-\text{O})$ and $r(\text{O}-\text{F})$ in the O_2F radical are 1.200 and 1.649 Å , respectively, and the $\text{F}-\text{O}-\text{O}$ bond angle is 111.2° , which is somewhat larger²⁵ than in the FOOF molecule. An increase in the $\text{O}-\text{F}$ bond length in the O_2F radical as compared with the O_2F_2 molecule agrees well with a decrease in the $\text{O}-\text{F}$ bond strength when going from O_2F_2 to O_2F . The $\text{F}-\text{O}_2\text{F}$ bond strength in dioxygen difluoride is $\sim 19.6\text{ kcal mol}^{-1}$ at 0 K .²⁷ In the O_2F radical, the fluorine atom is less strongly bound to oxygen: the dissociation energy is $11.7 \pm 0.5\text{ kcal mol}^{-1}$ (0 K).²⁸ Virtually the same value $11.9 \pm 0.2\text{ kcal mol}^{-1}$ (0 K) was obtained in calculations²⁷ from the third law of thermodynamics when studying the thermodynamic properties of the $\text{F} + \text{O}_2$ reaction mixture.

Like peroxy radicals,²⁹ dioxygen monofluoride strongly absorbs in the UV range ($200\text{--}300\text{ nm}$). The absorption

maximum for the O₂F radical was shown³⁰ to lie at 206.5 nm (the absorption cross-section $\sigma = 1.35 \times 10^{-17} \text{ cm}^2$), at 215 or 220 nm.^{27,28,31} At 298 K,³¹ intense absorption of the O₂F radical was observed at 215 nm with the absorption cross-section $\sigma = 1.15 \times 10^{-17} \text{ cm}^2$ (for O₂F₂ molecules, $\sigma = 4.2 \times 10^{-18} \text{ cm}^2$).³¹ At 300 K, the absorption maximum was observed at 220 nm, the absorption cross-section being equal to $1.3 \times 10^{-17} \text{ cm}^2$ (Ref. 28) and $1.6 \times 10^{-17} \text{ cm}^2$ (Ref. 27).

The IR spectrum of the O₂F radicals in the gas phase has been studied.^{21,26,32,33} Using an IR Fourier spectrometer (resolution of 0.003 cm^{-1}) and a cell with an optical path of 100 m, the vibrational spectrum of the O₂F radical was obtained with the most intense absorption bands at 579.32 (ν_3), 940.22 ($\nu_2 + \nu_3$), 1142.46 ($2\nu_3$), 1486.93 (ν_1), 1495.60 ($\nu_2 + 2\nu_3$) and 2948.09 ($2\nu_1$).²¹ All vibrational frequencies of gaseous O₂F appeared to be lower than those of matrix-isolated O₂F. The bending vibrational frequency ν_2 was in the range of $365\text{--}370 \text{ cm}^{-1}$. An attempt⁹ to resolve the rotational structure of the O–O stretching band has failed; however, this structure was eventually resolved.²¹ These results show that detachment of a fluorine atom from the O₂F₂ molecule results in a substantial increase in the O–O stretching mode frequency, the latter approaching a vibrational frequency of 1580 cm^{-1} for the O₂ molecule.

In spectrokinetic studies²⁸ of the equilibrium in the gas-phase reaction



in a temperature range of 295 to 359 K, the enthalpy of formation of the O₂F radical was found to be $\Delta H_{298}^\circ(\text{O}_2\text{F}) = 6.24 \pm 0.50 \text{ kcal mol}^{-1}$ (the radicals were generated by pulse irradiation of a gas mixture with electrons of 2 MeV energy). A kinetic study of the reaction of fluorine and oxygen atoms³¹ gave a value of $5.49 \pm 0.40 \text{ kcal mol}^{-1}$ (298 K). A later study²⁷ showed similar values for enthalpy (Table 3). Table 3 lists $\Delta H_0^\circ(\text{O}_2\text{F})$ values calculated using B3LYP¹⁴ and B3PW91⁶ functionals and the QCISD(T)/6-31G(*d,p*) method³⁴ (QCI is quadratic configuration interaction).

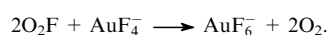
Generally, the O₂F radical behaves as a mere source of fluorine atoms rather than as a radical. Its relatively low reactivity is explained by the fact that abstraction of the F atom, which represents the active part of the radical, requires an activation energy of $\sim 12.6 \text{ kcal mol}^{-1}$ (Ref. 35). The O₂F radical is inert with respect to other peroxy radicals, whereas the HO₂ radical reacts quickly at room temperature with RO₂ with the rate constants lying within $(4\text{--}12) \times 10^{-12} \text{ cm}^3 \text{ molecule}^{-1} \text{ s}^{-1}$ (Ref. 29).

Table 3. The enthalpy of formation of the O₂F radical.

<i>T</i> /K	$\Delta H_{\text{exp}}^\circ / \text{kcal mol}^{-1}$	$\Delta H_{\text{theor}}^\circ / \text{kcal mol}^{-1}$	Ref.
298	6.24 ± 0.50	—	28
	5.49 ± 0.40	—	31
	6.132	—	27
	—	5.93	34
	—	6.0	6
0	—	6.1 ± 0.5^a	11
	6.571	—	27
	—	7.2 ± 2.0	14
	—	8.9 ± 3.0	34
	—	6.5 ± 0.5^a	11

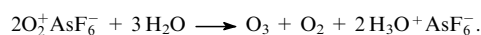
^a This value is included in the recommended NIST–JANAF Thermochemical Table.

Solutions containing O₂F radicals are stable at temperatures $\leq 223 \text{ K}$. They can be used for oxidative fluorination. For example, Au(III) is oxidised to Au(V)



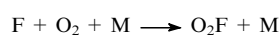
Similarly, the Ag(II) ions are oxidised to Ag(III), Ni(II) is oxidised to Ni(IV) and Pt(IV) is oxidised to Pt(V).

Controlled hydrolysis of a solution of a dioxygenyl salt in HF at 195 K represents a rare example of the chemical synthesis of ozone.³⁶

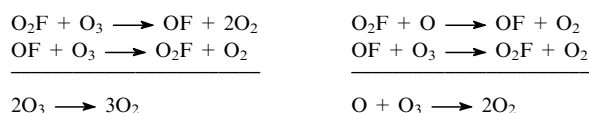


The same result was obtained with other available and handy dioxygenyl salts, *viz.*, fluoroantimonates O₂⁺SbF₆[−] and O₂⁺Sb₂F₁₁[−]. It was assumed³⁶ that the reaction of dioxygenyl O₂⁺ with a water molecule gives an O₂ molecule and an H₂O⁺ cation, the latter decomposing with elimination of H⁺. Hydroxyl formed upon the H₂O⁺ decomposition reacts with O₂⁺ producing protonated ozone OOOH⁺, which transforms into ozone upon elimination of H⁺.

The recent active studies on the properties of dioxygen difluoride and the O₂F radicals were partly associated with the hazards of atmospheric contamination by halogen-containing refrigerants and propellants that produce halogen atoms upon photolysis. The reactions of the fluorine atoms with methane, water and other hydrogen-containing compounds present in the atmosphere of Earth have low activation barriers³⁷ and result in HF, *i.e.*, stable reservoir molecules rained out of the atmosphere. However, the main mechanism for transformation of the fluorine atoms in the atmosphere is the reaction



(hereinafter M is any species), which produces the O₂F radicals. Moreover, due to a high oxygen concentration and a high rate of fluorine atom reaction with oxygen, the ratio of the equilibrium concentrations [O₂F] : [F] in the stratosphere may exceed 10^4 (see Refs 35, 38, 39). The radicals O₂F in turn can take part in catalytic cycles of ozone destruction^{36,38–41}



The efficiencies of the reactions of oxygen, water and methane with F atoms in the atmosphere depends on the altitude: at altitudes of 4–42 km, the reactions with oxygen resulting in O₂F₂ prevail; below 4 km and above 42 km, the reactions with H₂O and CH₄, which produce HF, are predominant.⁴² At altitudes above 28 km, photolysis of O₂F proceeds actively, which inhibits accumulation of these radicals.³⁹

The reaction of the F atoms with the oxygen molecules is not the only source of the O₂F radicals. The following reaction has been hypothesised:⁴³



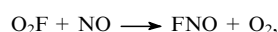
which, however, cannot play any noticeable role due to the lower chlorine dioxide content in the atmosphere as compared with oxygen.

Studies of certain reactions of the O₂F radicals at 295 K by means of pulse radiolysis coupled with UV absorption spectroscopy have shown³⁵ that the reactivity of the O₂F radical is relatively low, the upper limits of rate constants of its reactions with O₃, CH₄ and CO being 3.4×10^{-16} , 4.1×10^{-15} and $5.1 \times 10^{-16} \text{ cm}^3 \text{ molecule}^{-1} \text{ s}^{-1}$, respectively.³⁵ Whence it follows that O₂F radicals pose no threat to the ozone layer.

The reaction



proceeds virtually completely by the channel



probably, *via* an intermediate complex ON–FO₂. The rate constant for the reaction (1) is $(1.47 \pm 0.08) \times 10^{-12} \text{ cm}^3 \text{ molecule}^{-1} \text{ s}^{-1}$. The reaction



proceeds at 295 K with the rate constant $k_2 = (1.05 \pm 0.15) \times 10^{-13} \text{ cm}^3 \text{ molecule}^{-1} \text{ s}^{-1}$ (Ref. 40). Kinetic studies of reactions (1) and (2) under continuous flow conditions using microwave electric discharge and mass spectrometry have confirmed their bimolecular mechanisms.³⁹ At a total pressure of 1 Torr, the following rate constants were obtained ($\text{cm}^3 \text{ molecule}^{-1} \text{ s}^{-1}$):

$$k_1 = (7.5 \pm 0.5) \times 10^{-12} \exp\left(\frac{-688 \pm 377}{T}\right) \text{ at } 190 \text{ K} < T < 298 \text{ K}$$

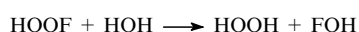
and

$$k_2 = (3.8 \pm 0.8) \times 10^{-11} \exp\left(\frac{-2042 \pm 456}{T}\right) \text{ at } 260 \text{ K} < T < 315 \text{ K}.$$

At room temperature, the upper limits of the rate constants for the reactions of O_2F with O_3 and CH_4 were 3×10^{-15} and $2 \times 10^{-16} \text{ cm}^3 \text{ molecule}^{-1} \text{ s}^{-1}$, respectively.

3. Compounds HOOF and ClOOF

The HOOF and ClOOF molecules are of particular interest for atmospheric chemistry. A reaction of OF with OH may result in a compound HOOF, which is kind of hybrid between hydrogen peroxide and dioxygen difluoride. A non-empirical estimate⁴⁰ has shown that the HOO/OOF dihedral angle in a skewed HOOF molecule (the C_1 group of point symmetry) is $\sim 83^\circ$ and the internuclear distance $r(\text{O}-\text{O}) = 1.339 \text{ \AA}$, these values being intermediate between those in H_2O_2 and O_2F_2 molecules. The HOOF molecule can be sufficiently stable and decomposes to F and HO_2 species. The enthalpy of HOOF formation can be estimated by using the following isodesmic reaction:



and was found to be $0.4 \pm 2 \text{ kcal mol}^{-1}$ (at 0 K).

Chlorine fluorine peroxide ClOOF can be an intermediate in the reaction of radicals $\text{ClO} + \text{OF}$. An estimate⁴³ gave a value of 85.1° for the dihedral angle in the skewed ClOOF molecule. The enthalpy of formation of ClOOF at 300 K was assessed to be $36.8 \pm 2 \text{ kcal mol}^{-1}$ (Ref. 43) and $18.5 \text{ kcal mol}^{-1}$ (Ref. 13). The presence of a stronger bond F–O in the ClOOF molecule as compared with HOOF, allows one to assume that ClOOF decomposes to Cl and O_2F . Dissociation of ClOOF to F and ClO_2 is energetically less advantageous.^{13,43} The peroxide ClOOF is by 18 kcal mol^{-1} more advantageous with respect to energy than the chlorite FOCIO.¹³

III. Chlorine oxides Cl_2O_2

In contrast to fluorine which forms a single compound, *viz.*, dioxygen difluoride, chlorine oxides with the composition X_2O_2 are of greater diversity.

The first mention in the literature of a compound with the formula Cl_2O_2 dates back to 1949. In the ^{38}Cl radiotracer investigations of mechanisms of reactions of chlorine with chlorous acid, of the chloride ion with the chlorate ion and of chlorous acid disproportionation, each of these reactions was assumed⁴⁴ to involve an intermediate which had an asymmetrical structure of either ClClO_2 or ClOCIO and decomposed to ClO_2 .

Of all possible structures built of two chlorine atoms and two oxygen atoms which include three-membered and four-membered cycles, only chloryl chloride ClClO_2 (C_s symmetry), chlorine peroxide ClOOCIO (C_2 symmetry) and chlorine chlorite ClOCIO (C_1 symmetry) can exist. Among these isomers, ClOOCIO is the most stable one. Chloryl chloride ranks higher in the energy scale as compared with chlorine peroxide (by $0.9\text{--}5 \text{ kcal mol}^{-1}$ according to different estimates^{45–48}) and chlorine chlorite (by $7\text{--}10 \text{ kcal mol}^{-1}$, see Refs 45–49).

An estimate⁵⁰ of the Gibbs energy for an equilibrium mixture of all Cl_2O_2 isomers in the ideal-gas state has shown that at low

temperatures the ClOOCIO isomer prevails, whereas at higher temperatures the fraction of ClClO_2 increases.

Temperature, K	100	200	300
Fraction of ClClO_2	0.4	8.8	21.6
in a mixture of Cl_2O_2 isomers (%)			

The yield of chlorine chlorite at $T \leq 590 \text{ K}$ did not exceed 1%; however, its content in the mixture increased substantially with further increases in the temperature.

1. Chloryl chloride

Attempts to obtain chloryl chloride by the reaction of chloryl fluoride ClO_2F or chloryl perchlorate ClO_2ClO_4 with certain chlorine-containing compounds (NOCl , NO_2Cl , AlCl_3 , BCl_3 , HCl) were undertaken as early as in the 1950's (see, *e.g.*, Ref. 51), but resulted in formation of products of chloryl chloride decomposition, *viz.*, ClO_2 and Cl_2 in a 2:1 ratio. Only in 1992, could the fluorine atom in ClO_2F be exchanged for a chlorine atom from AlCl_3 , BCl_3 and HCl to give chloryl chloride in amounts sufficient for spectroscopic measurements; however, an attempt to isolate pure ClClO_2 has failed.⁵² Chloryl chloride was synthesised by passing ClO_2F over AlCl_3 under a pressure of $0.1\text{--}1 \text{ mbar}$, the product being collected at 77 K .⁵² The reactions of ClO_2F with BCl_3 and HCl also resulted in ClClO_2 , while the reaction of ClO_2F with NOCl afforded predominantly NO_2Cl .

In a different preparation of ClClO_2 , stoichiometric amounts of ClO_2F and HCl were mixed in a reactor and then the mixture was expanded into an absorption cell, the temperature in the reactor and the cell being kept at $\sim 255 \text{ K}$.⁵³ Chloryl chloride was also formed in the reaction of photochemically generated chlorine atoms with chlorine dioxide and in the recombination of ClO radicals on ice.⁵⁴ At room temperature, with a ClClO_2 partial pressure of 1 mbar and a total gas pressure of 4 mbar, the ClClO_2 half-life is 1 min. Under stratospheric conditions, chloryl chloride is more stable, but easily undergoes photolysis.

The UV absorption spectrum of ClClO_2 in a neon matrix demonstrated two bands devoid of definite structures with maxima at 236 and 296 nm and half-widths of ~ 40 and $\sim 45 \text{ nm}$, respectively.⁵² The absorption maxima in the gas-phase ClClO_2 spectrum were at 231 ($\sigma = 1.3 \times 10^{-17} \text{ cm}^2$) and 296 nm ($\sigma = 1.5 \times 10^{-17} \text{ cm}^2$).

The IR spectra of matrix-isolated and gaseous ClClO_2 demonstrated six fundamentals $\nu_1\text{--}\nu_6$. Table 4 shows the vibrational frequencies for the matrix-isolated $^{35}\text{Cl}^{35}\text{Cl}^{16}\text{O}_2$ (neon matrix)⁵² and compares them with the vibrational frequencies calculated by the CCSD/TZ2P method⁴⁷ (singles and doubles coupled-cluster). Geometrical parameters of the ClClO_2 molecule (Ref. 52) were later refined based on the rotational spectra^{53,54} of chloryl chloride (Table 5). For comparison, Table 5 shows the geometrical parameters estimated by the MP2 method using 6-31G*

Table 4. Vibrational frequencies in the spectrum of the ClClO_2 molecule.

Frequency	Experimental data ⁵²	Calculations ^a using the CCSD/TZ2P method ⁴⁷	Mode
ν_1	1041.20	1039	Cl–O stretch, symmetric
ν_2	522.50	524	OCIO bend
ν_3	440.43	459	ClClO bend, symmetric
ν_4	271.37	285	Cl–Cl stretch
ν_5	1216.37	1205	Cl–O stretch, antisymmetric
ν_6	251.40	254	ClClO bend, antisymmetric

^a Of all the values calculated using the MP2, CCSD and CCSD(T) methods with TZ2P and TZ2Pf basis sets, the CCSD/TZ2P method provided the best agreement with experimental data.

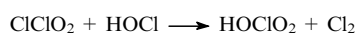
Table 5. Geometrical parameters and dipole moment (μ) for the ClClO₂ molecule.

Parameter	Experimental data			Quantum-chemical calculations	
	IR ⁵²	MW ⁵³	MW ⁵⁴	MP2/6-31G* (see Ref. 46)	MP2/TZ2Pf (see Ref. 47) ^a
$r(\text{Cl}-\text{Cl})/\text{\AA}$	2.22	2.1966	2.1978	2.459	2.269
$r(\text{Cl}-\text{O})/\text{\AA}$	1.44	1.4367	1.4360	1.469	1.442
$\text{Cl}-\text{Cl}-\text{O}$ /deg.	103.5	104.14	104.06	104.2	103.8
$\text{O}-\text{Cl}-\text{O}$ /deg.	116.0	114.96	115.05	116.7	115.0
μ/D		1.570		3.378	2.20

^aThe values shown were calculated by the MP2/TZ2Pf method that provides the best agreement with experimental data.

(Ref. 46) and TZ2Pf (Ref. 47) basis sets. The internuclear distance Cl—Cl in a ClClO₂ molecule exceeds that in the Cl₂ molecule by almost 0.21 Å. Chloryl chloride molecules represent asymmetric prolate rotors with the rotational constants $A = 9450.9218$, $B = 3588.0617$ and $C = 2787.9468$ MHz (for ³⁵Cl³⁵Cl¹⁶O₂).

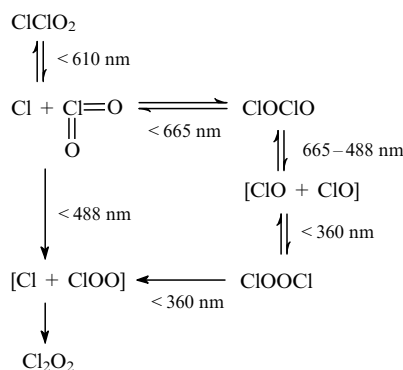
A non-empirical quantum-chemical calculation⁴⁶ of the enthalpy of formation carried out by the MP2 method using 6-31 + G(3d, 2p) and 6-31G* basis sets for the following isodesmic reaction:



gave values of $\Delta H_0^\circ(\text{ClClO}_2)$ equal to 33.8 [MP2/6-31 + G(3d, 2p)] and 34.6 kcal mol^{−1} (MP2/6-31G*). The enthalpy of formation of ClClO₂ was also calculated⁴⁷ using the second-order Møller–Plesset perturbation theory and the CCSD and CCSD(T) methods with TZ2P and TZ2Pf basis sets. The CCSD(T)/TZ2P method gave a value of 35.1 kcal mol^{−1}, which is most similar to the experimental one.

Photolysis of matrix-isolated ClClO₂ caused its rearrangement into ClOClO and ClOOCl.⁵⁵ A more detailed study⁵⁶ has shown that the effect of light with a threshold wavelength of 610 nm on argon-matrix-isolated ClClO₂ results in immediate transformation of the latter into chlorine chlorite ClOClO without formation of any long-lived intermediates. A chlorine atom formed upon ClClO₂ dissociation can attack the ClO₂ residue either at the chlorine atom giving ClClO₂ or at the oxygen atom to give ClOClO. The action of light with a threshold wavelength of 665 nm on ClOClO causes its dissociation to either Cl and OClO (with subsequent regeneration of ClClO₂) or two ClO radicals (with subsequent regeneration of ClOOCl). A scheme of photolysis of argon matrix-isolated ClClO₂ has been described⁵⁶ and the wavelengths at which dissociation of Cl₂O₂ isomers takes place were specified (Scheme 1).

Scheme 1



By using narrow-band filters (665, 610 and 360 nm), all three isomers, *viz.*, ClOClO, ClClO₂ and ClOOCl, respectively, could be identified. The calculated⁵⁶ values of dissociation energies (E_{dis})

for chlorine chlorite and chloryl chloride were substantially lower than the photon energy, which points to the excessive energy of the photofragments.

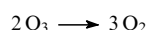
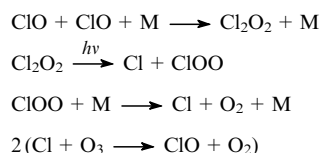
Reaction	$E_{\text{dis}}/\text{kcal mol}^{-1}$
$\text{ClOClO} \longrightarrow 2 \text{ClO}$	6
$\text{ClOClO} \longrightarrow \text{Cl} + \text{OClO}$	~9.5
$\text{ClClO}_2 \longrightarrow \text{Cl} + \text{OClO}$	~19

In the photolysis of neon matrix-isolated ClClO₂, only chlorine and oxygen are formed, and no photoisomerisation of ClClO₂ to ClOOCl takes place.

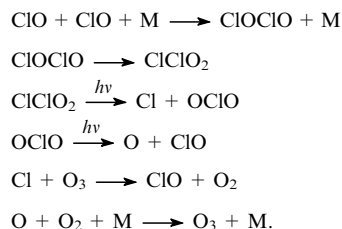
A study⁵⁷ of photoisomerisation of argon-matrix-isolated chlorine, bromine and iodine chlorites (XOClO, X = Cl, Br, I) obtained by addition of X atoms to OClO has shown that all three chlorites isomerised to the corresponding chloryl halides XClO₂. In turn, ClClO₂ and BrClO₂ were transformed into ClOClO and BrOClO; this process could be repeated many times until XClO₂ decomposed to oxygen and the halogen.

It was assumed⁵² that chloryl chloride takes part in stratospheric ozone destruction (Scheme 2),⁵² although one can simulate⁴⁶ a 'zero' cycle (Scheme 3), which does not result in ozone loss.⁴⁶

Scheme 2



Scheme 3



For decades, the ClO radicals were the subject of spectroscopic and kinetic studies (the first works on this subject were carried out as far back as 20–30 years ago); however, little attention was paid to their dimerisation (self-reaction). The possibility of Cl₂O₂ formation upon recombination of the ClO radicals and further involvement of the Cl₂O₂ molecules in the presumed catalytic cycle of ozone depletion (see Scheme 2) were the reasons for the appearance of numerous publications devoted to recombination of the ClO radicals and properties of the dimer formed.

2. Chlorine peroxide

An IR spectroscopic study⁵⁸ of recombination of the ClO radicals generated at 220–240 K under continuous flow conditions by the reaction of Cl atoms with ozone has shown that chlorine peroxide ClOOCl, which can take part in the aforementioned catalytic cycle, is the dominant recombination product. Although it was soon shown^{55, 59–62} that the IR spectral bands pertain most probably to dichlorine trioxide (chlorine sesquioxide Cl₂O₃), the main conclusion on the involvement of Cl₂O₂ in the catalytic cycle remained true.

When studying the spectrum of the ClO radical recombination products in the submillimetre range (415–435 GHz) at a temperature below 240 K, several Cl₂O₂ isomers and chlorine dioxide OClO were identified,⁶³ chlorine peroxide ClOOCl being the main product. The ClOOCl molecule has a chain structure with two equivalent chlorine atoms and two equivalent oxygen atoms (C₂

Table 6. Geometrical parameters and dipole moment (μ) for the chlorine peroxide molecule.

Parameter	Experimental data	Quantum-chemical calculations	
	MW ⁶³	MP2/6-31G* (see Ref. 46)	MP2/TZ2Pf (see Ref. 47)
$r(\text{Cl}-\text{O})/\text{\AA}$	1.7044	1.741	1.711
$r(\text{O}-\text{O})/\text{\AA}$	1.4259	1.420	1.407
$\text{Cl}-\text{O}-\text{O}/\text{deg.}$	110.07	109.0	108.9
ClOO/OOCl	81.03	85.0	83.0
μ/D	0.72	0.921	0.84

symmetry). Molecules of chlorine peroxide represent slightly prolate asymmetric rotors with the constants $A = 13109.4463$, $B = 2409.7892$ and $C = 2139.6786$ MHz.⁶³ Earlier,⁶⁴ the following constants were obtained: $A = 12967$, $B = 2333$ and $C = 2085$ MHz. Table 6 shows internuclear distances and bond angles for chlorine peroxide molecules (see also Ref. 65).

The calculated values of the internal rotational barrier for ClOOCl are as follows:

ClOOCl conformation	$E/\text{kcal mol}^{-1}$	
	data from Ref. 66	data from Ref. 67
<i>cis</i>	8.8	10.1
<i>trans</i>	4.9	5.4

According to Ref. 63, the dipole moment of a ClOOCl molecule is 0.72 D, although the value of 0.76 D was thought⁶⁷ to be the most reliable one for the dipole moment.

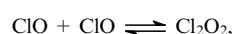
An IR spectrum of argon-matrix-isolated ClOOCl at 12 K demonstrated absorption bands at 752.6 (O–O, stretch), 649.8 and 647.6 cm^{-1} (Cl–O, stretches);⁵⁵ the absorption bands at 750 and 650 cm^{-1} were also present in the spectrum of gaseous chlorine peroxide.⁶⁰ In a later work,⁵⁶ the IR spectrum of ClOOCl isolated in an argon matrix was studied. For a molecule with an isotopic composition of $^{35}\text{Cl}^{16}\text{O}^{16}\text{O}^{35}\text{Cl}$, the frequencies 753.97 (ν_1), 543.0 (ν_2), 647.67 (ν_3) and 418.5 cm^{-1} (ν_6) were found and the values 310 (ν_3) and 127 cm^{-1} (ν_4) were calculated.

In the UV absorption spectrum of ClOOCl,⁶⁸ the absorption maximum was observed at 245 nm and the absorption cross-section (σ) was equal to $6.4 \times 10^{-18} \text{ cm}^2$ (at 350 nm, the absorption cross-section was $< 1 \times 10^{-19} \text{ cm}^2$). An adsorption maximum was also found⁶⁰ at 245 nm ($\sigma = 6.5 \times 10^{-18} \text{ cm}^2$), and measurable cross-section values could be obtained up to 410 nm. The fact that this UV spectrum pertained to chlorine peroxide was confirmed by calculations.⁴⁸ Later,⁶⁹ an UV spectrum of ClOOCl obtained by chlorine monoxide photolysis ($\lambda = 254 \text{ nm}$) was studied; the absorption maximum was found at 244 nm ($\sigma = 6.4 \times 10^{-18} \text{ cm}^2$). The measurements were carried out at 195 K in the 200–400 nm range.

In a number of studies, the enthalpies of ClOOCl formation and energies of bond dissociation were calculated, which did not coincide completely but did not differ dramatically from one another. The enthalpy of ClO dimerisation found⁶⁸ from the temperature dependence of the equilibrium constant

$$K_{\text{eq}} = \exp\left(\frac{\Delta S_1^\circ}{R}\right) \exp\left(-\frac{\Delta H_1^\circ}{RT}\right)$$

for the reaction

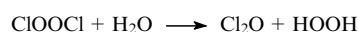


was equal to $-17 \pm 0.7 \text{ kcal mol}^{-1}$. An experimental value of the enthalpy of ClOOCl formation (ΔH_{298}°) was equal to $31.3 \pm 0.7 \text{ kcal mol}^{-1}$. A non-empirical calculation⁴⁶ of the enthalpy of ClOOCl formation carried out within the framework

of the second-order Møller–Plesset perturbation theory with the 6-31 + G(3d) and 6-31G* basis sets gave the values $\Delta H_0^\circ(\text{ClOOCl}) = 35.7$ (MP2/6-31 + G(3d) and 32.6 kcal mol^{-1} (MP2/6-31G*), and an estimate⁴⁷ obtained by the CCSD method was $\Delta H_0^\circ(\text{ClOOCl}) = 34.2 \text{ kcal mol}^{-1}$. Using an experimental value of the heat of ClO formation and a calculated value of $\Delta H_0^\circ(\text{ClOOCl})$ with a correction made for $T = 298 \text{ K}$, the energy of ClOOCl dissociation



was determined⁴⁷ to be $D(\text{ClO}-\text{OCl}) = 14.9 \text{ kcal mol}^{-1}$. The fact that the enthalpy value of $34.2 \text{ kcal mol}^{-1}$ calculated by using the isodesmic reaction



deviated from the experimental value may be due to an error introduced by determination of the heat of formation of Cl_2O .⁴⁷ Using another value for the heat of Cl_2O formation, the following parameters were obtained:⁴⁷ $\Delta H_0^\circ(\text{ClOOCl}) = 32.7 \text{ kcal mol}^{-1}$ and $D(\text{ClO}-\text{OCl}) = 16.4 \text{ kcal mol}^{-1}$, which were in better agreement with the experimental data.

According to an estimate,⁵⁸ dissociation of chlorine peroxide ClOOCl to ClO + ClO requires $\sim 16.7 \text{ kcal mol}^{-1}$, whereas the dissociation to Cl + ClOO requires more than 19 kcal mol^{-1} . The value of $\Delta H_0^\circ(\text{ClOOCl})$ was calculated⁷⁰ to be $33 \pm 2 \text{ kcal mol}^{-1}$. In a kinetic study⁷¹ devoted to reactions of ClOOCl thermal decomposition and ClO dimerisation, the energy of the O–O bond dissociation ($18.1 \text{ kcal mol}^{-1}$) was calculated and the enthalpy of ClOOCl formation ($30.5 \pm 0.7 \text{ kcal mol}^{-1}$) was determined. Apparently, without introducing a huge error, one can assume the dissociation energies of Cl–OOCl and ClO–OCl bonds to be 21 and 18 kcal mol^{-1} , respectively.^{69, 72}

Thus, the molecule of chlorine peroxide differs sharply from the FOOF molecule in the bond strength: the O–O bond in ClOOCl is much weaker as compared with that in FOOF. Ionisation of ClOOCl makes this bond still weaker: for an ionic dimer ClOOCl^+ , the values $D_{298}(\text{ClO}-\text{OCl}^+) = \sim 11.5 \pm 4.3 \text{ kcal mol}^{-1}$ and $\Delta H_{298}^\circ(\text{ClOOCl}^+) = 287.5 \pm 2.9 \text{ kcal mol}^{-1}$ were found.⁷³

3. The ClOO and OClO radicals

It was assumed⁵⁸ that the photolysis of ClOOCl in the polar stratosphere results in the formation of Cl atoms and ClOO radicals. An investigation⁷⁴ confirmed this assumption. It was found that it is these products that were formed upon laser pulse photolysis of chlorine peroxide ($\lambda = 308 \text{ nm}$, 235 K) with a primary quantum yield of 1.03 ± 0.12 . The photodissociation of ClOOCl to Cl atoms and ClOO radicals was also mentioned in Ref. 68; however, the possibility of another dissociation channel resulting in two ClO radicals⁵⁶ cannot be ruled out. In contrast to Cl atoms, ClO radicals do not catalyse the ozone destruction; hence, the ratio of the dissociation products $[\text{Cl}]:[\text{ClO}]$ is important when assessing the ozone-depletion effect of ClOOCl. Experiments⁷⁵ on the ClOOCl photolysis ($\lambda = 248$ and 308 nm) have shown that irradiation mainly cleaves the stronger Cl–O bond, the $[\text{Cl}]:[\text{ClO}]$ ratio being 0.88:0.12 (248 nm) and 0.90:0.10 (308 nm). Mass-spectrometric studies failed to detect the intermediate ClOO that forms in the Cl–O bond scission, because of its fast dissociation. Photolysis of chlorine peroxide at $\lambda = 308 \text{ nm}$ resulted in its dissociation to Cl atoms and O_2 molecules, whereas photolysis at 248 nm produced in addition ClO, O and ClOO.⁷⁶

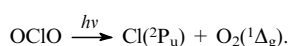
Abstraction of a chlorine atom from the ClOOCl molecule results in a ClOO radical, which is an isomer of the well-known chlorine dioxide OClO. The possibility of existence of the ClOO radical as an intermediate product in the pulse photolysis of chlorine–oxygen mixtures was reported by Porter and Wright⁷⁷ as far back as the early 1950's. The ClOO radical was by 3–4 kcal mol^{-1} energetically more favourable as compared with the OClO radical, the former being very reactive, however, in contrast, chlorine dioxide was stable at room temperature and

could exist as a radical for an indefinitely long period without any sign of dimerisation. Association of OCIO with the formation of weakly bound dimers was observed only in the solid state.^{78,79} Both ClO₂ isomers can be involved in the stratospheric ozone destruction, which explains the attention they have attracted in recent years (photochemistry of chlorine dioxide is the subject of numerous studies, see, *e.g.*, Refs 80–111). Experiments on OCIO photolysis most frequently used radiation with wavelengths of 365–368 nm; the absorption of OCIO begins at ~510 nm.

Photolysis of OCIO can result in both dissociation of the molecule and its photochemical isomerisation. A model of concerted isomerisation of the OCIO molecule which proceeds *via* ClOO isomers in the lower excited state ²A' was proposed. From this state, the radical ClOO can either emit a photon and pass to the ground state ²A'' with the energy 25–30 kcal mol⁻¹ lower than the energy of the ²A' state or dissociate. The ground state ²A'' of ClOO radicals obtained by photoisomerisation of chlorine dioxide and stabilised in an aluminosilicate matrix at 77 K was confirmed by analysis of the ESR spectrum.⁸¹

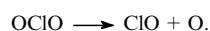
Decomposition of photo-excited OCIO molecules results in Cl atoms and O₂ molecules. Chlorine atoms can destroy ozone. Decomposition of OCIO can proceed by a different pathway, namely, with ClO and O formation. The latter species can regenerate ozone; however, dimerisation of ClO is preferable. Dimerisation of ClO and photoisomerisation of OCIO result in the formation of ClOOC or ClOO which destroy ozone. The direction of OCIO reactions, *viz.*, isomerisation or dissociation, and the mechanisms of these processes depend strongly on the photolysis conditions. In low-temperature inert matrices, chlorine dioxide transforms almost completely to the ClOO isomer. The ClOO radicals represent the only photoproduct upon photolysis of OCIO in an amorphous ice matrix (360 nm, 80 K).¹⁰⁰ Photolysis of OCIO at 150 K also produced ClOO together with ClClO₂. The latter was formed in the reaction of Cl atoms with chlorine dioxide.^{97,103} Chloryl chloride was also observed among the photolysis products of thin OCIO films either condensed at 100 K (up to 70 monolayers) or adsorbed on ice (0.5–2 monolayers).¹⁰⁵

Photolysis of aqueous and other solutions of chlorine dioxide results in the formation of chlorine atoms. The quantum yield and the mechanism of Cl atom formation were the subjects of a discussion. Thus it was assumed⁹⁷ that chlorine dioxide is first isomerised to ClOO, which is decomposed to Cl and O₂. On the other hand, it was supposed⁸⁹ that nearly 90% of excited OCIO molecules dissociate to O and ClO in an aqueous solution at room temperature at $\lambda = 365$ nm and only 10% of the molecules isomerise to ClOO, the latter decomposing to Cl and O₂ (the rate constant is $\sim 6.7 \times 10^9$ s⁻¹). However, the possibility of chlorine atom formation as the primary photoproduct has not been ruled out



According to data from Ref. 98, the 10% yield of Cl atoms comprised 9.5% of Cl obtained upon ClOO decomposition and 0.5% of Cl formed upon direct photodissociation. The same conclusion was made by the authors^{110,111} who studied photolysis of an aqueous solution of chlorine dioxide at $\lambda = 400$ nm. They have found that nearly 90% of excited OCIO molecules dissociate to ClO and O with subsequent recombination of these fragments. In this process, the quantum yield of the Cl atoms was about 10%, of which 2% were formed upon decomposition of ClOO and 8% were formed upon dissociation. They managed to observe ClOO radicals with a lifetime of ~4 ns.

Chang and Simon¹⁰⁴ assumed that a 'hot' ClOO isomer formed upon photolysis of OCIO undergoes relaxation in 9 ps and then dissociates. Irradiation of ClOO with light with a wavelength of 365 nm increased the yield of Cl atoms owing to the photolysis of vibrationally excited ClO radicals formed by the dominant photodissociation channel¹⁰⁸



A femtosecond spectroscopic study of the photolysis of an aqueous solution of OCIO has shown that ClO and O fragments quickly recombine to give vibrationally excited OCIO which relaxed to the ground state in 10 ps. Irradiation of OCIO with light with $\lambda = 400$ nm produced only Cl and O₂ as the photolysis products with a quantum yield of 0.07 ± 0.03 .^{106,107}

Gas-phase photoisomerisation of OCIO molecules seems to be highly unlikely.^{90,101}

In the UV spectrum, the absorption maximum of ClOO radicals was found at 248 nm [$\sigma = (3.4 \pm 0.3) \times 10^{-17}$ cm², 298 K] (Ref. 112) and at 246 nm [$\sigma = (2.98 \pm 0.23) \times 10^{-17}$ cm², 191 K] (Ref. 113).

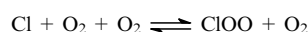
An IR spectrum of ClOO radicals generated by either photoisomerisation of argon-matrix-isolated OCIO or the reaction of Cl atoms with oxygen molecules at 17 K demonstrated the following vibrational frequencies: 1442.8 (ν_1), 408.3 (ν_2), 192.4 (ν_3) cm⁻¹ and an overtone of 375.6 cm⁻¹ ($2\nu_3$) (C_s point symmetry group).⁹⁵ IR-Fourier spectra measured for eight neon-matrix-isolated ClOO radicals with different isotope compositions contained all fundamental frequencies, four overtones and five combined frequencies.⁷⁹ For example, the spectrum of ³⁵Cl¹⁶O¹⁶O radicals contained the frequencies 1438.56 (ν_1), 413.73 (ν_2), 201.38 cm⁻¹ (ν_3) (anharmonicity-corrected frequencies were 1477.8, 432.4 and 214.8 cm⁻¹). The O–O stretch frequency for the ClOO radical (1477.8) was close to that for the O₂F radical (1487 cm⁻¹).

The exact values of geometrical parameters for ClOO radicals are unknown. Based on IR spectra measured during the photolysis of a Cl₂ + O₂ mixture at 4 K, estimates were made¹¹⁴ for bond lengths and bond angles in a ClOO radical (Table 7). For this radical, the following values were proposed:¹¹⁵ $r(\text{O}–\text{O}) = 1.31$ Å and $r(\text{O}–\text{Cl}) = 1.835$ Å. Noticeably different geometrical parameters of ClOO radicals were calculated by different methods, *viz.*, by the high-level nonempirical CMRCI (contracted multireference configuration interaction) method,¹¹⁶ by using the MP2 theory with different basis sets¹¹⁷ and by means of the density functional theory (DFT)¹¹⁸ (see Table 7). According to calculations,¹¹⁶ the dipole moment of ClOO is 1.113 D.

Table 7. Bond lengths and bond angle in the ClOO radical.

Parameter	Experimental data IR ¹¹⁴	Quantum-chemical calculations		
		CMRCI ¹¹⁶	MP2 ¹¹⁷	DFT ¹¹⁸
$r(\text{O}–\text{O})/\text{Å}$	1.23	1.201	1.174–1.247	1.2154
$r(\text{Cl}–\text{O})/\text{Å}$	1.83	2.139	1.923–2.203	1.9286
$\text{Cl}–\text{O}–\text{O}$ /deg.	110	115.7	114.1–118.6	115.74

In a kinetic study of the reaction of Cl atoms with O₂ molecules and the following equilibrium:

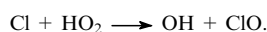


(181–200 K, oxygen pressure of 15–40 Torr), the rate constant for Cl + O₂ association was found to be $(8.9 \pm 2.9) \times 10^{-33}$ cm⁶ molecule⁻² s⁻¹ (186.5 ± 5.5 K).¹¹⁵ According to this study,¹¹⁵ the equilibrium constant (K_{eq}) of the reaction Cl + O₂ is 18.9 atm⁻¹ (185.4 K). A similar value ($K_{\text{eq}} = 20.4$ atm⁻¹) was found at the same temperature in a different study.¹¹² The enthalpy of formation of ClOO radical was found¹¹² to be $\Delta H_{298}^\circ(\text{ClOO}) = 23.4 \pm 0.5$ kcal mol⁻¹; calculations¹¹⁹ gave the value of 24.2 ± 2 kcal mol⁻¹. In experimental studies,^{112,115} calculations according to the third law of thermodynamics gave the following values for the dissociation energy $D_0(\text{Cl}–\text{OO})$: 4.76 ± 0.49 (Ref. 115) and 4.83 ± 0.05 kcal mol⁻¹ (Ref. 112). The calculated value of $D_0(\text{Cl}–\text{OO})$ was 4.0 ± 2 kcal mol⁻¹ (see Ref. 119). Quantum-chemical calculations using the density func-

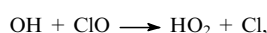
tional method showed that the dissociation energy of the ClO—O bond is 62.4 kcal mol⁻¹. Thus, it is evident that the ClOO radical has a strong O—O bond and a weak Cl—OO bond and in this respect resembles the FOO radical. A rather weak Cl—O bond allows us to consider the ClOO radical as an O₂ molecule with a ‘chaperon’, viz., a chlorine atom.¹²⁰

4. Compound HOOCI

Substitution of a hydrogen atom for a chlorine atom in chlorine peroxide gives HOOCI. This compound has not yet been isolated, however, it is of interest for atmospheric chemistry. Reactions Cl + HO₂ and ClO + OH can result in the formation of HOOCI. The reaction of Cl with HO₂ probably produces an excited HOOCI molecule with the lifetime at 298 K estimated as 1 ns.¹²¹ HOOCI molecules can decompose by three channels, viz., to Cl + HO₂, HCl + O₂ and OH + ClO. A study¹²² of the Cl + HO₂ reaction under continuous flow conditions at 250–420 K and a pressure of 0.9–1.5 Torr have shown that in this temperature range its rate constant depends little on the temperature and is equal to $(4.2 \pm 0.7) \times 10^{-11}$ cm³ molecule⁻¹ s⁻¹. At 298 K, the reaction proceeds by roughly 20% by the channel



At 243–298 K, the reaction of OH and ClO radicals largely proceeds by the channel



probably, with the formation of an excited HOOCI intermediate.¹²³ The other reaction channel

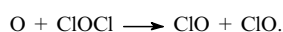


is realised to a small degree due to the high energy barrier associated with rearrangement of the intermediate.

The probability of stabilisation of excited HOOCI molecules is low under both atmospheric and laboratory conditions.¹²⁴ However, a non-empirical calculation using the CCSD(T)/TZ2P method has shown¹²⁵ that the thermal stability of HOOCI even exceeds that of ClOOCl; hence, when studying atmospheric processes, one must bear in mind the possibility of the existence of HOOCI. In the same work,¹²⁵ geometrical parameters of the HOOCI molecule were estimated [$r(\text{O}—\text{O}) = 1.443$ Å, $r(\text{Cl}—\text{O}) = 1.746$ Å, $r(\text{H}—\text{O}) = 0.968$ Å, bond angles Cl—O—O and O—O—H were 108.6° and 100.6°, respectively, the dihedral angle ClOO/OOH was 98.1°] as well as the dipole moment (1.74 D). The enthalpy of HOOCI formation was shown to be 1.5 ± 1 or 0.2 ± 1 kcal mol⁻¹. The calculated frequencies of HOOCI harmonic vibrations ω_1 – ω_6 were 3744, 1399, 835, 633, 392 and 361 cm⁻¹, respectively. The skewed structure of HOOCI was also confirmed by calculations.¹²⁶ It was also found¹²⁶ that the HOOCI isomer is most stable among the isomers of the general formula HClO₂, the energies of branched Y-shaped HClO₂ and a chain HOCIO (chlorous acid) forms exceeding the energy of the HOOCI form by 51.0 and 8.3 kcal mol⁻¹, respectively. The calculated¹²⁶ enthalpies of formation of HOOCI, HOCIO and HClO₂ molecules were 1.6, 11.9 and 56.2 kcal mol⁻¹, respectively [according to other estimates,¹³ $\Delta H_{300}^\circ(\text{HOOCI}) = -0.1$ kcal mol⁻¹]. The geometrical parameters of the HOOCI molecule calculated using the MP2/6-31G(d,p) method [$r(\text{O}—\text{O}) = 1.408$ Å, $r(\text{O}—\text{Cl}) = 1.751$ Å]¹¹⁶ were similar to those found in Ref. 125.

5. Chlorine chlorite and Cl₂O₂⁺ cation

In studies of disproportionation of chlorine-containing compounds, it was assumed that chlorine chlorite ClOClO can be an intermediate in these reactions.¹²⁷ Apparently, chlorine chlorite is the intermediate¹²⁸ in the reaction



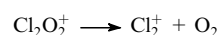
A mass-spectrometric study⁷³ of ClO dimers has shown that several Cl₂O₂ isomers exist, of which ClOClO is the least stable.

Table 8. Calculated values of bond lengths and bond and torsion angles for the ClOCl'O' molecule.

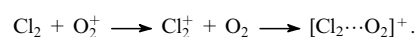
Parameter	Quantum-chemical calculations	
	MP2/6-31G* (see Ref. 46)	CCSD/TZ2P ⁴⁷
$r(\text{Cl}—\text{O})/\text{\AA}$	1.713	1.717
$r(\text{O}—\text{Cl}')/\text{\AA}$	1.909	1.739
$r(\text{Cl}'—\text{O}')/\text{\AA}$	1.512	1.517
$\text{Cl}—\text{O}—\text{Cl}'/\text{deg.}$	109.7	111.6
$\text{O}—\text{Cl}'—\text{O}'/\text{deg.}$	116.8	112.4
$\text{ClOCl}'/\text{OCl}'\text{O}'/\text{deg.}$	67.1	76.6

According to different estimates,^{13,46,47} the enthalpy of ClOClO formation is 40.8–44.3 kcal mol⁻¹. Table 8 shows the results of quantum-chemical calculations^{46,47} of geometrical parameters for the ClOClO isomer.

Salts that involve Cl₂O₂⁺ as a cation have been synthesised.¹²⁹ A reaction of hexafluoroantimonate O₂⁺SbF₆⁻ with chlorine in anhydrous HF at 195–233 K gave Cl₂O₂⁺SbF₆⁻; the addition of antimony pentafluoride to the same reactants resulted in the formation of Cl₂O₂⁺Sb₂F₁₁⁻. Black-violet crystals of both salts precipitated when the solutions were cooled to 193 K. Structural studies showed that the salts contain the Cl₂O₂⁺ cations shaped as flat trapezia in which the ‘chlorine part’ is spaced at 2.425 Å from the ‘oxygen part’, which amounts to ~75% of the sum of the van der Waals radii of Cl and O. The internuclear distances Cl—Cl and O—O were 1.916 and 1.185 Å, respectively. In the Raman spectrum of the Cl₂O₂⁺Sb₂F₁₁⁻ salt, an O—O stretch was observed at 1534 cm⁻¹ and Cl—Cl stretches were found at 586 and 593 cm⁻¹. Despite the apparent weakness of the cation structure, the salts are sufficiently stable: Cl₂O₂⁺SbF₆⁻ decomposes at 273 K, and Cl₂O₂⁺Sb₂F₁₁⁻ is stable up to 313 K. The dissociation energy of the Cl₂O₂⁺ cation



is equal to 12.8 kcal mol⁻¹. The formation of Cl₂O₂⁺ cations occurs as a result of chlorine oxidation by a dioxygenyl cation.



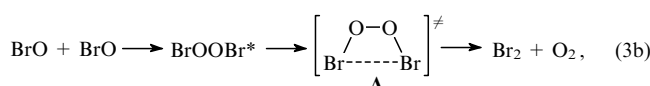
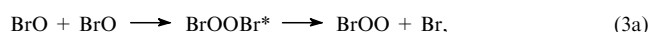
IV. Bromine and iodine oxides

1. Bromine oxides

Currently, bromine oxides remain insufficiently explored compounds despite the growing interest in them.¹³⁰ Probably, this is associated with their low stabilities. Only bromide monoxide Br₂O, bromine bromate BrOBrO₂ and bromic anhydride O₂BrO—BrO₂ have been characterised in most detail. Despite being known since the 1930s, BrO₂ has probably never been obtained in pure form. Moreover, a substance with this molecular formula is believed to be in fact either a mixture of Br₂O₃ and Br₂O₅ (see Ref. 130) or bromine perbromate BrOBrO₃ (Ref. 131).

The oxide Br₂O₂ has never been isolated either. However, this was probably observed¹³² in the IR spectroscopic studies of the products of atomic–molecular reactions of bromine and oxygen in solid argon. Moreover, it is most probable that this oxide is an intermediate in the recombination of the BrO radicals.

A study of disproportionation of the BrO radicals generated by photolysis of either bromine–ozone or bromine–oxygen mixtures



has shown¹³³ that reaction (3) is of the second order. The branching ratio for reactions (3a) and (3) k_{3a}/k_3 was equal to

Table 9. Geometrical parameters of the BrOOBr molecule calculated by different methods.

Parameter	Quantum-chemical calculations		
	BLYP, SVWN and B3LYP ¹³⁹	MP2, CCSD(T), B3LYP ¹⁴⁰	MP2/6-31 + G(2d) ¹⁴¹
$r(\text{O}-\text{O})/\text{\AA}$	1.264–1.335	1.359–1.410	1.4068
$r(\text{Br}-\text{O})/\text{\AA}$	1.922–2.082	1.861–1.900	1.8861
$\text{Br}-\text{O}-\text{O}/\text{deg.}$	113.3–115.6	109.6–112.6	111.46
$\text{BrOO/OOBr}/\text{deg.}$	79.2–85.6	82.2–84.6	84.75

0.84±0.03 (at 298 K). According to the data from Ref. 134, the branching ratio k_{3b}/k_3 is equal to 0.12±0.04. The vibrationally excited intermediate BrOOBr* either dissociates to BrOO and Br or passes to a more stable state and then dissociates to Br₂ and O₂ via a four-centred complex A.

Studies of the kinetics and mechanism of the self-reaction of the BrO radicals generated by pulse photolysis of bromine–ozone mixtures at 220 and 298 K and a pressure of different gases of 75–600 Torr have revealed¹³⁵ absorption at 312 nm, which was not reported earlier. The absorption at 220 K was attributed to the Br₂O₂ dimer. The rate constant for reaction (3) was equal to $(2.75\pm0.50)\times10^{-12}\text{ cm}^3\text{ molecule}^{-1}\text{ s}^{-1}$ at 298 K independent of pressure and changed from $(2.00\pm0.41)\times10^{-12}$ (100 Torr) to $(3.10\pm0.30)\times10^{-12}\text{ cm}^3\text{ molecule}^{-1}\text{ s}^{-1}$ (400 Torr) at 220 K. In the same work, the pressure-independent ratios $k_{3a}/k_3 = 0.84$ (298 K) and 0.68 (220 K) were found. Estimates¹³⁵ have shown that the lifetime of Br₂O₂ does not exceed 1 min in the stratosphere at 195 K.

In a kinetic study,¹³⁶ the absence of the OBrO radical among the products of the BrO + BrO reaction was reported. Apparently, the metastable intermediate BrOBrO the decomposition of which would have given OBrO either was not formed at all or quickly isomerised to BrOOBr. For reaction (3), the following rate constants were found ($\text{cm}^3\text{ molecule}^{-1}\text{ s}^{-1}$):¹³⁶ $k_3 = (2.98\pm0.42)\times10^{-12}$, $k_{3a} = (2.49\pm0.42)\times10^{-12}$, $k_{3b} = (4.69\pm0.68)\times10^{-13}$ at 298 K and 760 Torr (oxygen as the buffer gas). These values are similar to those obtained in a different study.¹³⁵ According to data from Ref. 137, in the temperature range of 204–388 K, the rate constant for reaction (3) depends on the temperature in the following way:

$$k_3 = (1.70 \pm 0.45) \times 10^{-12} \exp\left(\frac{215 \pm 50}{T}\right).$$

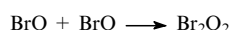
At 298 K, $k_3 = (3.51\pm0.35)\times10^{-12}\text{ cm}^3\text{ molecule}^{-1}\text{ s}^{-1}$. When simulating the atmospheric processes, it is recommended (bearing in mind the results of previous studies) to use the value

$$k_3 = (1.50 \pm 0.46) \times 10^{-12} \exp\left(\frac{230 \pm 100}{T}\right) \text{ cm}^3\text{ molecule}^{-1}\text{ s}^{-1}.$$

A detailed study¹³⁸ of the kinetics and mechanism of the self-reaction of BrO radicals in the temperature range of 220–298 K has shown that at $T < 250$ K a new reaction channel appears



At 222 K, the rate constants k_{3c} and k_{-3c} are equal to $8.2 \times 10^{-32}\text{ cm}^6\text{ molecule}^{-2}\text{ s}^{-1}$ and $2.5 \times 10^{-18}\text{ cm}^3\text{ molecule}^{-1}\text{ s}^{-1}$, respectively. The equilibrium constant is 1.937×10^5 (235 K) and $1.26 \times 10^6\text{ atm}^{-1}$ (222 K). An enthalpy change in the reaction



was estimated to be $-14\pm0.02\text{ kcal mol}^{-1}$.

The absorption maximum in the UV spectrum of the Br₂O₂ dimer was found at 305 nm, the cross-section $\sigma = 1.4 \times 10^{-17}\text{ cm}^2$ (at 350 nm, the cross-section was $1.28 \times 10^{-17}\text{ cm}^2$).¹³⁸

Like Cl₂O₂, compound Br₂O₂ can exist in several isomeric forms. Among three possible isomers of Br₂O₂, bromine peroxide

BrOOBr is the most stable.^{139,140} A calculation¹³⁹ using BLYP, SVWN and B3LYP density functionals have shown that the energies of BrBrO₂ and BrOBrO isomers are higher than that of the BrOOBr isomer by 8.4 and 11.3 kcal mol⁻¹, respectively. Table 9 shows the results of quantum-chemical calculations^{139–141} of geometrical parameters for the bromine peroxide molecule. Depending on the calculation method, the internuclear distance $r(\text{O}-\text{O})$ varies from 1.264 to 1.410 Å, and $r(\text{Br}-\text{O})$ varies from 1.861 to 2.082 Å, the bond angle Br–O–O varies from 109.6 to 115.6° and the torsion angle BrOO/OOBr varies from 79.2 to 85.6°. The vibrational spectrum of the BrOOBr molecule was also calculated.^{139–141} The frequencies of O–O stretches (1103, 1046 and 878 cm⁻¹) obtained¹³⁹ by three different methods differ substantially from the calculated frequencies 746 cm⁻¹ (Ref. 140) and 737 cm⁻¹ (Ref. 141).

The enthalpy of BrOOBr formation was estimated¹³ to be 41 kcal mol⁻¹ (300 K). Calculated within the framework of different approximations, the enthalpies of BrOOBr, BrBrO₂ and BrOBrO formation at 0 K are, correspondingly, 46.1, 52.9 and 54.8 kcal mol⁻¹ (Ref. 139) and 44±1, 57±6 and 56±4 kcal mol⁻¹ (Ref. 140).

It was shown¹⁴² that the reaction of bromine atoms with O₂ molecules in an argon matrix at 10 K gives BrOO radicals. The frequency of 1487.0 cm⁻¹ in the IR spectrum of the BrOO radicals was assigned to the O–O stretch. In a recent study¹⁴³ which analysed the IR spectrum of argon-matrix-isolated BrOO radicals with different isotope compositions at 17 K, the frequencies of 1485.1, 1444.0 and 1402.3 cm⁻¹ were attributed to the O–O stretches in Br¹⁶O¹⁶O, Br¹⁶O¹⁸O and Br¹⁸O¹⁸O, respectively. Non-empirical calculations using the QCISD(T) method¹⁴⁴ gave the frequencies of the Br–O stretch (450 cm⁻¹) and the Br–O–O bend (261 cm⁻¹).

Like its chlorine analogue, the BrOO radical is more stable than its symmetrical isomer OBrO by approximately 5 kcal mol⁻¹ (Ref. 145) or 17–18 kcal mol⁻¹ (Ref. 146).

By using five different density functionals, the internuclear distances Br–O and O–O and the Br–O–O bond angle were calculated¹⁴⁶ for the BrOO radical in its ground state ²A'' (Table 10). In the other studies,^{144,145} higher values were obtained for the Br–O bond length and lower values were found for the O–O bond length.

Table 10. Geometrical parameters of the BrOO radical.

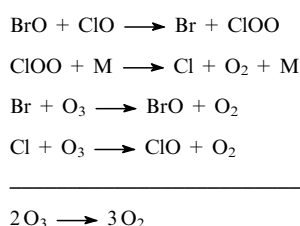
Parameter	Quantum-chemical calculations			
	BHLYP ¹⁴⁶	BP86 ¹⁴⁶	QCISD(T) ¹⁴⁴	[UMP/2, CCSD(T)] ¹⁴⁵
$r(\text{Br}-\text{O})/\text{\AA}$	2.178	2.150	2.302	2.291
$r(\text{O}-\text{O})/\text{\AA}$	1.253	1.242	1.232	1.214
$\text{Br}-\text{O}-\text{O}/\text{deg.}$	118	118		116.4

According to estimates,¹⁴⁷ the strength of the Br–O bond is ~1 kcal mol⁻¹. A later estimate¹⁴⁵ gave practically the same value, viz., 1.2–1.7 kcal mol⁻¹. Dissociation of BrOO radicals to BrO and O requires more than 50 kcal mol⁻¹ (Ref. 145). The enthalpy of BrOO formation is 35.1 kcal mol⁻¹ (300 K).¹³

Irradiation of BrOO radicals isolated in a solid argon matrix at 275 nm resulted in reversible photoisomerisation to give OBrO.¹⁴³ If the matrix also contained oxygen, photolysis of BrOO produced O₃ and BrO. Apparently, in this case a reaction of excited BrOO radicals with oxygen molecules proceeds.¹⁴⁸

Contamination of the atmosphere of Earth with bromine-containing compounds proceeds both in a natural way and as a result of human activities. Methyl bromide is the main source of stratospheric bromine. Its content in the atmosphere was recently assessed to be ~10 ppt (1 ppt = 10⁻¹²).¹⁴⁹ The lifetime of CH₃Br in the atmosphere is less than two years, it readily photolyses in the lower stratosphere. It was concluded¹⁵⁰ that, of all possible bromine-involving catalytic cycles of ozone depletion, the cycle with the reaction BrO + ClO as the rate-determining step (Scheme 4) is the most efficient.

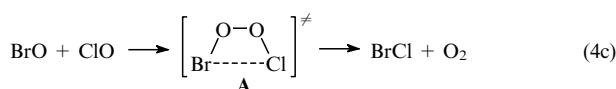
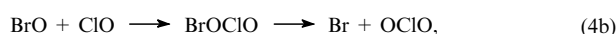
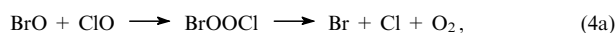
Scheme 4



This cycle is particularly remarkable due to the fact that the loss of two radicals that are inactive with respect to ozone results in appearance of very reactive bromine and chlorine atoms.¹⁵¹ The contribution of such a cycle into the halogen-controlled ozone depletion can reach 20%–25%.¹⁵² Many studies were devoted to the BrO + ClO reaction (*e.g.*, see Refs 153–161 and references therein).

2. Compounds BrOOCl, BrOCIO and HOOBr

The class of compounds covered by this review also involves BrOOCl and BrOCIO. These can form as intermediates in the BrO + ClO reaction



It was found^{154, 156} that the rate constant for reaction (4) is $(8.2 \pm 1.0) \times 10^{-12} \text{ cm}^3 \text{ molecule}^{-1} \text{ s}^{-1}$ and does not depend on the temperature in the range of 241–408 K. In the same studies, the following branching ratios were found: $k_{4a}/k_4 = 0.45 \pm 0.10$, $k_{4b}/k_4 = 0.55 \pm 0.10$ and $k_{4c}/k_4 < 0.02$. The presence of channel (4c) was concluded by Toohey and Anderson,¹⁵⁵ and the formation of BrCl in considerable amounts was experimentally observed,^{157, 158, 160, 161} which suggests that this channel makes a substantial contribution to reaction (4). Using the gas-discharge technique and mass spectrometry and a combination of pulse photolysis and UV absorption spectroscopy, the value $k_4 = (1.29 \pm 0.16) \times 10^{-11} \text{ cm}^3 \text{ molecule}^{-1} \text{ s}^{-1}$ (298 K) and the ratio $k_{4c}/k_4 = 0.08 \pm 0.03$ were obtained.^{158, 159} Like many other bimolecular radical–radical reactions, reaction (4) is characterised by an inverse temperature dependence. Thus the following values were obtained for the rate constant of reaction (4) in the temperature range of 220–400 K ($\text{cm}^3 \text{ molecule}^{-1} \text{ s}^{-1}$):

$$k_4 = (4.70 \pm 0.50) \times 10^{-12} \exp\left(\frac{320 \pm 40}{T}\right) \quad (\text{Ref. 158})$$

and

$$k_4 = (6.1 \pm 1.2) \times 10^{-12} \exp\left(\frac{240 \pm 60}{T}\right) \quad (\text{Ref. 159}).$$

Values of rate constants for reaction (4) similar to the aforementioned values,^{158, 159} were found in the studies devoted to the kinetics of this reaction and involving mass-spectrometric detection of the products:¹⁶⁰ $k_4 = (1.13 \pm 0.15) \times 10^{-11} \text{ cm}^3 \text{ molecule}^{-1} \text{ s}^{-1}$, $k_{4b}/k_4 = 0.43 \pm 0.10$ and $k_{4c}/k_4 = 0.12 \pm 0.04$ (298 K). Thus, the BrO + ClO reaction proceeds with formation of two intermediates, *viz.*, BrOCIO which gives OCIO [channel (4b)] and BrOOCl which either decomposes to Br, Cl and O₂ [channel (4a)] or rearranges to the four-centred state A with subsequent elimination of BrCl [channel (4c)].

A calculation¹⁴⁰ has shown that, of the mixed oxides XX'O₂ (X = Br and X' = Cl), the peroxide BrOOCl is the most stable; the enthalpy of its formation was found to be $39 \pm 2 \text{ kcal mol}^{-1}$ (0 K)¹⁴⁰ or $38.9 \text{ kcal mol}^{-1}$ (0 K).¹³⁹ In an earlier work,¹⁵⁵ the geometrical parameters of the BrOOCl molecule were estimated: $r(\text{Br}-\text{O}) = 1.8 \text{ \AA}$, $r(\text{Cl}-\text{O}) = 1.7 \text{ \AA}$, $r(\text{O}-\text{O}) = 1.2 \text{ \AA}$ and the BrOO/OOBr dihedral angle was ~70°. A calculation¹⁴⁰ using the MP2 perturbation theory gave the following values: $r(\text{Br}-\text{O}) = 1.859 \text{ \AA}$, $r(\text{Cl}-\text{O}) = 1.710 \text{ \AA}$, $r(\text{O}-\text{O}) = 1.412 \text{ \AA}$, bond angles Br–O–O and Cl–O–O were both equal to 109° and the dihedral angle was 84.5°. The values close to those mentioned above were also obtained in calculations using the B3LYP density functional.

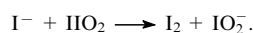
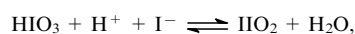
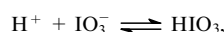
It was assumed¹⁶² that the reaction of the BrO radical with hydroxyl involves the formation of a short-lived vibrationally excited complex HOOBr. The main and probably the only channel of this reaction is



The rate constant for this reaction was estimated to be $(7.5 \pm 4.2) \times 10^{-11} \text{ cm}^3 \text{ molecule}^{-1} \text{ s}^{-1}$ at 300 K and 1 Torr.¹⁶² The enthalpy of HOOBr formation was determined to be 5 kcal mol^{-1} (298 K)¹⁶² which is similar to the value of $4.2 \text{ kcal mol}^{-1}$ (300 K)¹³ and to the calculated¹³⁹ value of $8.6 \text{ kcal mol}^{-1}$ (0 K). The formation of the HOBrO intermediate in the BrO + OH reaction cannot be ruled out either; however, isomerisation of HOOBr to HOBrO is hindered due to the high energy barrier.¹⁶³

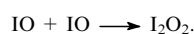
3. Iodine oxides

An assumption of the existence of I₂O₂ and its hydrate H₂I₂O₃ as intermediates in the reaction of the iodate ions with the iodide ions in an acidic medium was put forward back in 1930 (see Ref. 164). In a study devoted to the mechanism of this reaction,¹⁶⁴ the following scheme of I₂O₂ formation (in the HIO₂ form) was proposed:

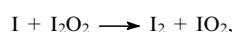


By analogy with the recombination of ClO and BrO radicals, one can assume that the reaction IO + IO also proceeds with the formation of I₂O₂ dimers as the intermediates, although the evidence of their existence is still insufficient.

When studying the recombination of IO radicals generated upon photolysis of CH₃I in the presence of ozone at 303 K at an atmospheric pressure (N₂ and O₂ as the diluent gases), the formation of the I₄O₉ aerosol was observed, which deposited on reactor walls as a yellow-white film.¹⁶⁵ It was assumed^{165, 166} that, at first, the bimolecular self-reaction of the IO radicals proceeds



The I₂O₂ formed reacts with I to give IO₂



and the latter transforms into amorphous I₄O₉.

The IO + IO reaction was studied by a combination of pulse photolysis and UV absorption spectroscopy in the temperature range of 250–373 K at a pressure of 650 Torr (nitrogen as the

diluent gas).¹⁶⁷ The rate constant for this reaction is independent of the temperature and has the following form:

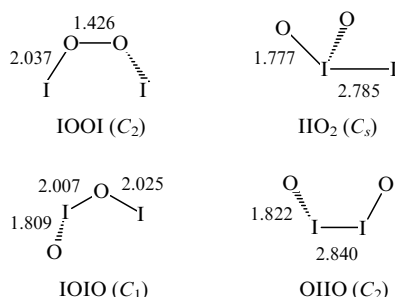
$$k = 1.73 \times 10^{-12} \exp \left(\frac{1020 \pm 200}{T} \right).$$

At 298 K, its value was $(5.6 \pm 1.2) \times 10^{-11}$ cm³ molecule⁻¹ s⁻¹. The rate constant at 300 K was determined¹⁶⁸ to be $(6.6 \pm 2) \times 10^{-11}$ cm³ molecule⁻¹ s⁻¹. Later,¹⁶⁹ the rate constant $k = (8 \pm 1.7) \times 10^{-11}$ cm³ molecule⁻¹ s⁻¹ was measured at room temperature and a pressure of 60–600 Torr.

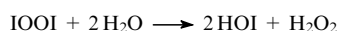
It was concluded¹⁷⁰ that I₂O₂ dimers can form in the self-reaction of the IO radicals, although this possibility has never been confirmed in spectroscopic studies. According to certain data,¹⁷⁰ the rate constant for this reaction is temperature-independent in the range of 220–320 K and is equal to $(9.9 \pm 1.5) \times 10^{-11}$ cm³ molecule⁻¹ s⁻¹.

A non-empirical calculation using the QCISD(T)/6-311 + G(3df) basis set¹⁷¹ has shown that all I₂O₂ isomers are unstable with respect to the elements at 298 K.

Below, four possible isomers of I₂O₂ are shown as well as the calculated bond lengths (in Å) in them



In this family, the IIO₂ isomer is the most stable (in contrast to the corresponding chlorine and bromine analogues). The stability of I₂O₂ isomers decreases in the following sequence:¹⁷¹ IIO₂ > IOIO > IOOI > OIIO. In the IIO₂ molecule, the internuclear distance $r(\text{I}-\text{O}) = 1.777$ Å [calculated using the MP2/6-311 + G(3df) method] is the shortest distance as compared with the other I₂O₂ isomers, and the frequency of the I–O stretch is the highest (about 960 cm⁻¹). The lifetime of IIO₂ with respect to its decomposition to I and OIO at room temperature was estimated to be ~4 s. The geometrical parameters of iodine peroxide molecules IOOI were also calculated:¹⁷¹ $r(\text{I}-\text{O}) = 2.037$ Å, $r(\text{O}-\text{O}) = 1.426$ Å, the bond angle I–O–O and the torsion angle IOO/OOI were equal to 110 and 86°, respectively. The frequency of the I–O stretch was ~510 cm⁻¹. Using the following isodesmic reaction



the enthalpy of IOOI formation was calculated to be 37.5 kcal mol⁻¹ (at 298 K).¹⁷¹ As suggested by the authors of this work,¹⁷¹ OIO may be among the products of the IO + IO reaction.

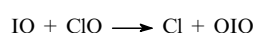
Apparently, IOO radicals are still less stable as compared with ClOO radicals.^{171, 172}

The reaction of IO and ClO radicals at 298 K and the total pressure of 1 Torr was studied by mass spectrometry¹⁷³



For reactions (5), the rate constant $k_5 = (1.1 \pm 0.2) \times 10^{-11}$ cm³ molecule⁻¹ s⁻¹ and the branching ratios $k_{5a}/k_5 = 0.55 \pm 0.03$, $k_{5b}/k_5 = 0.25 \pm 0.02$ and $k_{5c}/k_5 = 0.20 \pm 0.02$ were found.¹⁷³ The value $k_5 = (1.29 \pm 0.27) \times 10^{-11}$ cm³ molecule⁻¹ s⁻¹ (298 K) was also obtained.¹⁷²

The channel



was assumed to be highly improbable.

The most important source of iodine in the atmosphere is methyl iodide, which is liberated by algae and phytoplankton of the ocean and is rapidly photolysed in the troposphere. Iodine compounds can get to the stratosphere as a result of convection. Nuclear stations can also be a source of atmospheric contamination with iodine. The activity of iodine in the atmosphere is associated particularly with the absence of a photolytically stable reservoir of iodine-containing molecules.

* * *

Until recently, insufficient attention has been paid, for very clear reasons, to halogen–oxygen compounds X₂O₂, with the exception of dioxygen difluoride. The interest which has been aroused in these and related compounds was associated with the problem of stratospheric ozone depletion. The use of traditional and advanced methods for studying the properties of unstable compounds, as well as theoretical calculations of different levels allowed certain characteristics of both existing and imaginary compounds with the general formula X₂O₂ to be obtained. In this review, an attempt is undertaken to draw their ‘portraits’ based on the data taken from literature sources in which these compounds are discussed. The work dealing with other oxygen compounds of halogens are beyond the scope of this survey.

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- ^a — *Kinet. Catal. (Engl. Transl.)*

Synthesis and reactions of organic compounds containing bonds of Te to Group 14 elements

I D Sadekov

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Abstract. The data on the synthesis and reactions of organic compounds containing bonds of Te to Group 14 elements are generalised and systematised. The use of these compounds in the synthesis of organoelement compounds, complexes with organotellurium ligands, tellurium-containing clusters and metal tellurides is reviewed. The bibliography includes 99 references.

I. Introduction

The existence of four types of true, *i.e.*, containing at least one $Te-C$ bond, organotellurium compounds with Group 14 elements, *viz.*, $(R^1Te)_4E$, $(R^1Te)_3ER^2$, $(R^1Te)_2ER_2^2$ and $R^1TeER_3^2$ ($R^1 = Alk, Ar$; $R^2 = H, Alk, Ar$; $E = Si, Ge, Sn, Pb$), is possible in principle. Tellurides $R^1TeER_3^2$ are the most well studied among them. Compounds $(TeR)_4E$ have not been described so far, while the other two types are represented by only a few examples. The derivatives $(R_3E)_2Te$, the methods of synthesis and reactions of which are similar to those of tellurides $R^1TeER_3^2$ are also considered.

The interest in compounds $R^1TeER_3^2$ and $(R_3E)_2Te$ is determined by the fact that these are currently acquiring an ever increasing importance in the synthesis of organic and inorganic tellurium derivatives. Perfluoroalkyl trimethylstannyl tellurides $(R_FTeSnMe_3)$ are used for the preparation of telluroketones and previously unknown telluracyles.^{1–3} Compounds $R^1TeER_3^2$ are used as synthetic equivalents of organyl telluroate anions RTe^- which are easily oxidised in air and are used exclusively *in situ*.^{4–9} These types of compounds have been used in the synthesis of aryl methyl tellurides,⁸ aryl tellurobenzoates⁹ and aryl telluroformates^{6,7} in high yields. Triphenylgermyl derivatives and their stannyl analogues, *viz.*, $ArTeEPh_3$ ($E = Ge, Sn$), are convenient starting compounds for the synthesis of metal telluroates $(ArTe)_nM$ (M is metal),⁴ whereas $BuTeSiMe_3$ is used for the synthesis of tellurium-containing clusters.⁵ The reaction of bis-(trialkylsilyl) tellurides with some organoelement compounds,

which enables low-temperature synthesis of practically important metal tellurides M_xTe_y , attracts special attention.^{10,11}

The use of other compounds with $Te-E$ bonds for the synthesis of organic tellurium derivatives and some organic and organoelement compounds are described in more detail in the sections devoted to reactions of tellurides $R^1TeER_3^2$.

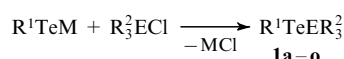
Earlier data on the synthesis and reactions of compounds $R^1TeER_3^2$ and $(R_3E)_2Te$ are described in the monographs.^{12–14}

Spatially hindered (organoelement)telluroles of the type R_3ETeH ($R = Me_3Si$, $E = Si, Ge$; $R = Ph$, $E = Si$) as well as tin and lead telluroates $[(Me_3Si)_3SiTe]_2E$ ($E = Sn, Pb$), which also contain $Te-E$ bonds, are used as the starting compounds in low-temperature synthesis of tellurides of these metals and are considered in the reviews.^{15,16}

II. Synthesis and reactions of compounds $R^1TeER_3^2$ ($E = Si, Ge, Sn, Pb$)

1. Synthesis of compounds $R^1TeER_3^2$

The most common approach to the synthesis of compounds $R^1TeER_3^2$ (**1**) with any element E is based on the reaction of alkali-metal telluroates R^1TeM with chlorides R_3^2ECl .^{4,5,17–19} Lithium telluroates are usually prepared by insertion of tellurium into the $C-Li$ bonds of alkyl(aryl)lithium,^{5,17–19} whereas sodium telluroates can be obtained by reducing diaryl ditellurides with either sodium borohydride in $PhH-EtOH$ ^{4,19} or metallic sodium in THF.¹⁸ The yields of compounds **1** usually vary from 60% to 80% with the exception of *p*-methoxyphenyl (triphenylgermyl) telluride (**1g**) obtained in 23% yield.⁴ Bis(trimethylsilyl) telluride and dialkyl ditellurides are side products in the synthesis of alkyl trimethylsilyl tellurides **1a,b**.^{5,17} $Ph_3SiTePh$ could not be obtained by this method.⁴



$M = Li, Na$.

Compound 1	E	R^1	R^2	Ref.
a	Si	Me	Me	17
b	Si	Bu	Me	5
c	Si	Ph	Me	17–19
d	Ge	Ph	Me	19
e	Ge	Ph	Ph	4, 19
f	Ge	Ph	4-MeOC ₆ H ₄	4
g	Ge	4-MeOC ₆ H ₄	Ph	4
h	Sn	Ph	Me	19

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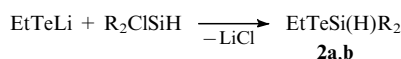
Received 30 July 2001

Uspekhi Khimii **71** (2) 113–125 (2002); translated by R L Birnova

Compound 1	E	R ¹	R ²	Ref.
i	Sn	Ph	Ph	4, 19
j	Sn	Ph	4-MeC ₆ H ₄	4
k	Sn	Ph	4-MeOC ₆ H ₄	4
l	Pb	Ph	Ph	4, 19
m	Pb	Ph	4-BrC ₆ H ₄	4
n	Pb	Ph	4-MeC ₆ H ₄	4
o	Pb	Ph	4-MeOC ₆ H ₄	4

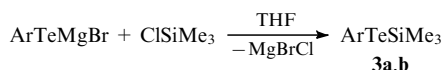
The silyl derivatives **1a–c** represent pale yellow fluids with an unpleasant odour; their analogues containing heavier Group 14 elements are colourless or pale yellow solids readily soluble in ordinary organic solvents.

The reaction of lithium ethanetellurolate with chlorosilanes was used in the synthesis of the silyl derivatives **2a,b** containing alkyl groups and a hydrogen atom at the silicon atom.²⁰



R = Me (**a**), Et (**b**).

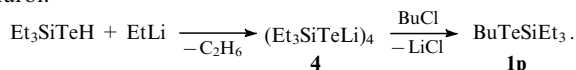
Aryl trimethylsilyl tellurides **3a,b** are obtained in 30%–40% yields by treatment of aryl telluromagnesium bromides with chlorotrimethylsilane in THF.^{21, 22}



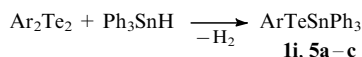
Ar = Ph (**a**), 4-MeC₆H₄ (**b**).

(Me₂Si)₂Te and Me₃SiO(CH₂)₄TePh were isolated along with compound **3a** in 10% and 45% yields, respectively.²¹ The latter seems to result from the tetrahydrofuran ring opening under the action of chlorotrimethylsilane and the reaction of Me₃SiO(CH₂)₄Cl formed with PhTeMgBr.

Yet another approach to the synthesis of compounds **1**, viz., the reaction of the lithium derivatives R₃ETeLi with alkyl halides, is represented by a single example. Thus butyl (triethylsilyl) telluride **1p** was synthesised²³ in 79% yield by treatment of tetrameric lithium triethylsilylanetellurolate (**4**) with butyl chloride. Compound **4** is prepared from ethyllithium and the corresponding tellurol.²³



Reactions of diorganyl ditellurides^{1–3, 24} and diorganyl tellurides^{6, 7, 25–27} with organoelement hydrides afford tellurides **1** containing Si, Ge and Sn atoms. The synthetic potential of this method is inferior to that based on the reaction of alkali-metal tellurolates with chlorides R₃TECl and is mainly employed for the synthesis of organyl (triorganylstannyl) tellurides **1** (E = Sn). The reaction of diaryl ditellurides with triphenylstannane proceeds under mild conditions (heating of the reactants at 60–70 °C without a solvent) and results in aryl (triphenylstannyl) tellurides **1i, 5a–c** in 50%–70% yields.²⁴

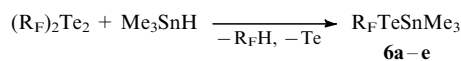


Ar = Ph (**1i**), 4-MeOC₆H₄ (**5a**), 4-EtOC₆H₄ (**5b**), 4-PhOC₆H₄ (**5c**).

If tributylstannane is used instead of triphenylstannane, no individual compounds similar to compounds **5** could be isolated. However, the mass spectra of oily reaction products contain peaks of molecular ions corresponding to aryl (tributylstannyl) tellurides ArTeSnBu₃.²⁴

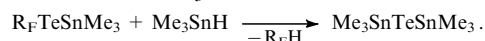
The reaction of bis(perfluoroalkyl) ditellurides with trimethylstannane is employed in the synthesis of perfluoroalkyl trimethylstannyl tellurides **6a–e**.^{1–3} Thus trifluoromethyl trimethylstannyl telluride **6a** was obtained in ~90% yield on warming of a 1:3 (CF₃)₂Te₂–Me₃SnH mixture in diethyl ether from –196 to 0 °C (see Ref. 1).

Compounds **6b–e** were synthesised under nearly identical conditions.^{2, 3} The reaction of the corresponding ditellurides with Me₃SnH (molar ratio 1:1) affords perfluorohydrocarbons and Te together with perfluoroalkyl trimethylstannyl tellurides.

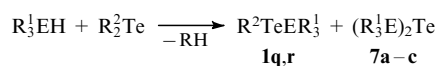


R_F = CF₃ (**a**), C₂F₅ (**b**), (CF₃)₂CF (**c**), C₃F₇ (**d**), C₄F₉ (**e**).

It is noteworthy that the yields of compounds **6** with a ditelluride:Me₃SnH molar ratio of 1:2 are much lower due to their reaction with Me₃SnH.²

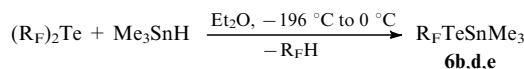


Reactions of diorganyl tellurides with organoelement hydrides proceed with the cleavage of one or two C–Te bonds resulting in compounds **1** or bis[triorganylsilyl (germyl, stannyl)] tellurides (R₃E)₂Te **7**. Sometimes, mixtures of both types of compounds are formed. The nature of the reactants is the main factor which determines the direction of these reactions. Thus in the case of dialkyl tellurides, a crucial role is played by the nature of the hydrides R₃EH the reactivities of which increase in the following order: Si < Ge < Sn. The reaction of triethylsilane with diethyl telluride (200 °C, 7 h) affords a mixture of compounds **1q** and **7a** (yields 12% and 55%, respectively). The reaction of triethylgermane with the same telluride (140 °C, 7 h) gives a mixture of compounds **1r** and **7b** in comparable yields (39% and 59%, respectively), whereas a similar reaction of triethylsilane yields only telluride **7c** even at 20 °C.^{25, 26}



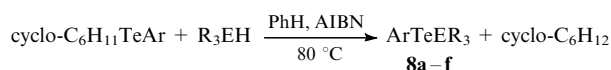
R¹ = R² = Et: E = Si (**1q, 7a**), Ge (**1r, 7b**), Sn (**7c**).

In contrast to dialkyl tellurides, the reaction of bis(perfluoroalkyl) tellurides with trimethylstannane (molar ratio 1:1) gives exclusively perfluoroalkyl trimethylstannyl tellurides **6b,d,e** in 50%–65% yields.^{2, 3}



R_F = C₂F₅ (**b**), C₃F₇ (**d**), C₄F₉ (**e**).

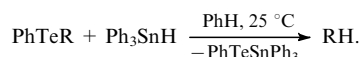
Irrespective of the nature of the hydrides R₃EH, their reaction with aryl cyclohexyl tellurides leads to the cleavage of only the C_{sp³}–Te bond. Thus tellurides **8a–f** were prepared by heating an equimolar mixture of the reactants in benzene in the presence of catalytic amounts of azoisobutyronitrile (AIBN).^{6, 7, 27, 28} Compounds **8** were not isolated due to their low stabilities and were used in subsequent conversions (see Section II.2) *in situ*.



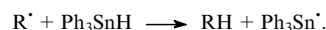
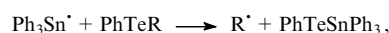
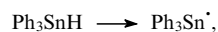
Compound 8	Ar	E	R	Ref.
a	Ph	Si	Me ₃ Si	6, 7, 28
b	4-FC ₆ H ₄	Si	Me ₃ Si	6, 7, 28
c	Ph	Ge	Bu	28
d	4-FC ₆ H ₄	Ge	Bu	28
e	Ph	Sn	Bu	27
f	4-FC ₆ H ₄	Sn	Bu	28

In contrast to tris(trimethylsilyl)silane, triphenylsilane does not split the C–Te bonds in aryl cyclohexyl tellurides.²⁸

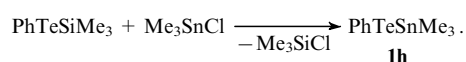
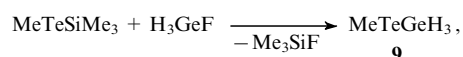
It is of note that reaction of alkyl (or cycloalkyl) phenyl tellurides with triphenylstannane was proposed²⁹ as an efficient preparative procedure for the synthesis of alkanes (or cycloalkanes) in high yields long before the publication of the works.^{6, 7, 27, 28}



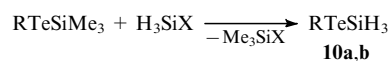
In all probability, this reaction follows a radical mechanism.²⁹



Germlyl (**9**) and stannyl (**1h**) derivatives were prepared in nearly quantitative yields by exchange reactions of organyl trimethylsilyl tellurides with the corresponding fluorogermane or chlorostannane.¹⁷



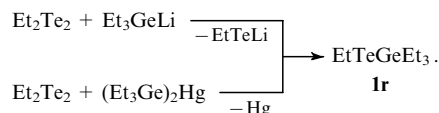
A similar reaction was used in the synthesis of organyl silyl tellurides **10a,b**.¹⁷



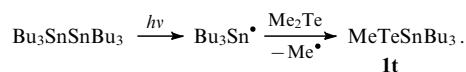
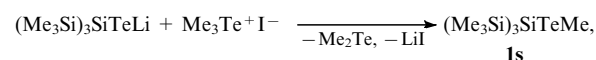
R = Me (**a**), Ph (**b**); X = Br, I.

The attempts to synthesise compounds of the type **10** by the reaction of lithium methane(benzene)telluroate with BrSiH_3 were unsuccessful, bis(silyl) telluride $(\text{H}_3\text{Si})_2\text{Te}$ being the only reaction product.¹⁷

Other reactions resulting in compounds **1** are represented by single examples. Thus ethyl (triethylgermyl) telluride (**1r**) was synthesised by reaction of diethyl ditelluride with triethylgermyl-lithium (yield 89%)²⁰ or from the same ditelluride and bis(triethylgermyl)mercury (yield 73%).³⁰



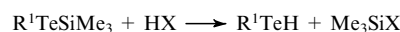
Methyl tris(trimethylsilyl)silyl telluride (**1s**) was synthesised by treatment of lithium tris(trimethylsilyl)silanetelluroate with trimethyltelluronium iodide.³¹ Photolysis of a hexabutyldistannane–dimethyl telluride mixture yields methyl tributylstannyl telluride (**1t**).³²



2. Reactions of compounds $\text{R}^1\text{TeER}_3^2$

In most cases, reactions of compounds **1** were studied using silyl and stannyl derivatives as examples. Some of these reactions represent valuable procedures for preparative synthesis of various organotellurium compounds including those used in synthetic organic chemistry.

The Te–Si bond in organyl triorganysilyl tellurides is easily cleaved under the action of hydrohalic acids, alcohols and water to give organyl tellurols and halogenosilanes, alkoxy-silanes or siloxanes, respectively.¹⁷

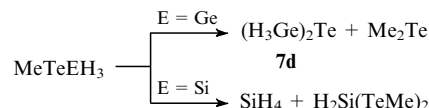


$\text{R}^1 = \text{Me, Ph; X} = \text{Br, I, Oalk, OH}.$

Benzenetellurol *in situ* manifests strong reducing properties.^{33–35} Several methods for the synthesis of this compound are known, they include methanolysis of phenyl trimethylsilyl telluride^{33–35} and reduction of diphenyl ditelluride with hypophos-

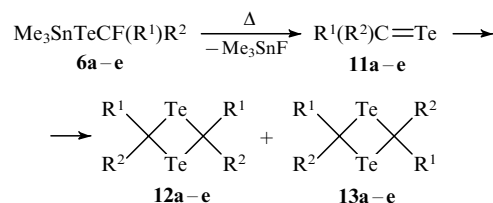
phorous acid or sodium borohydride.³³ The former approach is especially convenient. Phenyltellurol thus generated reduces nitro compounds into amines (in benzene or chloroform),^{33,34} alkenes and alkynes into alkanes,³⁴ aldehydes and ketones into alcohols³⁴ and reduction of carbonyl compounds in alcohols in the presence of catalytic amounts of ZnI_2 affords ethers.³⁵ These reactions proceed under mild conditions and in high yields.

Compounds **1** readily undergo disproportionation. Thus methyl germly telluride disproportionates into di(germyl) telluride (**7d**) and dimethyl telluride, whereas disproportionation of methyl silyl telluride yields bis(methyltelluro)silane and silane.¹⁷



The disproportionation of methyl trimethylstannyl telluride upon long-term storage or irradiation at 488 nm follows the same scheme as in the case of methyl germly telluride, bis(trimethylstannyl) telluride and dimethyl telluride being formed.¹⁷

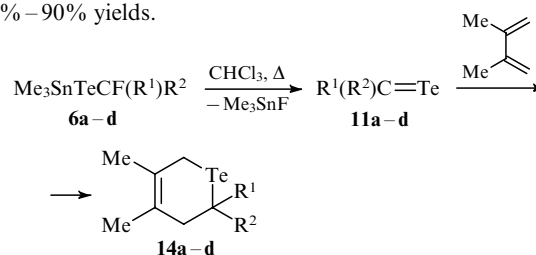
Pyrolysis of perfluoroalkyl trimethylstannyl tellurides **6** proceeds in quite a different manner.^{1–3} This results in trimethyl-fluorostannane and telluroketones **11**, which easily dimerise into the 1,3-ditellurethane derivatives **12** and **13**.^{1–3}



$\text{R}^1 = \text{F; R}^2 = \text{F}$ (**a**), CF_3 (**b**), C_2F_5 (**d**), C_3F_7 (**e**);

$\text{R}^1 = \text{R}^2 = \text{CF}_3$ (**c**).

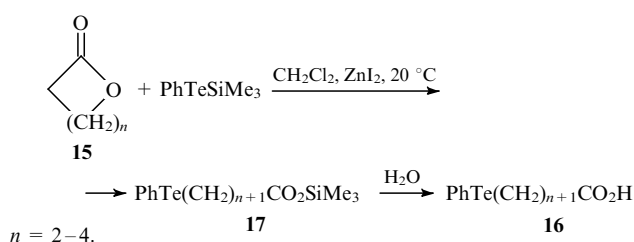
Heating of tellurides **6a–d** in chloroform with a large excess of 2,3-dimethylbutadiene yields initially the telluroketones **11a–d**, which then enter into a [4 + 2]-cycloaddition reaction^{1–3} to give 5,6-dihydro-3,4-dimethyl-2*H*-tellurine derivatives **14a–d** in 70%–90% yields.



$\text{R}^1 = \text{R}^2 = \text{F}$ (**a**); $\text{R}^1 = \text{F, R}^2 = \text{CF}_3$ (**b**); $\text{R}^1 = \text{R}^2 = \text{CF}_3$ (**c**);

$\text{R}^1 = \text{F, R}^2 = \text{C}_2\text{F}_5$ (**d**).

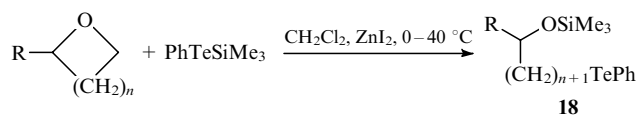
Phenyl trimethylsilyl telluride cleaves lactones and ethers under mild conditions (dichloromethane, 20 °C) in the presence of catalytic amounts of ZnI_2 to give C-tellurination and O-silylation products.¹⁸ Thus acids **16** are prepared from lactones **15** and PhTeSiMe_3 in > 80% yields. Intermediate *O*-trimethylsilyl esters **17** are hydrolysed upon work-up of reaction mixtures.



Phenyl trimethylsilyl telluride markedly exceeds related sulfur- and selenium-containing compounds in reactivity. The lac-

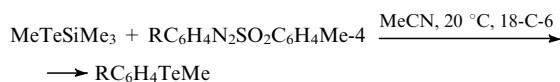
tone ring opening under the action of telluride occurs at 20 °C (PhSSiMe₃ reacts at 70 °C,³⁶ whereas PhSeSiMe₃, at 80–100 °C).³⁷

Oxirane and other cyclic ethers are cleaved with the same efficiency under the action of phenyl trimethylsilyl telluride to give trimethylsilyloxy-substituted tellurides **18**.¹⁸ Other examples of such reactions have also been described.¹⁸



R = Me, Et, n = 0; R = H, n = 1–4; R = Me, n = 2.

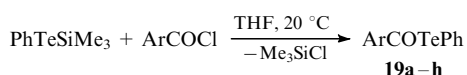
Organyl trimethylsilyl tellurides RTeSiMe₃ are synthetic equivalents of organyl tellurolate anions RTe[−] (see Refs 4–9). In some cases, the use of tellurides gives better results in comparison with alkali-metal tellurolates. Thus the reaction of MeTeSiMe₃, generated *in situ* from MeTeLi and Me₃SiCl, with arylazo sulfones in MeCN containing catalytic amounts of 18-crown-6 afforded aryl methyl tellurides in 36%–62% yields.⁸



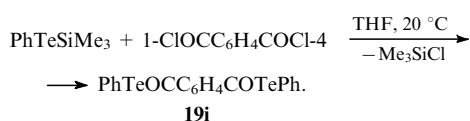
R = H, 4-Br, 4-COMe, 2-CO₂Me.

The use of MeTeLi prepared from MeLi and Te in THF does not lead to aryl methyl tellurides in this reaction. Deazosulfonation in THF does not take place, but substitution of MeCN for THF yields a mixture of dimethyl telluride and dimethyl ditelluride which are inert with respect to arylazosulfones.⁸

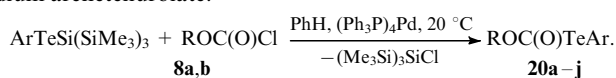
Under mild conditions (THF, 20 °C), phenyl trimethylsilyl telluride reacts with aryl chlorides to give phenyl tellurobenzoates **19a–i** (yield 62%–91%).⁹ The advantages of this procedure in comparison with the classical methods based on the use of sodium arenetellurolates lie in higher yields of the esters formed and the simplicity of their isolation from reaction mixtures.³⁸



Ar = 4-ClC₆H₄ (**a**), 3-ClC₆H₄ (**b**), 4-BrC₆H₄ (**c**), 4-NO₂C₆H₄ (**d**), 4-NCC₆H₄ (**e**), Ph (**f**), 4-MeC₆H₄ (**g**), 4-MeOC₆H₄ (**h**).

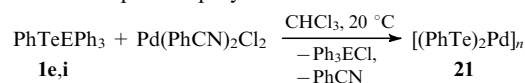


Aryl tris(trimethylsilyl)silyl tellurides **8a,b** used *in situ* react with chloroformates exclusively in the presence of catalytic amounts of tetrakis(triphenylphosphine)palladium(0) to give aryl tellurocarbonates **20a–j** (for the use of compounds **20a–j** as precursors of oxyacyl and alkyl radicals see Refs 39, 40). Aryl tellurocarbonates **20e,j** with a phenyl radical at the ester oxygen atom can be prepared^{6,7} only from compounds **8a,b**. They could not be obtained in the reaction of chloroformates with sodium arenetellurolate.^{6,7}



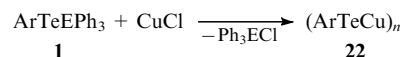
Compo- und 20	Ar	R	Compo- und 20	Ar	R
a	Ph	Me	f	4-FC ₆ H ₄	Me
b	Ph	Pr ⁱ	g	4-FC ₆ H ₄	Pr ⁱ
c	Ph	cyclo-C ₆ H ₁₁	h	4-FC ₆ H ₄	cyclo-C ₆ H ₁₁
d	Ph	C ₈ H ₁₇	i	4-FC ₆ H ₄	C ₈ H ₁₇
e	Ph	Ph	j	4-FC ₆ H ₄	Ph

Compounds **1** react with some metal halides to give the corresponding metal tellurolates. Thus the reaction of phenyl triphenylgermyl(stannyl) tellurides **1e,i** with the palladium(II) chloride–benzonitrile complex results in elimination of Ph₃ECl followed by the formation of red-brown palladium tellurolates **21** which seem to possess polymeric structures.⁴



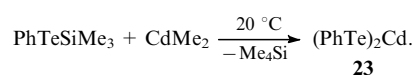
E = Ge (**1e**), Sn (**1i**).

The reaction of compounds **1** with CuCl in chloroform⁴ or acetonitrile⁴¹ gives polymeric copper(I) tellurolates **22**.

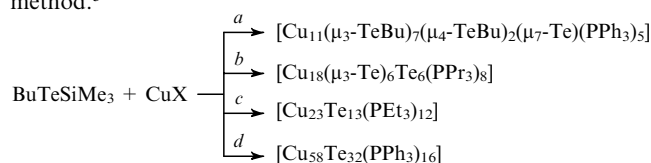


Ar = Ph, 4-EtOC₆H₄; E = Ge, Sn, Pb.

Metal tellurolates are also formed in those cases where phenyl trimethylsilyl telluride is used as a source of the ligand PhTe. Thus reaction of this compound with dimethylcadmium in CH₂Cl₂ gave cadmium(II) benzenetellurolate (**23**).¹⁰

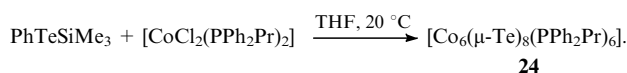


Reaction of organyl trimethylsilyl tellurides, particularly, BuTeSiMe₃, with copper(I) salts results in tellurium-containing clusters which were characterised by the X-ray diffraction method.⁵

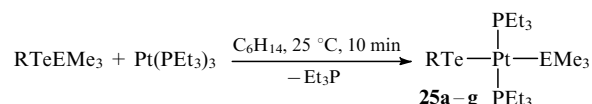


X = Cl, OAc; (a) PPh₃, THF; (b) PPr₃, diglyme; (c) PET₃, THF; (d) PPh₃, diglyme.

The cluster **24** is the only reaction product of phenyl trimethylsilyl telluride with a complex cobalt(II) salt.⁵



It has been shown recently⁴² that compounds RTeEMe₃, similar to (Me₃E)₂Te (E = Si, Sn), enter into oxidative addition with triethylphosphine platinum complexes Pt(PEt₃)_n (n = 3, 4) to give complexes **25a–g** in 76%–100% yields.



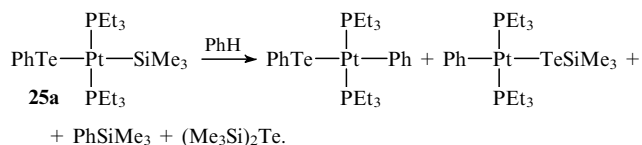
E = Si: R = Ph (**a**), 4-PhC₆H₄ (**b**), Bu (**c**), Me₃Si (**d**);

E = Ge, R = Ph (**e**); E = Sn: R = Ph (**f**), Me₃Sn (**g**).

The structures of compounds **25** were confirmed by NMR spectroscopy and the X-ray diffraction analysis using complex **25b**⁴² as an example. They represent solid red-coloured substances stable under an argon atmosphere but extremely sensitive to oxygen and moisture.⁴²

The reactivities of phenyl trimethylsilyl chalcogenides PhM(SiMe₃)₃ (M = S, Se, Te) in this reaction increase in the following order: S < Se < Te. Thus phenyl trimethylsilyl sulfide does not react with Pt(PEt₃)₃ even after 5-h heating at 50 °C, whereas phenyl trimethylsilyl selenide reacts with the Pt(0) complex at 25 °C, albeit at a much slower rate than its tellurium analogue.⁴²

Complexes **25** are gradually decomposed in benzene even at 25 °C. The following decomposition products of compound **25a** have been identified:⁴²



The decomposition reaction is reversible, *i.e.*, the addition of even 1 equiv. of PEt_3 inhibits this process.⁴²

III. Methods of synthesis and reactions of compounds $(\text{R}_3\text{E})_2\text{Te}$ (E = Si, Ge, Sn, Pb)

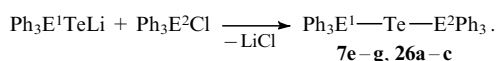
Compounds containing two bonds of Te to Group 14 elements include both symmetrical $(\text{R}_3\text{E})_2\text{Te}$ (E is a Group 14 element) (**7**) and non-symmetrical derivatives of the type $\text{R}_3^1\text{E}^1\text{TeER}_3^2$ (**26**). The methods of their syntheses and reactions of both types of compounds are very similar and will therefore be considered in the same section.

1. Methods of synthesis

Two reactions affording tellurides **7** are described in Section II. The first of them is the reaction of hydrides R_3EH with diorganyl tellurides. Depending on the nature of substrates, this reaction gives compounds **1** and **7** or their mixtures.^{25,26} The second reaction is disproportionation of tellurides **1**.¹⁷

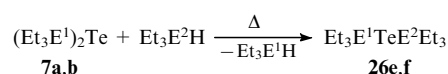
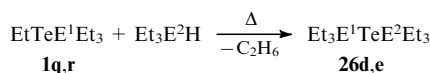
The addition of Me_3SiCl to an ethereal solution of PhTeMgBr leads to the formation of bis(trimethylsilyl) telluride,⁴³ apparently also as a result of disproportionation of PhTeSiMe_3 under the reaction conditions. It should be noted that the same reactants in THF (see Section II.1) give PhTeSiMe_3 .

The general method for the synthesis of both symmetrical (**7**) and non-symmetrical (**26**) tellurides is based on the reaction of organolithium derivatives $\text{R}_3^1\text{E}^1\text{TeLi}$ with chlorides $\text{R}_3^2\text{E}^2\text{Cl}$.^{44–48} However, this method is only seldom employed, *e.g.*, in the synthesis of phenyl derivatives containing various combinations of Ge, Sn and Pb atoms. This reaction was also used in the synthesis of bis(triphenylsilyl) telluride.⁴⁹



Compound	E ¹	E ²	Ref.
7e	Ge	Ge	46
7f	Sn	Sn	44, 45
7g	Pb	Pb	47
26a	Sn	Ge	46
26b	Sn	Pb	45
26c	Pb	Ge	46

Non-symmetrical derivatives **26d–f** are also obtained by reactions of triethyltin or -germanium hydrides with tellurides **1q,r** (yields 60%–90%)²⁶ or **7a,b**.⁵⁰

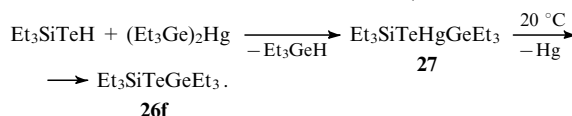


E¹ = Si (**1q, 7a**), Ge (**1r, 7b**); E¹ = Si, E² = Sn (**26d**); E¹ = Ge, E² = Sn (**26e**); E¹ = Si, E² = Ge (**26f**).

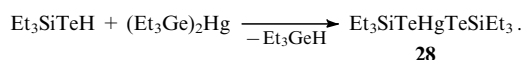
In these reactions, the reactivities of the hydrides decrease in the following order: Sn > Ge > Si. Thus the reaction of Et_3GeH with $(\text{Et}_3\text{Si})_2\text{Te}$ yields $(\text{Et}_3\text{Ge})_2\text{Te}$ (yield 79%) and Et_3SiH (yield 50%) at 235 °C for 6 h, while the reaction of Et_3SnH with

$(\text{Et}_3\text{Ge})_2\text{Te}$ results in $(\text{Et}_3\text{Sn})_2\text{Te}$ (yield 76%) and Et_3GeH (yield 57%) at 70 °C for 1 h.⁵⁰

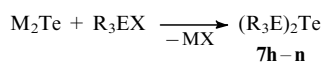
Reactions of the mercury derivatives $(\text{Et}_3\text{E}^1)_2\text{Hg}$ with the hydrides $\text{R}_3\text{E}^2\text{TeH}$ also yield non-symmetrical tellurides **26**,⁵¹ however, this method has been studied relatively little. Reaction of bis(triethylgermyl)mercury with Et_3SiTeH (molar ratio 1 : 1) yields compound **27** with the Si–Te–Hg–Ge fragment, which can easily eliminate the mercury atom to yield the non-symmetrical telluride **26f** under mild conditions (–78 °C, 2–3 min).



It is of note that in contrast to compound **27**, bis(triethylsilyltelluro)mercury (**28**) formed with a tellurol:mercury molar ratio of 2 : 1 is thermally stable and is not decomposed even on heating to 130 °C for 7 h.⁵¹



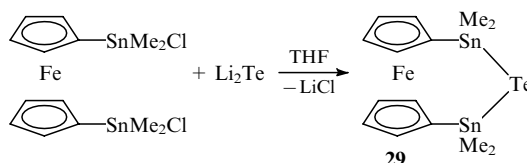
The synthesis of symmetrical tellurides **7** has been studied in much more detail than that of the non-symmetrical analogues **26**. Reaction of sodium⁵² or lithium^{21,53–57} tellurides with the halides R_3EX is the most general approach to their synthesis. The yields of tellurides **7** vary from very low (5%)⁵⁷ to quantitative.⁵⁵



M = Na, Li.

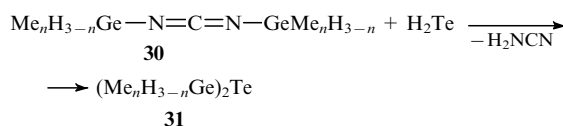
Compound 7	E	R ₃	Ref.
h	Si	H ₃	53, 55
i	Si	Me ₃	21, 52–54, 56
j	Si	Bu ^t Me ₂	56
k	Ge	(CF ₃) ₃	57
l	Ge	Me ₃	52
m	Sn	Me ₃	52
n	Pb	Me ₃	52

Reaction of 1,1'-bis(chlorodimethylstannyl)ferrocene⁵⁸ with lithium telluride was used to obtain 1,3-distanna-2-tellura[3]ferrocenophane **29** (yield 28%).⁵⁹



Sodium hydrotelluride was employed in the synthesis of bis(triphenylstannyl) telluride (**7f**).^{19,60}

Some digermyl tellurides were prepared using hydrogen telluride as the tellurium-containing reagent.⁶¹ Thus warming of a mixture of carbodiimides **30** with an excess of H_2Te from –196 °C to room temperature results in bis(germyl) tellurides **31** in 60%–90% yields.⁶¹

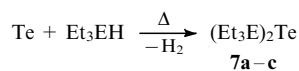


$n = 1-3$.

Silicon analogues of carbodiimides **30** do not enter into such reactions.⁶¹

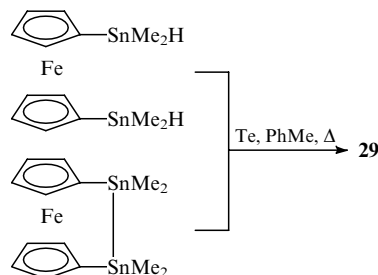
The symmetrical tellurides **7a–c** were obtained by heating hydrides R_3EH with tellurium powder.^{26,50,62,63} As in the previous cases, the reactivities of the hydrides increase in the following order: Si < Ge < Sn. Whereas the reaction of tellurium with

Et_3SnH proceeds at $130\text{ }^\circ\text{C}$ ^{26,62} and that with Et_3GeH , at $190\text{--}210\text{ }^\circ\text{C}$,^{26,62} the reaction of Te with Et_3SiH resulting in bis(triethylsilyl) telluride **7a** in 71% yield can be realised only at $280\text{ }^\circ\text{C}$.^{50,63}

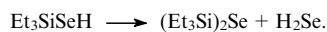


E = Si (**a**), Ge (**b**), Sn (**c**).

The reaction of 1,1'-bis(dimethylstannyl)ferrocene⁵⁸ with tellurium powder was used for the synthesis of telluride **29** (yield 90%);⁵⁹ the same compound was obtained in 79% yield by reaction of 1,1,2,2-tetramethyl-1,2-distanna[2]ferrocenophane with tellurium.⁵⁹



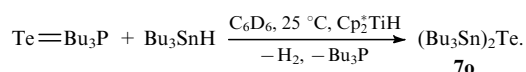
Depending on the nature of the hydride and the chalcogen, reactions of sulfur and selenium with hydrides R_3EH yield either organoelement hydrochalcogenides R_3EMH [E = Si,^{50,63} Ge;²⁶ M = S,⁶³ Se (see Refs 26, 50 and 63)] or their mixtures with compounds $(\text{R}_3\text{E})_2\text{M}$. The stabilities of hydrides R_3EMH increase in the following order: $\text{Te} < \text{Se} < \text{S}$. Thus heating of sulfur with triphenylsilane at $200\text{ }^\circ\text{C}$ gives triphenylsilylanethiol Ph_3SiSH as the only product (yield 70%),⁶³ whereas reaction of selenium with triethylsilane ($260\text{ }^\circ\text{C}$) results in a mixture of Et_3SiSeH (yield 62%) and $(\text{Et}_3\text{Si})_2\text{Se}$ (yield 32%).^{50,63} The latter represents a symmetrisation product.⁶³



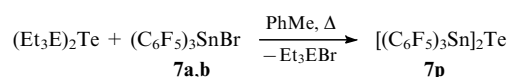
Whereas triethylsilylanetellurol Et_3SiTeH , which is the least stable of all chalcogenols, is symmetrised completely, the degree of conversion of more stable triethylsilylaneselenol into bis(triethylsilyl) selenide and H_2Se is only 40%.⁶³

It should be noted that reaction of selenium with germanes R_3GeH (R = Pr^i , cyclo- C_6H_{11}) yields predominantly germane selenols R_3GeSeH .

Tributylphosphine telluride $\text{Bu}_3\text{P}=\text{Te}$, a synthetic equivalent of metallic tellurium, was used instead of the latter in reactions with triorganylstannyl hydrides.⁶⁴ Its solubility in organic solvents makes it possible to synthesise bis(triorganylstannyl) tellurides, e.g., bis(tributylstannyl) telluride **7o**, under mild conditions in the presence of catalytic amounts (2 mol.%–10 mol.%) of Cp_2^*TiH ($\text{Cp}^* = \text{Me}_5\text{C}_5$). In the absence of a catalyst, the yield of the target product does not exceed 2%.⁶⁴

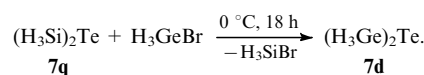


Tellurides **7** (E = Ge, Sn) were also synthesised by exchange reactions of compounds **7** containing more light weight Group 14 elements with the halides R_3EX . Thus bis[tris(pentafluorophenyl)stannyl] telluride **7p** was obtained (in 57% and 51% yields, respectively) by reaction of bis(triethylgermyl) (**7b**) or bis(triethylsilyl) tellurides (**7a**) with $(\text{C}_6\text{F}_5)_3\text{SnBr}$.⁶⁵ This reaction seems to involve stepwise exchange of Et_3E groups (E = Si, Ge) for $(\text{C}_6\text{F}_5)_3\text{Sn}$ groups and proceeds through four-membered transition states.

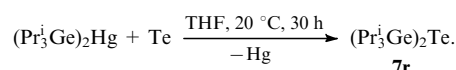


E = Si (**a**), Ge (**b**).

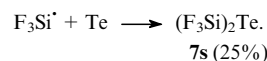
With an excess of germlyl bromide, di(silyl) telluride (**7q**) is quantitatively converted into di(germyl) telluride (**7d**), apparently, by the same mechanism.⁵⁵



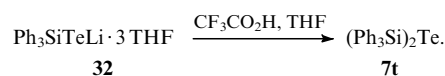
Other methods of synthesis of tellurides **7** were studied in separate reactions, although some of them can be used for the synthesis of a larger number of compounds. Thus bis(triisopropylgermyl) telluride (**7r**) was obtained in 78% yield by reaction of bis(triisopropylgermyl)mercury with tellurium powder.³⁰



Bis(trifluorosilyl) telluride (**7s**) was prepared by reaction of trifluorosilyl radicals generated by decomposition of hexafluorodisilane with tellurium vapour in a low-temperature matrix.^{66,67}

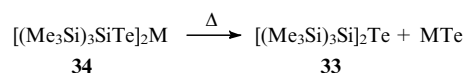


The synthesis of silyl derivatives of the type **7**, which contain sterically hindered silane residues, requires special strategies. Thus bis(triphenylsilyl) telluride (**7t**) was obtained by protonation of lithium triphenylsilylanetellurolate (**32**) in THF or by oxidation of this salt with atmospheric oxygen.⁴⁹



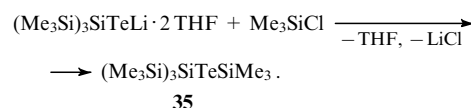
It should be noted that oxidation of tris(trimethylsilyl)silane-tellurol ($(\text{Me}_3\text{Si})_3\text{SiTeH}$ or its lithium salt results in the ditelluride $[(\text{Me}_3\text{Si})_3\text{Si}]_2\text{Te}_2$.^{68,69}

The symmetrical telluride **33** is formed together with the corresponding metal tellurides by pyrolysis of tellurolates **34**.¹⁶



M = Zn, Cd, Sn, Pb, Yb.

The symmetrical and non-symmetrical tellurides considered above containing two $\text{Te}-\text{E}$ bonds have identical substituents on the Group 14 elements. Presumably, telluride **35**⁶⁹ synthesised from lithium tris(trimethylsilyl)silylanetellurolate and trimethylchlorosilane is the only compound which has different substituents on these atoms.

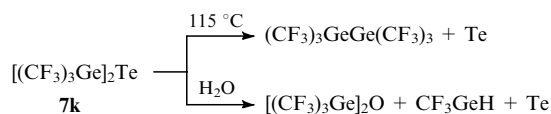


2. Reactions of compounds $(\text{R}_3\text{E})_2\text{Te}$

It should be noted that the majority of reactions of tellurides **7** and **26** have been studied for a limited number of compounds only; therefore, it is sometimes difficult to judge the general type of one or another reaction.

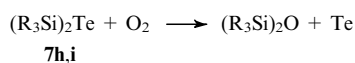
Most reactions of tellurides **7** (reactions of the non-symmetrical derivatives **26** have been studied relatively little) occur with elimination of tellurium. The hydride derivatives $(\text{H}_3\text{E})_2\text{Te}$ are photosensitive and are decomposed on rough glass surfaces even at room temperature,⁵³ while bis[tris(trifluoromethyl)germyl] telluride (**7k**) eliminates tellurium only at $115\text{ }^\circ\text{C}$.⁵⁷ Tellurides **7**

containing alkyl and trifluoromethyl radicals are rather easily hydrolysed.⁵⁷



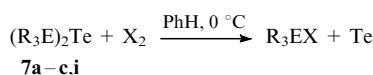
Symmetrical (**7e–g**) and non-symmetrical phenyl derivatives (**26a–c**) are thermally and hydrolytically stable compounds. Their stabilities with respect to moisture and oxygen increase in the following order: $(\text{Ph}_3\text{Ge})_2\text{Te} < (\text{Ph}_3\text{Pb})_2\text{Te}$ and $(\text{Ph}_3\text{Ge})_2\text{Te} < \text{Ph}_3\text{GeTeSnPh}_3 < \text{Ph}_3\text{GeTePbPh}_3$.⁴⁷ The non-symmetrical aliphatic derivatives $\text{R}_3^1\text{E}^1\text{TeE}^2\text{R}_3^2$ easily disproportionate to give the symmetrical tellurides $(\text{R}_3^1\text{E}^1)_2\text{Te}$ and $(\text{R}_3^2\text{E}^2)_2\text{Te}$.⁷⁰

The Te–E bonds in tellurides **7** are easily cleaved under the action of various oxidants. Thus the silyl derivatives **7h,i** react with oxygen to give elementary tellurium and the corresponding siloxane.⁵³



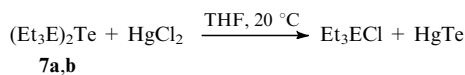
R = H (**h**), Me (**i**).

The oxidation of tellurides **7** by halogens proceeds under mild conditions and gives halides R_3EX (yields 50%–85%) and Te; some amount of R_2SnX_2 is formed in the case of stannyl derivatives.^{56,71}

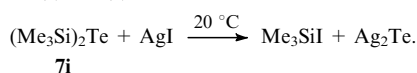


R = Et; E = Si (**a**), Ge (**b**), Sn (**c**); R = Me, E = Si (**i**); X = Cl, Br, I.

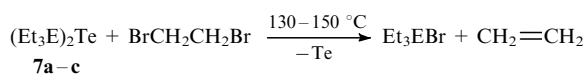
The reactions of the tellurides **7** with Ag(I) ⁴³ and Hg(II) ⁵¹ salts also afford halides R_3EX and, in addition, metal tellurides. Noteworthy, the reactions of these salts with diorganyl tellurides R_2Te give complexes with the compositions 1 : 1 or 1 : 2.⁷²



E = Si (**a**), Ge (**b**).

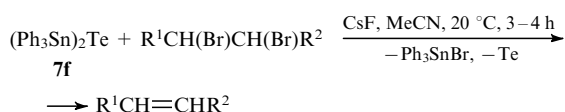


It has been shown for the first time⁶³ that the cleavage of E–Te bonds in compounds **7** is effected not only by free halogens but also by organic dihalides containing rather active halogen atoms. Thus boiling of ethyl derivatives **7a–c** with 1,2-dibromoethane leads to the formation of Et_3EBr , Te and ethylene.⁶³ The reaction with bis(triethylstannyl) telluride (**7c**) proceeds most smoothly.



E = Si (**a**), Ge (**b**), Sn (**c**).

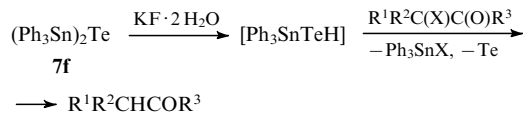
It is this reaction in particular that underlies the synthesis of alkenes from vicinal dibromides using bis(triphenylstannyl) telluride (**7f**) and CsF as a dehalogenating reagent.⁷³



$\text{R}^1 = \text{H}$; $\text{R}^2 = \text{Ph}$, $n\text{-C}_8\text{H}_{17}$, PhSO_2CH_2 ; $\text{R}^1 = \text{R}^2 = \text{Ph}$;
 $\text{R}^1-\text{R}^2 = \text{CH}_2\text{OCH}_2\text{OCH}_2$.

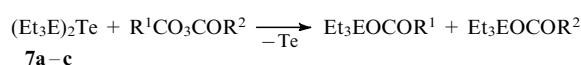
This reaction proceeds under mild conditions; alkenes are most frequently formed in virtually quantitative yields. Thus the reaction of *meso*-1,2-dibromo-1,2-diphenylethane with $(\text{Ph}_3\text{Sn})_2\text{Te}$ results in *trans*-stilbene in 94% yield.⁷³

Upon substitution of $\text{KF} \cdot \text{H}_2\text{O}$ for CsF, telluride **7f** effects dehalogenation of α -chloro(bromo) ketones under mild conditions (MeCN , 20°C).⁷³ With a molar reagent ratio **7f**: $\text{KF} \cdot 2\text{H}_2\text{O}$: α -halogeno ketone of 1 : 3 : 1, the ketones are formed in 60%–90% yields. The feasible mechanism of this reaction includes the intermediate formation of triphenylstannanetellurol.⁷⁴



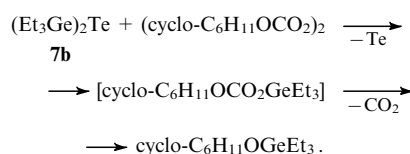
$\text{R}^1 = \text{R}^2 = \text{H}$; $\text{R}^3 = \text{Me}$, Et, Ph; $\text{R}^1 = \text{Me}$, $\text{R}^3 = \text{Ph}$; $\text{R}^2 = \text{H}$, Me;
 $\text{R}^1-\text{R}^3 = (\text{CH}_2)_4$, $\text{R}^2 = \text{H}$.

Cleavage of the Te–E bonds in tellurides **7a–c** proceeds smoothly under the action of symmetrical and non-symmetrical acyl peroxides.⁷⁵ This reaction gives high yields of elementary tellurium and triorganylsilyl (germyl, stannyl) esters of the corresponding acids.

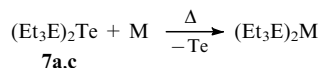


E = Si (**a**), Ge (**b**), Sn (**c**); $\text{R}^1 = \text{Ph}$, $\text{R}^2 = \text{Ph}$, Me.

Reaction of bis(triethylgermyl) telluride (**7b**) with dicyclohexyl percarbonate yields CO_2 and cyclohexyloxytriethylgermane together with Te, apparently as a result of decomposition of the initially formed triethylgermyl cyclohexanecarboxylate.⁷⁵

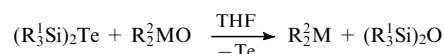


Like diaryl tellurides Ar_2Te ,⁷² tellurides **7a,c** eliminate Te upon heating with sulfur or selenium to give sulfides and selenides, respectively.^{50,63} As in the reaction with diaryl tellurides,⁷² sulfur surpasses selenium in activity. Thus reaction of $(\text{Et}_3\text{Sn})_2\text{Te}$ with sulfur proceeds at 20°C (90 h), whereas reaction of the same telluride with selenium requires heating at 150°C for 30 h.^{50,63}



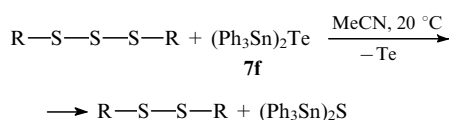
E = Si, M = S; E = Sn: M = S, Se.

Formally, reduction of diorganyl chalcogen oxides by bis(trialkylsilyl) tellurides is related to the same class of reactions.⁵⁶ This can be regarded as a preparative method for the synthesis of chalcogenides from chalcogen oxides because of their high yields (80%–100%) and easy separation from other products, *viz.*, hexaalkyldisiloxanes and elementary tellurium. It should be noted that bis(trimethylsilyl) sulfide and selenide are also rather efficient reagents.⁵⁶



$\text{R}^1 = \text{Me}$; $\text{R}^2 = \text{Ph}$, M = Te; $\text{R}^2 = \text{Me}$, M = S;
 $\text{R}_3^1 = \text{Bu}^t\text{Me}_2$; $\text{R}^2 = \text{Ph}$, M = Se; $\text{R}^2 = \text{Me}$, M = S.

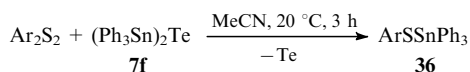
The use of bis(triphenylstannyl) telluride (**7f**) for monodesulfurisation of organic trisulfides⁷⁶ and synthesis of aryl triphenylstannyl sulfides⁷⁷ is based on easy elimination of the Te atom from compounds **7**. Various types of organic trisulfides (aryl-, benzyl-, alkyl-) are readily converted into the corresponding disulfides under the action of $(\text{Ph}_3\text{Sn})_2\text{Te}$. The rate of the desulfurisation reaction increases with an increase in the solvent polarity.



R = FC₆H₄, MeC₆H₄, Bn, PhCHMe, Me(CH₂)₂.

Other bis(triphenylstannyl) chalcogenides (Ph₃Sn)₂M (M = S, Se) can monosulfurise organic trisulfides; the reactivities of chalcogenides (Ph₃Sn)₂M decrease in the following order: Te > Se > S. Bis(triphenylstannyl) selenide causes desulfurisation of only diaryl and dibenzyl trisulfides, whereas desulfurisation by bis(triphenylstannyl) sulfide proceeds with very low yields and only upon long-term boiling of the reaction mixture.⁷⁶

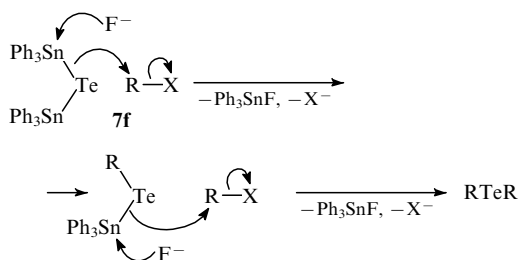
Reaction of telluride **7f** with diaryl disulfides under mild conditions (MeCN, 20 °C) results in aryl triphenylstannyl sulfides **36** in high, sometimes quantitative, yields.⁷⁷ Dialkyl and dibenzyl disulfides do not enter into such reactions. Compounds **36** can be synthesised from diaryl disulfides and bis(triphenylstannyl) selenide.⁷⁷ However, the latter is much less efficient than tellurides. 4-Methylphenyl triphenylstannyl sulfide is formed in a quantitative yield upon treatment of the corresponding disulfide with telluride **7f** and in only 28% yield when a selenium derivative is used, other conditions (solvent, temperature, reaction time) being the same.⁷⁷



Ar = 4-ClC₆H₄, 4-FC₆H₄, Ph, 4-MeC₆H₄, 2-C₁₀H₇.

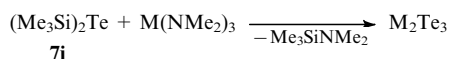
If organyl trimethylsilyl tellurides RTeSiMe₃ represent synthetic equivalents of organytellurolate anions RTe⁻ (see Section II.2), compounds **7** and particularly bis(triphenylstannyl) telluride **7f** act as synthetic equivalents of the telluride anion Te²⁻ (see Refs 73, 78).

Bis(triphenylstannyl) telluride **7f** used in combination with CsF (4 equiv.) is a mild tellurinizing reagent.^{73, 78} Reactions of this reagent with organic bromides and iodides in MeCN at 20 °C afford symmetrical diorganyl tellurides in high yields.^{73, 78} Aryl iodides and alkyl chlorides are inert with respect to compound **7f**, which makes it possible to synthesise diorganyl tellurides containing chlorine atoms. It is believed⁷³ that the synthesis of diorganyl tellurides proceeds in two steps and includes an attack of the fluoride ion on the tin atom.



X = Br, I; R = Prⁱ, Bn, Cl(CH₂)₆, Me(CH₂)₉, PhCOCH₂, CH₂CO₂Et, CH₂CO₂Me, CH₂CO₂Prⁿ, CH₂CO₂Bu^t, (CH₂)₃CO₂Et.

Reactions of bis(trialkylsilyl) tellurides with certain organo-element compounds occur with the cleavage of both Te—Si bonds and lead to the formation of tellurides of the corresponding metals rather than elementary Te; these reactions are of special interest. Thus reactions of bis(trimethylsilyl) telluride (**7i**) with tris(dimethylamino)antimony or -bismuth occur under very mild conditions (hexane, -30 °C) and yield polycrystalline antimony and bismuth tellurides¹¹ which manifest semiconducting properties.

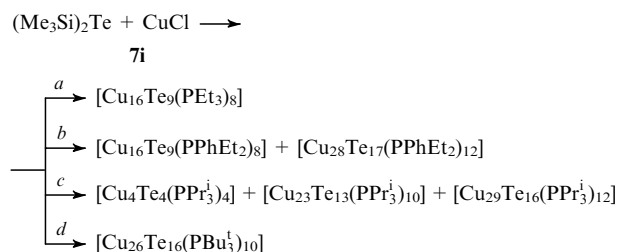


M = Sb, Bi.

Metal dialkyls can be used instead of dimethylamino derivatives. This method was used in the synthesis of Cd(II) telluride.¹⁰



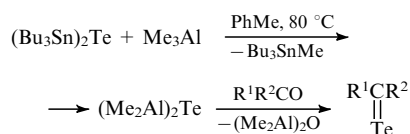
Reaction of bis(trimethylsilyl) telluride (**7i**) with copper(I) chloride in the presence of phosphines results in the formation of cluster copper complexes⁷⁹ which differ from those obtained using butyl trimethylsilyl telluride (see Section II.2).



(a) PEt₃, Et₂O; (b) PPhEt₂, Et₂O; (c) PPr₃ⁱ, Et₂O; (d) PBU₃^t, THF.

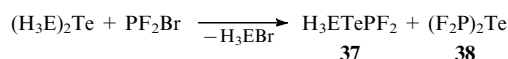
Reactions of tellurides **7** with other than Sb, Bi and Cd organoelement derivatives occur with the cleavage of two (less frequently, one) Te—E bonds; in this case, tellurium becomes a constituent of one of the reaction products.

Bis(tributylstannyl) telluride undergoes transmetalation with trimethylaluminium.^{80, 81} Bis(dimethylaluminium) telluride (Me₂Al)₂Te used *in situ* is an efficient tellurinizing reagent. Treatment of aldehydes, ketones⁸⁰ and *N*-methylformanilide⁸¹ with this reagent results in telluroaldehydes (ketones)⁸⁰ and *N*-methyltelluroformanilide,⁸¹ respectively.



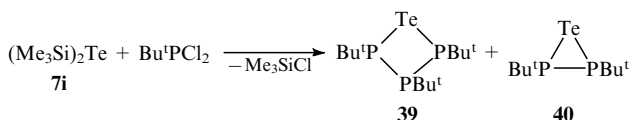
R¹ = H; R² = Prⁿ, Bu^t, Ph, N(Me)Ph; R¹R²CO — adamantanone, bicyclo[3.3.1]nonan-7-one.

Tellurides (H₃E)₂Te react with PF₂Br with the cleavage of one and two Te—E bonds to give a mixture of compounds **37** and **38**.⁸² These compounds were not isolated; their formation was deduced from the ¹H and ¹⁹F NMR spectra.



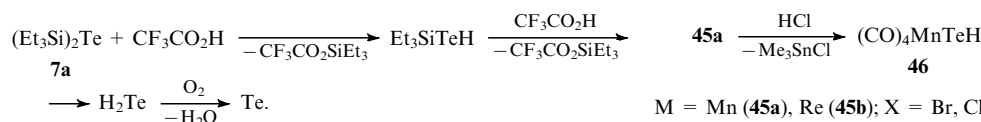
E = Si, Ge.

At the same time, reaction of bis(trimethylsilyl) telluride **7i** with Bu^tPCl₂ occurs with the cleavage of both Te—Si bonds resulting in a mixture of cyclic compounds **39** and **40**.⁸³



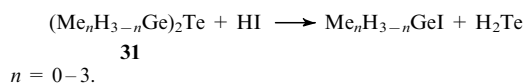
Reactions of bis(trialkylsilyl) tellurides with acyl chlorides and bisacyl tellurides have been considered in the recently published review.⁸⁴

The Te—E bond in tellurides **7** is easily cleaved by protic acids (HCl, anhydrous CF₃CO₂H).⁶³ Thus the first silanetellurol, *viz.*, triethylsilanetellurol, was obtained by treating bis(triethylsilyl) telluride (**7a**) with trifluoroacetic acid (molar ratio 1 : 1) at 20 °C. In the presence of an excess of the acid, the Te—Si bond of tellurol is cleaved to give triethylsilyl trifluoroacetate and elementary Te, presumably as a result of oxidation of the intermediate H₂Te.⁶³

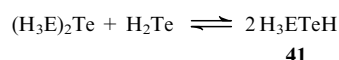


M = Mn (**45a**), Re (**45b**); X = Br, Cl.

Reaction of germyl tellurides **31** with gaseous HI at 20 °C results in the cleavage of both Te–Ge bonds^{55,61} to give germyl iodides and H₂Te.



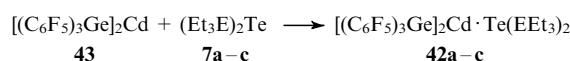
Silane- and germane-tellurols **41** are formed by an exchange reaction between the corresponding tellurides and H₂Te.⁸⁵ The equilibrium constants are equal to 0.90 (E = Si) and 0.95 (E = Ge).



E = Si, Ge.

The signals for the Te–H protons in the ¹H NMR spectra of tellurols **41** are observed at very high fields. Thus δ_{TeH} of silanetellurol is equal to –7.46 ppm, while that of germanetellurol is –7.44 ppm.⁸⁵

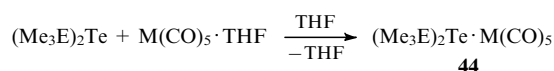
The Te–E bonds are not affected upon complexation of tellurides **7** with some Lewis acids. The stable complexes **42a–c** (1 : 1) were prepared from bis[tris(pentafluorophenyl)germyl]cadmium (**43**) and tellurides **7a–c**.⁸⁶ A complex with the composition 1 : 2 was also isolated in the case of the stannyl derivative.



E = Si (**a**), Ge (**b**), Sn (**c**).

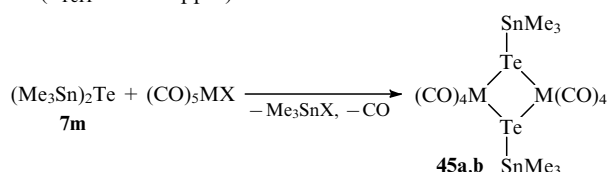
The complexes **42a–c** are rapidly oxidised in air. It is noteworthy that tellurides **7a–c** form predominantly 1 : 1 complexes, while diorganyl sulfides R₂S react with compound **43** to give 1 : 2 complexes. This is attributed to the decrease in the donor activity of the Te atoms of tellurides **7a–c** as a result of *d*_π–*p*_π coupling of Te with the E atoms and steric hindrances.⁸⁶

Tellurides **7** react with chromium, molybdenum and tungsten carbonyls (CO)₅M·THF (M = Cr, Mo, W) resulting in the displacement of the tetrahydrofuran molecule and the formation of complexes **44** which are sensitive to oxygen and atmospheric moisture.^{52,87} The yields of the latter are relatively low (17%–45%). The attempts to obtain complexes **44** by irradiation of solutions containing metal hexacarbonyls and tellurides failed due to decomposition of tellurides upon illumination.



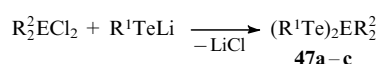
E = Ge, Sn, Pb; M = Cr, Mo, W.

Unlike bis(trimethylstannyl) selenide, which forms binuclear complexes **45** in high yields upon reaction with manganese and rhenium halogen carbonyls, bis(trimethylstannyl) tellurides (**7m**) react with these carbonyls to give complexes **45a,b** in very low yields (*e.g.*, the yield of compound **45a** is 11%, whereas the formation of complex **45b** followed only from spectroscopic data).⁸⁸ Treatment of complex **45a** with HCl in ether yields tellurol **46** (δ_{TeH} – 12.80 ppm).



IV. Other types of non-cyclic compounds containing Te–E bonds

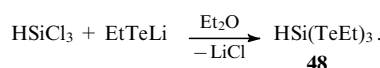
Apart from R¹TeER₂³ and (R₃E)₂Te derivatives, several non-cyclic compounds containing Te–E bonds, *e.g.*, di(organyl-telluro)silanes (germanes, stannanes) (R¹Te)₂ER₂² **47** (see Refs 17, 19, 20) and tris(ethyltelluro)silane (**48**), have been described.²⁰ Synthesis of both types of compounds was performed by reactions of the corresponding chloro derivatives of Group 14 elements with lithium tellurolates in THF¹⁹ or ether.²⁰



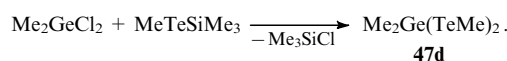
47a: E = Sn, R¹ = Ph, R² = Me;

47b: E = Sn, R¹ = Ph, R² = Bu¹;

47c: E = Si, R¹ = Et; R₂² = Et, H.



Dimethylbis(methyltelluro)germane (**47d**) was prepared by reaction of dimethylchlorogermane with methyl trimethylsilyl telluride.¹⁷

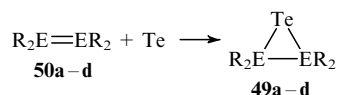


Reactions of compounds **47a–d** and **48** have not been studied yet.

V. Cyclic compounds containing Te–E bonds

A series of three-, four-, five- and six-membered cyclic compounds with rings built exclusively of Group 14 elements (Si, Ge, Sn) and tellurium have been described. The methods for the synthesis of rings containing 4 to 6 atoms are similar to those for non-cyclic tellurides (R₃E)₂Te, whereas reactions resulting in three-membered cycles have no analogues.

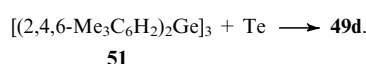
The reaction of compounds R₂E=ER₂ **50a–d** with tellurium powder is a common procedure for the synthesis of three-membered cyclic compounds **49a–d** containing two Group 14 elements and one tellurium atom. Synthesis of telluradisilirane (**49a**)⁸⁹ and telluradigermirane (**49b**)⁹⁰ is performed in benzene at 20 and 80 °C, respectively; telluradistannirane (**49c**)⁹¹ is prepared by boiling the reactants in toluene for 2 h. The yields are 66%, 80% and 71%, respectively.



E = Si, R = 2,4,6-Me₃C₆H₂ (**a**); E = Ge, R = 2,6-Et₂C₆H₃ (**b**);

E = Sn, R = 2,4,6-Pr¹₃C₆H₂ (**c**); E = Ge, R = 2,4,6-Me₃C₆H₂ (**d**).

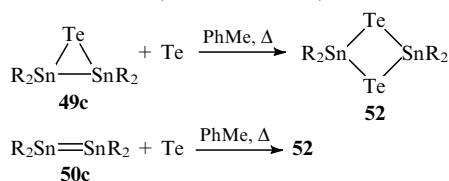
The synthesis of the Te,Ge-cycle **49d** was also carried out by boiling hexamethylcyclotrigermane (**51**) with tellurium powder in toluene.⁹⁰ Presumably, this reaction proceeds *via* the intermediate digermene **50** (E = Ge, R = 2,4,6-Me₃C₆H₂).



Compounds **49a–d** represent high-melting crystalline substances which are resistant against oxygen and atmospheric moisture. The germyl derivatives **49b,d** manifest thermochromic

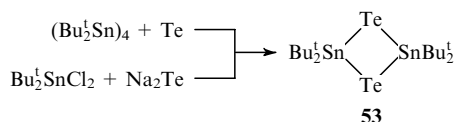
properties: they are colourless at -196°C but become pale yellow (20°C) and orange (140°C) colour.⁹⁰ The structures of the cyclic compounds **49a–c** were studied by the X-ray diffraction method.

Reaction of compound **49c** with an excess of tellurium powder in toluene affords cyclo-1,3-ditellura-2,4-distannane **52** in a quantitative yield.⁹¹ The same cycle is obtained in 73% yield by boiling a mixture of the corresponding distannene **50c** with tellurium powder in toluene (molar ratio 1 : 3).⁹¹

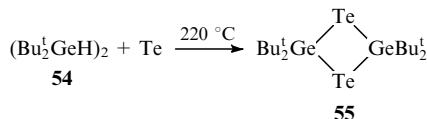


R = 2,4,6-Pr₃C₆H₂.

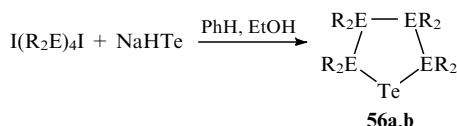
The *tert*-butyl analogue of compound **52**, viz., cyclo-1,3-ditellura-2,4-distannane **53**, was synthesised by reaction of tetrameric di(*tert*-butyl)tin with tellurium as well as by reaction of Bu₂^tSnCl₂ with sodium telluride.⁹²



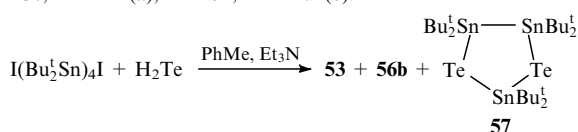
The reaction similar to that used in the synthesis of tellurides (R₃E)₂Te (see Section III.1) was used to prepare cyclo-1,3-ditellura-2,4-digermane **55**. Heating of the hydride **54** with tellurium powder gives a cyclic compound **55** in a nearly quantitative yield.⁹³ It is noteworthy that reaction of the hydride **54** with selenium yields a mixture of four- and five-membered cyclic products.⁹³



The synthesis of the five-membered derivatives R₈E₄Te (**56a,b**, E = Ge, Sn) was carried out using structurally similar derivatives of Group 14 elements. Octaphenyltelluratetragermacyclopentane (**56a**) was obtained by reaction of 1,4-diiodooctaphenyltetragermene with sodium hydrotelluride in a benzene–ethanol mixture.⁹⁴ Reaction of 1,4-diiodoocta(*tert*-butyl)tetrastannane with H₂Te in the presence of triethylamine leads to octa(*tert*-butyl)telluratetrastannacyclopentane (**56b**).⁹⁵ Since the reaction of triethylamine with H₂Te yields triethylammonium hydrotelluride Er₃NH⁺HTe[−], it may be assumed that the HTe[−] anion is a tellurium-containing substrate of this reaction. Sodium telluride is not suitable for the synthesis of the heterocycle **56b**, since it cleaves the Sn–Sn bonds in the starting compound. Compound **53** and the five-membered *tert*-butyl derivative of 1,3-ditellura-2,4,5-tristannacyclopentane **57** are by-products in the synthesis of telluratetrastannacyclopentane **56b**.⁹⁵



E = Ge, R = Ph (**a**); E = Sn, R = Bu^t (**b**).

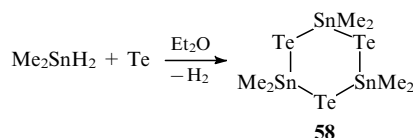


Compound **56b** is rather stable upon storage, whereas its germanium analogue **56a** is rapidly oxidised in air to give

Ph₂Ge–Ph₂Ge–O–GePh₂–GePh₂.⁹⁴ According to X-ray diffraction analysis data,⁹⁵ the ring in compound **56b** is practically planar.

2,4,5-Hexamethyl-1,3-ditellura-2,4,5-tristannacyclopentane, a representative of yet another type of five-membered cyclic compound containing Te and Sn atoms, was prepared by reaction of tellurium powder with dimethylstannane which in turn was synthesised by reduction of dichlorodimethylstannane with lithium aluminium hydride in an Et₂O–DMF mixture (30 : 1, by volume).⁹⁶ It was characterised by mass spectrometry as well as by ¹H (see Ref. 96) and ¹¹⁹Sn NMR spectroscopy (see Ref. 97).

Reduction of dichlorodimethylstannane or Me₂SnO with lithium aluminium hydride in Et₂O and subsequent reaction of dimethylstannane with tellurium powder results in 2,2,4,4,6,6-hexamethyl-1,3,5-tritellura-2,4,6-tristannacyclohexane (**58**) in 58% yield.⁹⁸



Compound **59** was also synthesised in 62% yield by reaction of dimethyldichlorostannane with sodium hydrotelluride synthesised from Te and NaBH₄ in water⁹⁹ and was characterised by the X-ray diffraction method⁹⁹ and mass spectrometry.⁹⁸

VI. Conclusion

The data presented suggest that compounds containing bonds of Te with Group 14 elements belong to a synthetically promising class of organoelement compounds. They can be used for the synthesis of organotellurium derivatives of various types, *e.g.*, organoelement tellurols, alkyl aryl tellurides, aryl tellurobenzoates and aryl telluroformates, various telluroketones and heterocycles. A promising, although still insufficiently studied area of application of these compounds is the synthesis of various metal tellurolates and tellurium-containing clusters and low-temperature synthesis of metal tellurides. These are only a very few examples which illustrate possible applications of compounds containing Te–E bonds in organic synthesis, particularly, in the synthesis of organic sulfur derivatives and some other organoelement compounds.

The expansion of the range of well-studied reactions, primarily those resulting in tellurolates and metal tellurides, a search for novel procedures for the synthesis and characterisation of various compounds, *e.g.*, R₃ETeR² and (R₃E)₂Te, elaboration of synthetic procedures for and studies of reactions of other types of compounds containing bonds of Te with Group 14 elements, *e.g.*, (R₃E)₄Te and (R¹Te)_nER_{4−n}² (*n* = 2, 3), present indisputable interest for both organotellurium chemistry and organic chemistry in general.

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Metal complex catalysis in organic electrosynthesis

Yu H Budnikova

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Abstract. Data on the use of electrochemically generated metal complex catalysts in organic synthesis are analysed, systematised and generalised. The considerable potential of organic electrochemistry is shown. Some electrochemical methods provide advantages in the synthesis of compounds where conventional chemical methods fail, are experimentally complicated or have environmental limitations. Particular attention is given to the mechanisms of electrocatalytic reactions. The bibliography includes 333 references.

I. Introduction

The development of environmentally safe and resource-saving chemical and technological processes is one of the strategically important lines of research in science and engineering. Homogeneous catalysis is finding increasing use in organic synthesis because it offers advantages over heterogeneous catalysis, particularly, from the viewpoint of selectivity and efficiency. Actually, complexes of transition metals, such as Ni, Pd or Co in low oxidation states, can react with many functional groups thus catalysing the formation of C–C, C–P, C–Si and other bonds. Electrochemical methods enable one to synthesise many organometallic compounds, study the reactivities of coordination compounds and elucidate possible reaction mechanisms.

In recent years, the use of electrochemically generated catalysts in reactions of organic compounds has assumed great importance both in organic synthesis and in thorough investigations into electron transfer, bond cleavage, substitution, addition

and other reactions. The results of these investigations find application in many fields of physical, organic and analytical chemistry. The major breakthrough in the use of electrochemical reactions in industry, particularly, in low-tonnage chemistry, occurred in the past few years. From an industrial standpoint, electrochemical reactions have a number of advantages. Thus the conversion, the rate and, within certain limits, the selectivity of the process can be easily controlled by means of such parameters as the current density and the potential.^{1–3}

Methods of indirect reduction and oxidation of organic compounds where the formation and regeneration of reactants occurs at an electrode find increasing use in modern organic synthesis. These methods enable one to perform various transformations of organic compounds under conditions of efficient and environmentally safe processes.⁴ Presently, the electric energy cost is only an insignificant part of the cost price of the product and it is expected that it will grow more slowly than the price of chemical reagents.⁵ Electrochemical processes are environmentally non-polluting and the control over these processes can be easily automated. Electrochemical reactions can provide higher selectivity as compared to conventional chemical transformations with simultaneous reduction of energy consumption and attainment of higher current densities.

Electrochemical metal complex catalysis attracts interest because it enables one to carry out reactions under mild conditions (moderate temperature, ambient pressure) and in a virtually closed system with the use of a minimum amount of the catalyst (mediator), which is cyclically regenerated. It should be noted that mediator processes are not only of practical importance but also offer a unique possibility of studying reaction mechanisms of reduction and oxidation of various substrates by electrochemical methods. For the simple cases, the mathematical approach was elaborated. This approach is based on approximating formulae, which provide a way of determining the rate constants of individual steps of the overall process of formation, consumption and regeneration of the mediator and enable one to obtain information on the energy characteristics of these steps and on the influence of various external factors. For this purpose, the

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dependencies of the current (its catalytic increase as a measure of the rate of the process) and the potential on the conditions of electrolysis are used.

The ever-increasing number of studies are aimed at replacing traditional catalysts based on toxic heavy metals with environmentally safer and cheaper compounds.

The present review surveys the principal results, which were obtained in organic synthesis with the use of electrochemical methods under the conditions of metal complex catalysis in the last 15 years. Some electrochemical reactions related to metal complexes, such as reversible haptotropic shifts, ligand exchange, modelling of molecular switches and modelling of the active sites of metalloenzymes as well as the architecture of electrochemically functionalised fullerenes are beyond the scope of the present review.

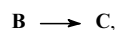
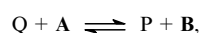
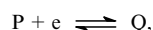
II. General principles of metal complex electrocatalysis in organic synthesis and methods of investigation of reaction mechanisms

1. General principles

Reactions involving transition metal complexes can be divided into two classes. One class includes reactions, such as isomerisation, dimerisation or oligomerisation of unsaturated compounds, in which no redox processes occur. In these reactions, the function of the catalyst is to control the kinetics and selectivity of thermodynamically possible processes. In this case, electrochemical methods employing transition metal catalysis are used as an alternative to conventional procedures for generation of some low-valent species that are difficult to access.⁶ However, the above-mentioned reactions are not, in essence, electrochemical processes because they require no electricity consumption and, hence, they are not considered in the present review.

The reactions of the second class involve both catalysts (transition metal complexes) and a stoichiometric number of electrons (either from a reducing agent or from an electrochemical source). This class can be subdivided into two groups according to the type of action of the catalyst.

In the first group of reactions, the transition metal complex can serve as a carrier of electrons from their source to the reagent. Generally, these processes proceed by the so-called outer-sphere mechanism without the formation of an intermediate complex of the substrate (**A**) with the catalyst (the redox P/Q pair) and the mediator is regenerated electrochemically.^{7–12}



where **P** is a mediator, **Q** is a catalyst, **A** is a substrate, **B** is a reduction product and **C** is the target product.

The function of the redox catalyst (mediator **P**) is to transfer an electron from the electrode to the substrate after which the initial product of reduction of the substrate **B** is transformed into the final product **C** in the course of the chemical reaction. In the case of the rapid irreversible conversion of **B** into **C**, the substrate can be reduced under the conditions of homogeneous electron transfer in the direction opposite to the standard potential drop ($E_{P/Q}^\circ > E_{A/B}^\circ$),^{7,8} which substantially extends the possibilities of redox catalysis. The apparent benefit of using redox catalysts is achieved only when these catalysts are stable and can be rapidly regenerated at an electrode in high current yield at potentials which are more positive than the potentials of direct electroreduction of the substrate, or at potentials which are less positive than the potentials of direct electrooxidation of the substrate. In addition, the catalysts must rapidly react with the substrate.

Hence, it is advantageous to use such metal complex catalysis in two cases: (1) if the employment of the homogeneous electron transfer leads to acceleration of the process as a whole, *i.e.*, if the

kinetic barrier of the electrochemical process is lowered and the potential approaches the thermodynamical value owing to transfer of the electron to the bulk of the solution and a decrease in the overpotential of the electrochemical reaction; (2) in processes involving substrates whose homogeneous redox reactions proceed more rapidly than heterogeneous reactions for one or another reason.

The second group of faradaic and catalytic reactions includes those proceeding by the inner-sphere mechanism, *i.e.*, processes involving the formation of various intermediate coordination compounds (**PA** or **QA**) in the course of the reaction. This approach was described for the first time 15 years ago and was considered in the reviews.^{13–19}

The inner-sphere electron transfer has some advantages over the outer-sphere mechanism for the following reasons.

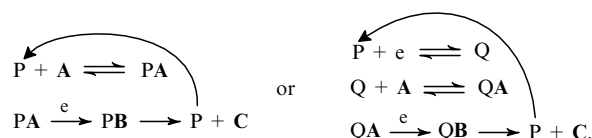
1. Redox processes are independent of the difference between the potentials of the mediator and the substrate and, hence, a large reduction in the overpotential becomes possible.

2. The inner-sphere transfer has a lower activation barrier.

3. Only one electron can be transferred in the outer-sphere process, whereas two or more electrons can be transferred through the inner-sphere mechanism. This is of particular importance in biocatalysis and in activation of small molecules.

In the last decade, attempts have been made to provide theoretical justification for these processes and to extend the range of catalytic reactions. However, many details of the reaction mechanisms remain unclear.

The mechanism of action of metal complex catalysts can be represented by the following scheme



Since transformations of the substrate in the coordination sphere of the metal complex play a decisive role in the catalytic cycle, this type of catalysis is termed coordination electrocatalysis.¹³ The electrochemical step of the process and the chemical reaction of the substrate share a common catalyst–substrate complex. The function of the catalyst is to bind and activate the substrate in the coordination sphere of the metal complex with the resulting increase in the reactivity of the substrate in the electron exchange with the electrode. Unlike redox catalysis, coordination electrocatalysis requires that either the mediator **P** or the catalyst **Q** be coordinatively unsaturated or their ligands be readily leaving groups, which is necessary for the formation of the intermediate **PA** and **QA** complexes. Different approaches to investigation of mediator processes were first described approximately two decades ago and were covered in the reviews.^{7–19}

Abundant data on complex formation and activation of substrates that are kinetically inert in redox reactions are presently available,^{14,20} which facilitates the choice of an appropriate metal complex.

For the reactions considered below, electrochemical methods do not necessarily have advantages over conventional chemical methods. However, it should be noted that electrochemical methods make it possible to generate unusual low-valent intermediates, which cannot be prepared with the use of chemical reducing agents. In addition, many reactions require reduction of intermediates of the catalytic cycle, which can be readily accomplished in the electrochemical process by controlling the potential of the working electrode.

In recent years, electrochemical methods were substantially simplified and became cheaper. Many electrochemical reactions are carried out in the direct current mode with the use of constructionally simple current sources. Undivided cells find increasing use because divided cells are less efficient in polar aprotic solvents and require a large amount of a supporting electrolyte. Processes with the use of sacrificial anodes have

considerable promise both for direct and catalytic reactions. In the latter case, the conductivity is enhanced and metal ions generated at an anode can influence the reactivities of chemical intermediates.^{21, 22}

Data on the electrochemical and chemical behaviour of the simplest transition metal complexes were surveyed in the reviews and papers.^{22–33}

2. Methods of investigation of the mechanisms of reactions catalysed by transition metals

Reactions catalysed by transition metals proceed through catalytic cycles involving metal complexes in different oxidation states. Most of the metal complexes are either oxidised or reduced, or both. Consequently, they can be readily detected and characterised by electrochemical methods (voltammetry, amperometry, chronoamperometry, *etc.*). These methods also allow one to estimate the reactivities of metal complexes. Presently, stationary and transient voltammetry are the most readily available methods.

Stationary voltammetry is used for characterising a metal complex which is already present in solution and is characterised by the redox potential and its concentration is determined by the reduction or oxidation current. The reactivity of the complex with respect to the substrate can be examined by monitoring the change in its redox current as a function of time using, for example, the method of rotating disc electrode. If a new electroactive metal complex is formed in the course of the reaction, it can also be detected from its redox peak and its yield in the reaction is determined by the redox current. By this means, both the reagents and the products of the chemical step and its kinetics can be characterised. The stationary state method enables one to obtain kinetic data for chemical reactions whose half-lives $t_{1/2}$ are larger than several tens of seconds.

Transient voltammetry is used for proving the existence of the equilibrium between different complexes by estimating the relative change in the current at the redox peaks of different species as the scan rate is changed. The redox process of one species at the electrode surface leads to a shift of the equilibrium in the diffusion layer. The concentration of the species, which is measured from their redox current, reflects not their true concentration but the dynamic concentration [the CE (chemical–electrochemical) mechanism]. The scan rate fixes the time scale. The equilibrium is more difficult to shift as the time is decreased. In the limit, at very high scan rates, the dynamical equilibrium is frozen though it can be realised within longer periods of time (low scan rates). This method allows one to determine the equilibrium concentrations of different complexes and then their equilibrium constants. In these cases, the thermodynamics and kinetics of the equilibrium can be characterised using staircase transient voltammetry or chronoamperometry (the pulse duration θ) of redox waves of various species. In this case, electrochemical methods are similar to

NMR spectroscopy because progressive freezing of the equilibrium as the scan rate is increased (voltammetry) or as the pulse duration θ is decreased (chronoamperometry) is analogous to coalescence in NMR spectroscopy. In the equilibrium reactions, the major species observed in solution are not necessarily reactive because they can be involved in the endergonic equilibrium (which is established with energy absorption). Since conventional methods provide a way of controlling the reaction, efficient reactive species can be identified only in detailed kinetic studies.

Cyclic voltammetry can also be used for generation of stable or short-lived organometallic species through successive electron transfers and chemical reactions in the course of redox processes involving metal complexes. A knowledge of the absolute number of electrons involved in an electrochemical process enables one to determine oxidation states of a cascade of complexes, which can be generated from a particularly stable complex. The kinetics of reactions of electrogenerated species with a particular substrate can be controlled by increasing the scan rate in cyclic voltammetry (or decreasing the pulse duration in chronoamperometry), *i.e.*, by reducing the time scale of the chemical reaction. Analysis of the changes in the voltammogram as a function of the scan rate (or the time) makes it possible to obtain the kinetic data for chemical reactions whose half-lives $t_{1/2}$ range from 0.1 s to 10 ns. Hence, intermediate species can be generated and/or identified and their reactivities can be characterised.

However, although electrochemical methods provide a way of studying the kinetics and thermodynamics of reactions, they give no information on the structures of intermediates. Electrochemical methods in combination with NMR spectroscopy allow the elucidation of the characteristic features of the reaction mechanisms and provide detailed structural data. Other spectral methods can also be combined with electrochemical methods to obtain kinetic and structural parameters of the complex reaction system. The efficiency of this approach was demonstrated in many studies on elementary stages, such as oxidative addition, ligand exchange and reductive elimination.

III. Homocoupling of organic halides

1. Homocoupling of organic monohalides

Reductive dimerisation of organic halides is the first known reaction involving both faradaic reduction and catalysis by transition metal complexes. In 1976, Jennings *et al.*³⁴ reported electrodimersation of alkyl bromides in DMF by electrolysis between two metal electrodes (Ni, Al or Cu) in the presence of iron or nickel acetylacetonates and triphenylphosphine. Later on, other analogous reactions were carried out, the electrochemical properties of catalyst precursors were studied and the reaction mechanisms were investigated.^{35–44} The results published within the last decade are summarised in Table 1. Although dimerisation products can be obtained in high yields, these reactions are of

Table 1. Products of electroreductive coupling catalysed by Ni and Co compounds.

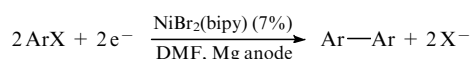
Substrate	Metal – ligand	Solvent	Product	Yield (%)	Ref.
EtBr	Ni – phen	DMF	C ₄ H ₁₀		35
n-C ₆ H ₁₃ Br	Ni – bipy	DMF or NMP	C ₁₂ H ₂₆	85	36
n-C ₅ H ₁₁ Br	Ni – bipy	DMF or NMP	C ₁₀ H ₂₂	89	36
MeOC ₂ H ₄ Br	Ni – bipy	DMF or NMP	(MeOC ₂ H ₄) ₂	60	36
MeO ₂ CC ₅ H ₁₀ Br	Ni – bipy	DMF or NMP	MeO ₂ CC ₁₀ H ₂₀ CO ₂ Me	65	36
Cl(CH ₂) ₄ Br	Ni – bipy	DMF or NMP	Cl(CH ₂) ₈ Cl	38	36
CH ₂ =CHCH ₂ Cl	Co – bipy	H ₂ O	(CH ₂ =CHCH ₂) ₂		37
PhCHCl ₂	Ni – salen	DMF	PhCH(Cl)CH(Cl)Ph + PhCH=CHPh		40
	Co – salen	DMF	PhCH ₂ CH ₂ Ph + PhCH=CHPh		41, 42
X(CH ₂) _n Cl (X = Br, I; n = 2–6)	Ni – salen	DMF	Cl(CH ₂) _{2n} Cl	80–90	43, 44

Note: phen is 1,10-phenanthroline; bipy is 2,2'-bipyridyl; NMP is *N*-methyl-2-pyrrolidone; salen is the bis(salicylidene)ethylenediamine dianion.

limited synthetic usefulness because most of them can be carried out using either chemical or electrochemical methods in the absence of catalysts.⁴⁵

The synthesis of biaryls from aryl halides attracts great interest because these compounds are of practical use, whereas they are difficult to prepare by chemical methods. First electro-syntheses were carried out in 1980s simultaneously by several research groups^{46–49} with the use of $\text{NiCl}_2\text{PPh}_3$ (1%–20%) as the catalyst precursor in the presence of an excess of PPh_3 . Later on, nickel complexes with 2,2'-bipyridyl and bidentate phosphines, *viz.*, 1,2-bis(diphenylphosphino)ethane (dppe) and 1,2-bis(dialkylphosphino)benzene, were prepared.^{50, 51}

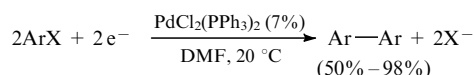
The Ni(II) complex with bipy, which can be reduced to the Ni(0) complex, proved to be an efficient catalyst of dimerisation of aryl compounds.^{52, 53} In combination with sacrificial anodes, this process can be performed in an undivided cell under very simple experimental conditions in the presence of an excess of bipyridyl.



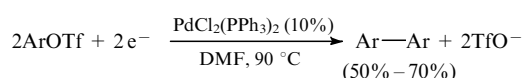
$\text{Ar} = \text{Ph}, 3\text{-MeC}_6\text{H}_4, 4\text{-MeCOC}_6\text{H}_4, 2\text{-naphthyl}; \text{X} = \text{I}, \text{Br}, \text{Cl}.$

Interestingly, biaryls were obtained in only slightly lower yields when the reactions were carried out in alcohols, such as methanol or ethanol, instead of DMF with the use of a sacrificial iron or aluminium anode.^{54, 55} A nickel complex with either bipy or di(2-bipyridyl)amine can serve as a catalyst. The results obtained in the cited studies evidence the possibility of formation of organonickel intermediates, which are stable in protic solvents and give rise to biaryls. Efficient arylation of activated alkenes was carried out under the same conditions.⁵⁵

The electrosynthesis of biaryls from bromo- or iodoarenes⁵⁶ can be carried out in the presence of $\text{PdCl}_2(\text{PPh}_3)_2$ as the catalyst precursor. Aryl triflate can also serve as the substrate,^{57, 58} but the latter process requires higher temperature. These homocoupling reactions catalysed by Ni or Pd complexes can also be performed using conventional chemical methods in the presence of zinc as a reducing agent to obtain biaryls in comparable yields.⁵⁸

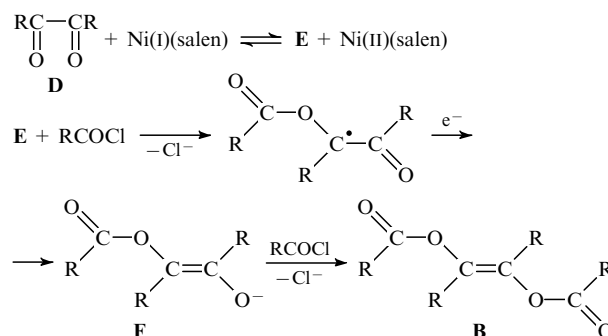
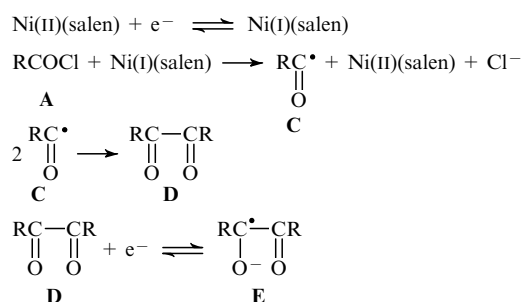


$\text{Ar} = \text{Ph}, 4\text{-Bu}^t\text{C}_6\text{H}_4, 4\text{-MeCOC}_6\text{H}_4, 4\text{-Me}_2\text{NC}_6\text{H}_4; \text{X} = \text{I}, \text{Br}.$



$\text{Ar} = \text{Ph}, 4\text{-NCC}_6\text{H}_4, 4\text{-CF}_3\text{C}_6\text{H}_4, 4\text{-ClC}_6\text{H}_4; \text{Tf} = \text{O}_2\text{SCF}_3.$

Catalytic reduction of cyclohexanecarboxylic acid chloride (**A**) in the presence of the electrochemically generated Ni(I)(salen) complex yielded the tetramer, *viz.*, 1,2-dicyclohexylethene-1,2-diol dicyclohexanoate (**B**).⁵⁹ The first step involves electron transfer from the Ni(I)(salen) complex to acyl chloride to form the acyl radical **C**. The radical anion **E** is generated from diketone **D** either by electroreduction or by the reaction with the Ni(I)(salen) complex. Subsequent reactions of the intermediates **E** and **F** with the initial acid chloride give rise to the reaction product **B**.

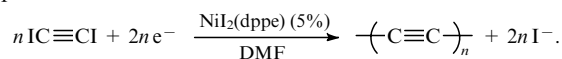


$\text{R} = \text{cyclo-C}_6\text{H}_{11}.$

However, the function of Ni(I)(salen) is conceivably more complex than the mere role of an outer-sphere electron carrier to form acyl radicals. Heterogeneous reduction of acyl chlorides RCOCl ($\text{R} = \text{Alk}$), which also proceeds through acyl radicals, yields aldehydes rather than the tetramers.

2. Homocoupling of organic dihalides

Electroreductive coupling of organic dihalides is one of the approaches to the synthesis of polymers. Polyynes were prepared from diiodoacetylene in the presence of the Ni complex with dppe.⁶⁰

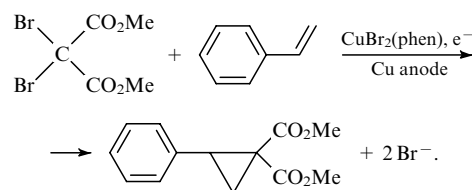


Electroreductive coupling of aromatic and heteroaromatic dihalides was examined.⁶¹

The results of studies on reductive electropolymerisation of aryl dihalides are summarised in Table 2.^{51, 62–72} Depending on the experimental conditions, polymers either deposit from the bulk of the solution in the course of electrolysis or precipitate as films on the electrode surface. This method is also suitable for preparing copolymers from a mixture of two aryl dihalides. Recently, the mechanism of polymerisation catalysed by the Ni complex with bipy was investigated.⁷³

Homogeneous catalytic reduction of α,ω -alkanediyl dihalides under the action of electrochemically generated Ni(I)(salen) complexes was studied. Thus, 1,8-dichlorooctane was prepared from 1-bromo-4-chloro- and 1-chloro-4-iodobutane in a yield of higher than 88%. It was demonstrated that the reaction followed the radical pathway.^{73, 74}

Electrochemical reductive coupling of some *gem*-dihalides, in particular, of dimethyl dibromomalonate in the presence of the copper complex with 1,10-phenanthroline and a sacrificial copper anode gave rise to cyclopropanes.⁷⁵



Studies by cyclic voltammetry and chronoamperometry showed that reduction of dimethyl dibromomalonate with the Cu(I) complex is a catalytic process, which is kinetically controlled by the rate of concerted electron transfer and cleavage of the carbon–bromine bond. In the presence of styrene, cyclopropane is formed through the addition of $\text{R}_2\text{C}\cdot\text{Br}$ ($\text{R} = \text{MeO}_2\text{C}$) at the double bond.⁷⁵ The radical intermediate is subsequently reduced to the corresponding anion, no transformations into carbene or alkylcopper intermediates being observed. In the reactions with other *gem*-dihalides, the products are formed by the chain mechanism involving addition.

Table 2. Reductive electropolymerisation of aryl dihalides with the use of a nickel catalyst.

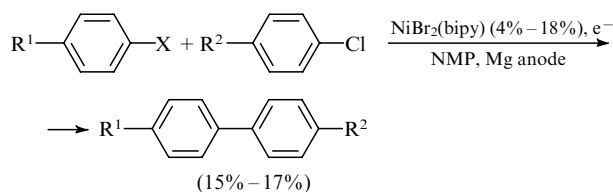
Substrate	Metal – ligand	Solvent	Ref.
	Ni – dppe	DMSO	51
	Ni – dppe	DMA ^a	62
	Ni – PPh ₃	MeCN	63
	Ni – bipy	DMA ^a	64
	Ni – bipy	DMA ^a	64
	Ni – bipy	DMA ^a	64
	Ni – bipy	DMA ^a	65–67
(R = Alk, aminoalkyldisiloxane)			
	Ni – bipy + PPh ₃	MeCN	68, 69
	Ni – bipy	MeCN	70
	Ni – bipy	DMA ^a	71, 72
(R = Alk, aminoalkyldisiloxane)			

^a DMA is *N,N*-dimethylacetamide.

IV. Cross-coupling of organic halides

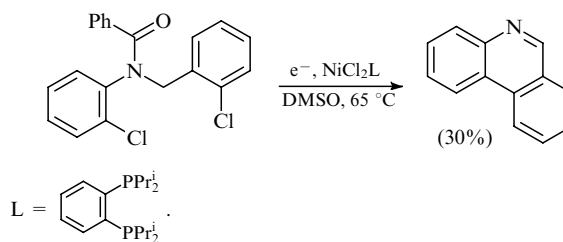
1. Cross-coupling of aryl halides

Asymmetrical biaryls, particularly, those containing electron-donating and electron-withdrawing groups in the aromatic nucleus, find use in nonlinear optics. Attempts were made to prepare these compounds, which are difficult to access, from mixtures of two different aryl halides employing electrochemical methods in combination with catalysis by Ni or Pd complexes. The chief drawback of this approach is the low selectivity of the process due to competitive cross- and homocoupling. It was demonstrated⁷⁶ that the reactions involving two aryl halides, which possess similar reactivities in the oxidative addition step, afforded three possible products (one asymmetrical and two symmetrical) in a ratio corresponding to statistical distribution (2:1:1). If the reactivities of the starting aryl halides differ substantially, an asymmetrical product can be obtained in satisfactory yield only upon slow addition of the more reactive aryl halide in the course of electrolysis.⁷⁶

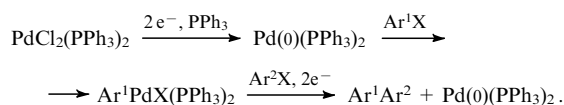


$R^1 = \text{MeO}, \text{Me}_2\text{N}, \text{MeS}; R^2 = \text{F}, \text{CN}, \text{CF}_3; X = \text{Br}, \text{Cl}.$

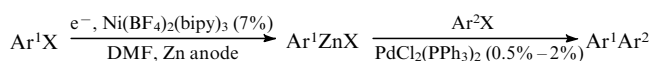
Intramolecular cross-coupling catalysed by the Ni complex with 1,2-bis(diisopropylphosphino)benzene was reported.⁵¹



In the electrochemical syntheses of asymmetrical biaryls, high selectivity is achieved in two-step processes. The reaction involving a stoichiometric amount of the $\text{PdCl}_2(\text{PPh}_3)_2$ complex is an example.^{56, 77, 78} The Pd(0) complex generated at an electrode first reacted with a molecule of one aryl halide followed by electroreduction of the resulting σ -arylpalladium complex in the presence of another aryl halide to give asymmetrical biaryls in good yields.



Yet another two-step synthesis of biaryls was carried out with the use of the catalytic Ni – bipy system. Electroreduction of aryl halides in the presence of Zn^{2+} ions and an excess of bipy with the use of a sacrificial zinc anode afforded not biaryls but arylzinc compounds stable in the reaction medium.⁷⁹ The addition of another aryl halide and a catalytic amount of $\text{PdCl}_2(\text{PPh}_3)_2$ to this reaction mixture gave rise to asymmetrical biaryls in high yields (Table 3).⁸⁰



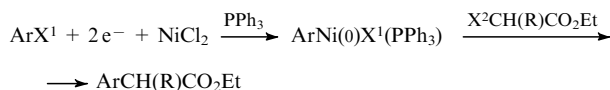
This method is also applicable to coupling reactions of aryl halides with allyl chlorides.⁷⁹ Functional substituents in aryl halides do not interfere with the reaction.

Table 3. Two-step cross-coupling of aryl halides catalysed first by Ni complexes and then by Pd complexes.⁸⁰

Ar ¹ X	Ar ² X	Yield (%)
4-ClC ₆ H ₄ CF ₃	4-BrC ₆ H ₄ OMe	83
4-ClC ₆ H ₄ CF ₃	4-BrC ₆ H ₄ CN	83
4-BrC ₆ H ₄ OMe	4-BrC ₆ H ₄ CN	90
4-BrC ₆ H ₄ OMe	4-BrC ₆ H ₄ NO ₂	84
4-ClC ₆ H ₄ CO ₂ Me	4-BrC ₆ H ₄ OMe	84
4-BrC ₆ H ₄ NMe ₂	4-BrC ₆ H ₄ NO ₂	84
4-BrC ₆ H ₄ NMe ₂	4-BrC ₆ H ₄ CN	83
2-BrC ₆ H ₄ OMe	2-BrC ₆ H ₄ CN	55

2. Cross-coupling of aryl halides with activated alkyl halides

The syntheses of pharmaceuticals, agrochemicals and perfumes make use of arylacetic or arylpropionic acids and benzyl ketones as important intermediates. These compounds can be prepared by electrochemical methods. It was shown that esters of α -halocarboxylic acids can react with arylnickel compounds, which are generated electrochemically from aryl halide in a divided cell, to give esters of arylacetic or arylpropionic acids.⁸¹ The chief drawback of this two-step procedure is the use of a large excess of PPh_3 , which is necessary for preventing homocoupling.



$\text{R} = \text{H, Me; X}^1, \text{X}^2 = \text{Cl, Br.}$

Recently, a more efficient procedure, which combines the use of a sacrificial anode with catalysis by nickel complexes, was developed. To reduce undesirable homocoupling to a minimum, the most reactive substrate, *viz.*, activated alkyl halide, was slowly added to the reaction mixture at 60–80 °C. This procedure was applied to cross-coupling of aryl halides with α -chloro esters (Table 4),^{82,83} α -chloro ketones (Table 5)^{83–85} and allyl and vinyl derivatives (Table 6).⁸⁴

Table 4. Electroreductive cross-coupling of aryl halides with α -chloro esters catalysed by the $\text{NiBr}_2(\text{bipy})$ complex.^{82,83}

$\text{ArX} + \text{ClCH(R)CO}_2\text{Me} \xrightarrow[\text{DMF, Zn or Al anode}]{\text{e}^-, \text{NiBr}_2(\text{bipy}) (5\% - 10\%)} \text{ArCH(R)CO}_2\text{Me}$		
ArX	R	Yield (%)
4-FC ₆ H ₄ Br	H	75
4-NCC ₆ H ₄ Br	H	60
4-Me ₂ NC ₆ H ₄ Br	H	67
4-FC ₆ H ₄ Br	Me	65
3-CF ₃ C ₆ H ₄ Br	Me	59
4-CF ₃ C ₆ H ₄ Br	Me	66
4-CNC ₆ H ₄ Br	Me	70
4-MeOC ₆ H ₄ Br	Me	51
4-MeOC ₆ H ₄ I	Me	85
2-Bromo-6-methoxynaphthalene	Me	55

This procedure was also successfully used in the asymmetric synthesis of 2-arylpropionic acids.⁸⁶ The resulting compounds possess higher biological activities than those of *S*-enantiomers [for example, in the case of 2-(3-phenoxyphenyl)propionic acid (phenopropfen) or 2-(6-methoxy-2-naphthyl)propionic acid (**1a**, $\text{R} = \text{H}$) (naproxen)]. However, conventional procedures for the synthesis generally afford racemates. The electrochemical syn-

Table 5. Electroreductive cross-coupling of aryl halides with α -chloro ketones catalysed by the $\text{NiBr}_2(\text{bipy})$ complex.^{83–85}

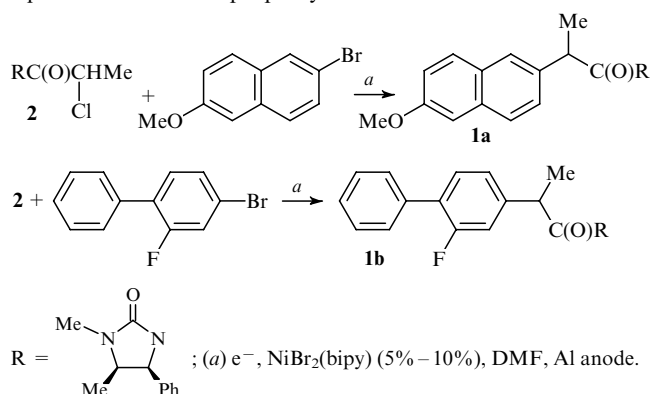
$\text{ArX} + \text{ClCH(R}^1\text{)COR}^2 \xrightarrow[\text{DMF, Zn or Al anode}]{\text{e}^-, \text{NiBr}_2(\text{bipy}) (5\% - 10\%)} \text{ArCH(R}^1\text{)COR}^2$			
ArX	R ¹	R ²	Yield (%)
4-FC ₆ H ₄ Br	H	Me	56
4-NCC ₆ H ₄ Br	H	Me	80
4-Me ₂ NC ₆ H ₄ Br	H	Me	52
4-FC ₆ H ₄ Br	H	Me	65
3-CF ₃ C ₆ H ₄ Br	H	Ph	52
4-CF ₃ C ₆ H ₄ Br	H	Ph	63
4-CNC ₆ H ₄ Br	Me	Me	70
4-MeOC ₆ H ₄ Br	Me	Me	70
4-MeOC ₆ H ₄ I	Me	Me	53
2-Bromo-6-methoxynaphthalene	Me	Me	45

Table 6. Electroreductive cross-coupling of aryl halides with vinyl or allyl derivatives catalysed by the $\text{NiBr}_2(\text{bipy})$ complex.⁸⁴

$\text{ArX} + \text{RX} \xrightarrow[\text{DMF, Zn or Al anode}]{\text{e}^-, \text{NiBr}_2(\text{bipy}) (5\% - 10\%)} \text{ArR}$		
ArX	RX (the ratio between Z and E isomers)	Yield of ArR (%) (the ratio between Z and E isomers)
3-CF ₃ C ₆ H ₄ Br	BrCH = CHMe (50 : 50)	66 (20 : 80)
4-NCC ₆ H ₄ Br	BrCH = CHMe (50 : 50)	66 (20 : 80)
4-MeOC ₆ H ₄ Br	BrCH = CHMe (50 : 50)	44 (25 : 75)
3-CF ₃ C ₆ H ₄ Br	AcOCH ₂ CH = CH ₂	56
4-CF ₃ C ₆ H ₄ Br	AcOCH ₂ CH = CH ₂	38
4-MeOC ₆ H ₄ Br	AcOCH ₂ CH = CH ₂	52
4-MeOC ₆ H ₄ Br	AcOCH ₂ CH = CHMe	63 ^a
4-MeOC ₆ H ₄ I	MeCH(Cl)CH = CH ₂	56 ^b

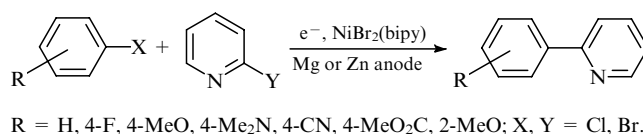
^a A mixture of $\text{ArCH} = \text{CHEt}$ and $\text{ArCH(Me)CH} = \text{CH}_2$ was obtained in a ratio of 86 : 12. ^b A mixture of $\text{ArCH} = \text{CHEt}$ and $\text{ArCH(Me)CH} = \text{CH}_2$ was obtained in a ratio of 96 : 4.

thesis allows asymmetric arylation of derivatives of α -chloropropionic acid using chiral auxiliary residues bound to the carboxy group. This reaction was used in the synthesis of (*S*)-fluorobipropfen starting from compound **1b**. Compounds **1a, b** were prepared in good yields and with a diastereomeric excess (*de*) using one equivalent of α -chloropropionylimide **2**.⁸⁶



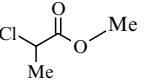
Compound	Yield (%)	ee	de	Major configuration
1a	62	85	93	<i>S</i>
1b	58	82	92	<i>S</i>

Recently, it has been demonstrated that cross-coupling of some aryl halides with heteroaryl halides proceeded in high yields under the action of the Ni(II) complex with *bipy*.^{87–89}



Products of cross-coupling of aryl halides are listed in Table 7. In the course of electrolysis, the nickel(II) complex was regenerated and its content in the electrolyte is at most 10 mol % with respect to Ar^1X . Organic halides were taken in equivalent ratios. In all cases, the electrosynthesis afforded asymmetrical biaryl as the major product. If aryl halides contain electron-withdrawing substituents in the aromatic nucleus, their cross-coupling reactions proceed in higher yields with the use of a zinc anode. Apparently, this is attributable to higher reactivity of magnesium

Table 7. Products of cross-coupling of organic halides under the action of the electrochemically generated Ni(0)(bipy) complexes. $Q = 2.0 - 2.5$ e per ArX molecule.

Ar ¹ X	Ar ² X or RX	Yield (%)	Anode	Ref.
4-MeOC ₆ H ₄ Br	2-ClC ₅ H ₄ N	77	Mg	87
4-Me ₂ NC ₆ H ₄ Br	2-ClC ₅ H ₄ N	67	Mg	87
PhBr	2-ClC ₅ H ₄ N	70	Mg	87, 89
4-FC ₆ H ₄ Br	2-ClC ₅ H ₄ N	66	Zn	87
4-MeOC(O)C ₆ H ₄ Cl	2-ClC ₅ H ₄ N	33	Mg	87
4-MeOC(O)C ₆ H ₄ Cl	2-ClC ₅ H ₄ N	76	Zn	87
2-MeOC ₆ H ₄ Br	2-ClC ₅ H ₄ N	58	Mg	87
4-CNC ₆ H ₄ Br	2-BrC ₅ H ₄ N	60	Zn	87
	2-BrC ₅ H ₄ N	78	Mg	88
	2-BrC ₅ H ₄ N	50	Mg	88
	2-BrC ₅ H ₄ N	50	Zn	88
	2-BrC ₅ H ₄ N	60	Mg	87
		59	Al	88
		41	Al	88
	MeCH=C(Me)Br	80 ^a	Al	88
PhBr	Me ₃ SiCl	65	Mg	89

^a $Z:E = 25:75$.

and its compounds with respect to electron-withdrawing functional groups resulting in transformations of the latter as side reactions. The mechanism of cross coupling was studied in detail and discussed in Ref. 89.

V. Formation of compounds containing the metal – carbon bond

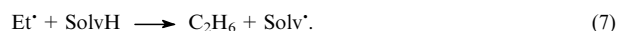
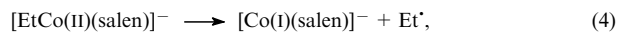
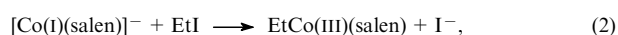
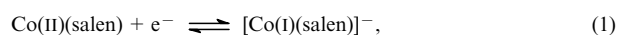
Cathodic alkylation of catalysts upon reduction of alkyl halides is characteristic of various chelate complexes of transition metals, which form rather stable compounds with the alkyl–metal σ -bond (such as cobalamine, phthalocyanine, salen and dithiocarbamate complexes of Co, Fe, Ru, Rh, Ni and Cr).^{90, 91}

The electrochemistry of vitamin B₁₂ and reactions of its reduced form (B_{12s}) with organic halides have been studied extensively.^{92–99}

Schrauzer and coworkers^{95–97} examined alkylation of vitamin B_{12s}, cobaloximes and other chelate Co(I) complexes [including Co(I)(salen)] with alkyl halides. Generally, these reactions proceed through the S_N2 mechanism including the supernucleophilic derivative of vitamin B₁₂, viz., B_{12s}, in which cobalt exists in the Co(I) state. Alkylcobalt intermediates were demonstrated⁹⁷ to decompose either photolytically or pyrolytically to form alkyl radicals. Rusling and coworkers⁹⁸ studied electrocatalytic reduction of 1,2-dibromoethane and 1,2-dibromobutane under the action of vitamin B_{12s} and found that these vicinal dibromides were transformed into alkenes without the intermediate formation of the alkylcobalt(III) complex. Later on, the catalytic reactions involving B_{12s} were compared with those involving Co(I)(salen)⁹⁹ and the rate of reduction of 1,2-dibromocyclohexane was found to

depend on the formal potential of the Co(II)–Co(I) pair. In addition, it was demonstrated¹⁰⁰ that reduction of benzyl bromide under the action of Co(I)(salen) gave rise to either benzyl radicals or carbanions depending on the potential at which the intermediate benzylcobalt(III) complex is subjected to electrolysis.

Costa and coworkers^{101–103} examined electrochemical reduction of salen complexes of organocobalt(III) and catalytic reactions of organic halides with the electrochemically generated Co(I)(salen) species. Methyl- and ethylcobalt(III)(salen) were electrochemically reduced to Co(I)(salen) and the alkyl radical.¹⁰¹ It was shown that Co(I)(salen) slowly reacted with *tert*-butyl bromide or chloride to give 2-methylpropene and molecular hydrogen. Apparently, the initially formed unstable intermediate decomposed into Co(II)(salen) and the highly reactive *tert*-butyl radical due to steric hindrances induced by the *tert*-butyl group, no organocobalt(III) derivatives being generated.¹⁰³ Peters and coworkers¹⁰⁴ studied these reactions in most detail. Thus, the products of the reaction of Co(II)(salen) with iodoethane were identified and characterised, the reaction scheme was proposed, its kinetic and thermodynamical parameters were measured, the UV spectrum of the EtCo(salen) intermediate was recorded, the electrochemical reduction of this intermediate was characterised and simulation of the mechanism was performed. Preparative electrolysis showed that one electron was consumed per iodoethane molecule. The compositions of the reaction products depend primarily on the solvent. Thus the dimer, viz., n-butane, and ethane were obtained as the major products in acetonitrile and DMF, respectively (in all cases, ethylene was present in small amounts). The reaction scheme includes the following steps:

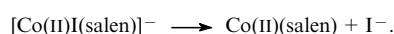
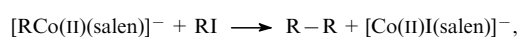


SolvH is the solvent.

It was suggested that the solvents have different effects on the relative rates of the last three steps [reactions (5)–(7)]. Dimerisation of ethyl radicals dominated over disproportionation (in acetonitrile, the yield of n-butane was 7.2 times higher than that of ethylene; in DMF, this ratio ranged from 3 to 4). In all cases, the yield of ethane was higher than that of ethylene because hydrogen atoms are readily detached from the solvent under the action of ethyl radicals, the detachment from DMF proceeding more readily than that from MeCN [reaction (7)]. To confirm the proposed mechanism, EtCo(III)(salen), which was prepared by the reaction of electrochemically generated Co(I)(salen) with EtI [reaction (2)], was reduced at a controlled potential. In this process, one electron was demonstrated to be consumed per molecule of the σ -complex with the resulting formation of the green Co(I)(salen) complex and the ethyl radical [reactions (3)–(4)].¹⁰⁴

Upon reduction of 1,8-diiodooctane under the same conditions,¹⁰⁵ two σ -complexes, viz., 8-iodooctylcobalt(III)salen and μ -(1,8-n-octyl)bis[cobalt(III)(salen)], were detected (both by electrochemical methods and UV spectroscopy) as intermediates, their relative amounts being dependent on the substrate : catalyst ratio.

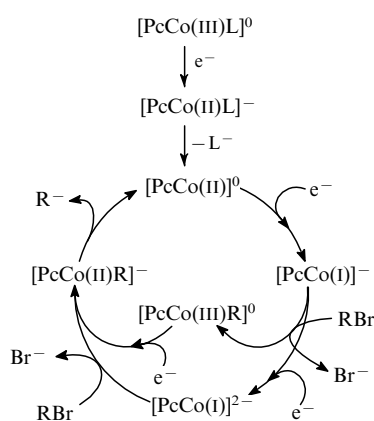
The mechanism proposed in the study⁹⁹ was supported by the results of the investigation¹⁰⁶ on catalytic reduction of alkyl halides with the Co(II)(salen) complex at microelectrodes, the reaction scheme being supplemented by two more steps.



Electrochemical alkylation of mercury metal with butyl bromide in the presence of bis(dimethylglyoximate)(pyridino)Co(II) [Co(DH)₂Py₂] was examined.¹⁰⁷ It was suggested that Co(II) was initially reduced to Co(I). Then the Co(I) complex reacted with BuBr to give BuCo(III)(DH)₂Py under the action of which the alkyl group was transferred to mercury metal.

Cathodic alkylation of the catalyst is typical of various chelate complexes of transition metals, which form rather stable compounds containing the alkyl–metal σ -bond, for example, of cobalamine, phthalocyanine, salen and dithiocarbamate complexes of Co, Fe, Ru, Rh, Ni and Cr.⁹⁰ These compounds contain metal atoms, which can exist in three successive oxidation states (for example, +3, +2 and +1 for Co), and possess the external π -system of the ligand favourable for stabilisation of the anionic complex. However, the ability of metal to exist in three oxidation states ($n+1$), n and ($n-1$) and the presence of a chelating ligand are not necessarily sufficient for alkylation of metal complex anions. For example, attempts to subject the Ir dimethylglyoximate complex to either chemical or electrochemical alkylation failed¹⁰⁸ in contrast to the analogous Co and Rh complexes. The potential of formation of the nucleophilic anion interacting with alkyl halides plays a large role in this process. If this potential is more negative than the potential of reduction of the alkylation product, the latter is not formed because of its irreversible reduction accompanied by the cleavage of the metal–alkyl bond. The potential of formation of the metal complex anion and the potential of reduction of the alkylation product depend on the nature of the metal atom, the chelating ligand, the solvent and the σ -bonded organic group.¹⁰⁹ For example, reduction of most metalloporphyrins, which contain an organic group σ -bonded to the metal atom, occurs at more negative potentials than reduction of metalloporphyrins with coordinated ligands. However, some ironporphyrins containing the Fe–Alk bond are reduced more readily than the corresponding complexes with ionic ligands.¹¹⁰ Studies of the electrochemical properties of a series of Co²⁺ complexes with substituted phthalocyanines in DMF allowed the conclusion that alkylation of electrochemically generated mono-anionic complexes in the presence of n-butyl bromide proceeded at the metal atom.⁹¹

Electrochemical reduction of n-butyl bromide was studied in the presence of the cobalt phthalocyanine complex PcCo(II) (Pc is substituted phthalocyanine) and the catalytic cycle was proposed.¹¹¹ This catalytic cycle was called ‘chemical catalysis of electrochemical reduction of alkyl halides’.¹¹¹



The above scheme is common to many chelate compounds of transition metals and rare-earth elements. At potentials more cathodic than the potential of reduction of the Co–Alk bond, electrolysis resulted in regeneration of the highly reactive [PcCo(I)]⁻ anion, which was rapidly alkylated with n-butyl bromide present in the solution and then reduced thus resuming the catalytic cycle.⁹¹

Metalloenzymes are natural catalysts in which metal ions exhibit different coordination modes. Vitamin-B₁₂-dependent enzymes containing the cobalt atom as the catalytic site catalyse

different isomerisation reactions accompanied by skeleton rearrangements.^{112–123} New models were proposed^{115–123} for enzyme catalysis on the basis of a hydrophobic analogue of vitamin B₁₂ in which the peripheral amide groups of natural vitamin B₁₂ are replaced by ester groups and this complex was demonstrated to be an efficient catalyst of electrochemical rearrangements of the carbon skeleton of 1-bromopropane derivatives containing two electron-withdrawing groups (COMe, CO₂Et or CN) at position 2.

Among other catalytic processes, the electrochemical transformation of nitrate anions into ammonia was carried out in water under the action of the Co(I) complex with 2,3-dimethyl-1,4,8,11-tetraazacyclotetradeca-1,3-diene, which was prepared from the corresponding Co(II) complex.¹²⁴

Some theoretical and applied problems of the use of cobalt complexes with ligands, which can stabilise metals in low-valent states, in electrocatalytic dehalogenation, homocoupling and cross-coupling reactions and in functionalisation of white phosphorus were covered in the studies.^{125,126} It was shown that electrochemical reduction of organic halides proceeded under the action of either the Co⁺(bipy) or Co[–](bipy)₂[–] complexes. Intermediates of the catalytic cycle, *viz.*, cobalt σ -complexes, were isolated and characterised. It was demonstrated that arylation (alkylation) of white phosphorus occurred under the simultaneous action of electrochemically generated nucleophilic [Co(I)(bipy) or RCoX₂(bipy)] and electrophilic (Mⁿ⁺, RX) reagents. Functionalisation of P₄ can follow two pathways, *viz.*, P₄ can react with ArCoX₂(bipy) or it can be reduced with the Co(I)(bipy) complex to the δ -P₃-cyclotriphenylphosphorus complex of cobalt, which, in turn, reacts with organic halides to form compounds containing the P–C bond.

The Ni σ -complexes are difficult to access and little studied. However, these compounds can be readily synthesised by electrochemical methods under mild conditions. It is known⁸⁹ that these complexes are intermediates of electrocatalytic cycles of cross-coupling, functionalisation of alkenes and reactions of aldehydes proceeding in the presence of Ni(0) complexes. In some cases, Ni σ -complexes can be isolated in pure form and they can be considered as model compounds for gaining insight into the mechanisms of organometallic synthesis.⁸⁹ Recently,⁸⁹ several σ -complexes containing Ni in different oxidation states [for example, RNiX(bipy), R₂NiX(bipy) and R₂Ni(bipy)] and exhibiting different reactivities were found to exist.

VI. Addition of organic halides to unsaturated groups

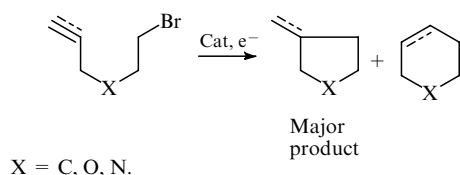
1. Addition at double and triple carbon – carbon bonds

First studies of electroreductive addition of organic halides at double or triple carbon – carbon bonds go back to the 1980s. Two main procedures using various catalysts were developed. In both processes, the key step involves the radical addition to unsaturated hydrocarbons. The first approach, which was considered primarily by Scheffold *et al.*,^{127,128} is based on the use of vitamin B₁₂ or related cobalt complexes as mediators of indirect electroreduction (in some cases, in combination with photolysis). The second approach, which was proposed by Gosden and Pletcher,¹²⁹ is based on the use of nickel complexes with macrocyclic tetradentate ligands, which can stabilise Ni(I) species.

In recent years, various organonickel and organocobalt compounds were studied and their redox properties and reactivities were examined depending on the nature of the ligand coordinated to the metal atom. The reactions described earlier were investigated once again with the aim of optimising the conditions and improving their efficiency. In particular, the reactions using the Ni(cyclam) complexes (cyclam is 1,4,8,11-tetraazacyclotetradecane) were examined and carbanion analogues were generated using the Ni(0) complexes in the presence of Michael acceptors.

a. Reactions with electron-rich double and triple carbon–carbon bonds

Most of reactions with electron-rich double and triple carbon–carbon bonds occur as free-radical cyclisation processes, which are used primarily for the preparation of five-membered rings with the desired stereochemistry.¹³⁰



Electrochemical processes involving cobalt complexes were studied in detail.^{127, 131} In recent years, the results of new studies on the application of cobalt complexes other than vitamin B₁₂ and nickel complexes with tetradentate macrocyclic ligands were reported. In these reactions, complexes of both types generate radical species.

Direct cyclisation of bromoacetals through cobaloxime(I) complexes was described as early as 1985.¹³² The reactions were carried out in a divided cell in the presence of a base (40% aqueous NaOH) and (chloropyridine)cobaloxime(III) (50%) as a catalyst precursor. Later on, it was found^{133, 134} that the amount of the catalyst can be reduced to 5% (the number of the catalytic cycles is ~50) and the presence of a base is not needed if the reaction is performed in a divided cell with a zinc anode.

This method was applied¹³³ to the synthesis of condensed bicyclic derivatives from various ethylene and acetylene compounds in the presence of (chloropyridine)cobaloxime(III) or Co[C₂(DO)(DOH)_{pn}] (see Table 8). Either saturated or unsaturated cyclic products can be obtained depending on the amount of the catalyst used, the cathodic potential and the presence of the hydrogen donor, for example, RSH (see Table 8).^{136, 138} Studies of some model reactions showed that the electrochemical method is more selective and efficient than conventional reduction with the use of Zn.¹³⁵

Nickel compounds, for example, the Ni(cyclam) complexes,¹²⁹ can also be used for generating radicals in electroreductive processes, including free-radical cyclisation reactions.

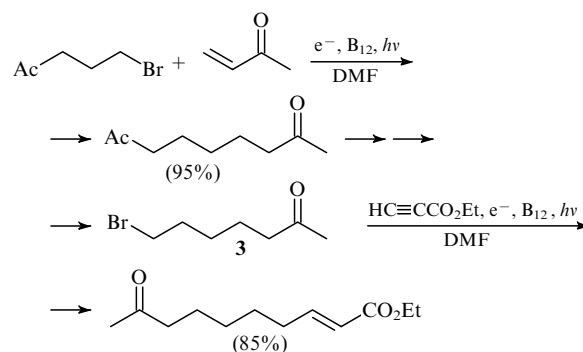
The Ni complexes with cyclam and its analogues and also with Ni(CR) and Ni(tet a) serve as efficient catalysts in DMF in the presence of NH₄ClO₄ as a proton source.^{136–138, 141} Electrochemically generated Ni(I) species rapidly react with organic halides to form alkynyl, alkenyl or aryl radicals whose intramolecular addition at double or triple bonds gives rise to cyclopentane derivatives (see Table 8).^{136–138} These reactions can also be carried out in an undivided cell with a magnesium anode, as exemplified¹³⁹ by the reactions of aryl halides bound to an unsaturated hydrocarbon chain (see Table 8). Nickel complexes with cyclam and other tetradentate donor ligands are catalysts of choice.^{139, 142, 143}

The Ni(salen) complex is a good alternative to the Ni(cyclam) complex for generating Ni(I)-containing intermediates. Thus cyclisation of 1-halo-6-phenylpent-5-yne proceeded much more efficiently than direct electroreduction of the substrate in the presence of 10% of a catalyst (see Table 8).¹⁴⁰ Electroreductive cyclisation of *N*-alkenyl-2-bromoanilines with the use of the Pd complex with PPh₃ as the catalyst¹⁴⁴ and electrocatalytic dehalogenation of α -haloacetic acids under the action of the reduced form of vitamin B₁₂ were reported.¹⁴⁵

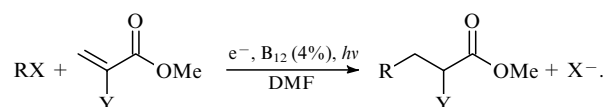
b. Addition to Michael acceptors

Radicals or carbanions and their equivalents, *viz.*, organometallic compounds, can be added to Michael acceptors. Free-radical reactions in the presence of nickel or cobalt complexes as catalysts have been studied previously.^{127–129}

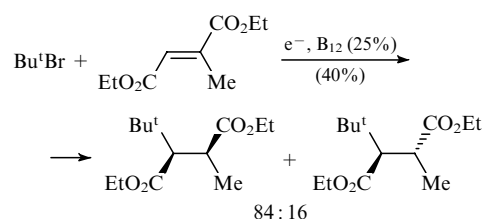
The synthesis of ethyl 8-oxodec-2-enoate, which was isolated from honey queen bees, provides a good example of the potential of the electrochemical approach to the preparation of natural products. This process involves two major electrochemical steps, *viz.*, the formation of the C–C bond catalysed by vitamin B₁₂ and initiated by visible light and the Michael addition of intermediate 3 at the triple bond.¹²⁸



This approach was applied to the synthesis of the pheromone of California red scale,¹⁴⁶ prostaglandin PGF_{2 α} ,¹⁴⁷ the pheromone of house mice¹²⁸ and jasmonates.¹⁴⁸ Alkylation and acylation of activated alkenes was used for the preparation of amino acid derivatives (Table 9).¹⁴⁹



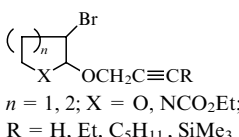
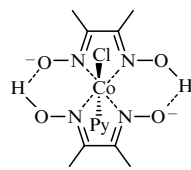
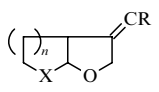
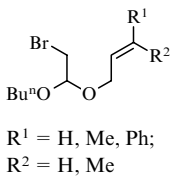
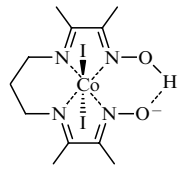
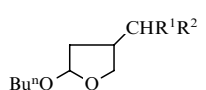
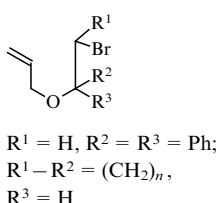
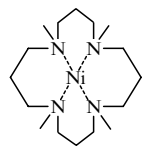
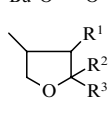
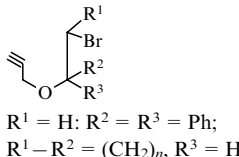
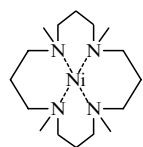
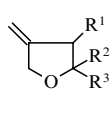
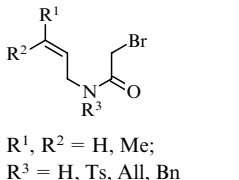
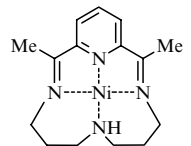
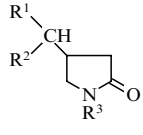
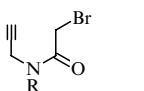
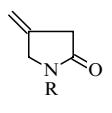
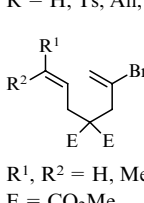
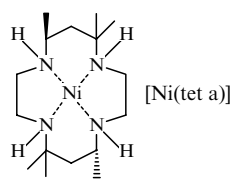
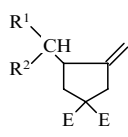
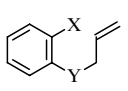
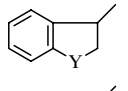
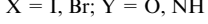
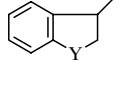
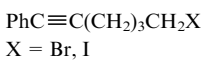
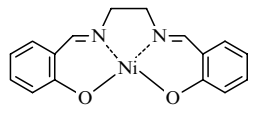
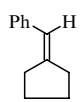
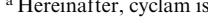
In some cases, protonation of an intermediate radical formed through the addition of alkyl halide to the Michael acceptor proceeds diastereoselectively. This situation is observed upon the addition of Bu^tBr to diethyl mesaconate catalysed by vitamin B₁₂.¹⁵⁰ However, standard reduction with zinc in the presence of vitamin B₁₂ proved to be more efficient because the stereoselectivity in the latter case was determined by the addition of amines.



The Ni(cyclam) complexes and related compounds can also be used for alkylation of Michael acceptors. For Ni(tet a) in acetonitrile, the number of catalytic cycles is small.¹⁵¹ However, this catalyst (2%) in DMF containing NH₄ClO₄ as the proton source shows efficiency in alkylation of unsaturated ethers, ketones or nitriles.¹⁵² In the case of terminal alkenes, the reaction products are obtained in good yields.

$R^1X + R^2CH=CR^3R^4 \xrightarrow[DMF, NH_4ClO_4]{e^-, Ni(tet a)^{2+}} \begin{matrix} R^1 & R^4 \\ & \\ R^2 & - & C & - & C \\ & & & & \\ & & R^3 \end{matrix}$				
R ¹ X	R ²	R ³	R ⁴	Yield (%)
BuBr	H	H	CO ₂ CH ₂ Ph	53
BuBr	H	H	CO ₂ H	32
Ph(CH ₂) ₃ Br	(CH ₂) ₄ CO	H		14
Ph(CH ₂) ₃ Br	Me	H	CO ₂ Me	13
Ph(CH ₂) ₃ Br	H	Me	CO ₂ Me	53
Ph(CH ₂) ₃ Br	H	H	CO ₂ Me	57
Ph(CH ₂) ₃ Br	H	H	CN	72
Ph(CH ₂) ₃ Br	H	H	COMe	37
Ph(CH ₂) ₂ CH(Me)Br	H	H	CO ₂ Me	60

Table 8. Reductive cyclisation catalysed by Co and Ni complexes.

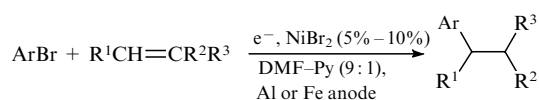
Substrate	Catalyst [short name]	Amount (mol %)	Reaction conditions	Reaction product	Yield (%)	Ref.
 $n = 1, 2$; $X = O, NCO_2Et$; $R = H, Et, C_5H_{11}, SiMe_3$	 [(chloropyridine)-cobaloxime(III)]	5	MeOH, 55–60 °C, Zn anode		54–80	133
 $R^1 = H, Me, Ph$; $R^2 = H, Me$	 $CoC_2(DO)(DOH)_{pn}$	5	MeCN $C_{12}H_{25}SH$		42–96	135
 $R^1 = H, R^2 = R^3 = Ph$; $R^1-R^2 = (CH_2)_n$, $R^3 = H$		20	DMF		68–97	135
 $R^1 = H; R^2 = R^3 = Ph$; $R^1-R^2 = (CH_2)_n, R^3 = H$		20	DMF		53–75	136
 $R^1 = H; R^2 = R^3 = Ph$; $R^1-R^2 = (CH_2)_n, R^3 = H$	 [Ni(CR)]	20	DMF or MeCN		85–86	136
 $R = H, Ts, All, Bn$	Ni(CR)	20	DMF or MeCN		11–67	137
 $R^1, R^2 = H, Me$; $E = CO_2Me$	 [Ni(tet a)]	20	DMF		7–33	137
 $X = I, Br; Y = O, NH$	Ni(tet a)	20	DMF		47–81	138
	Ni(cyclam) ^a	10	DMF, Mg anode		60–90	136, 138
 $X = Br, I$	 [Ni(salen)]	10	DMA		60–90	139
					84	140

^a Hereinafter, cyclam is 1,4,8,11-tetraazacyclotetradecane.

Table 9. Alkylation or acylation of activated alkenes catalysed by vitamin B₁₂.¹⁴⁹

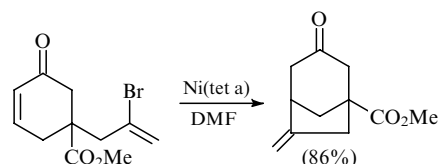
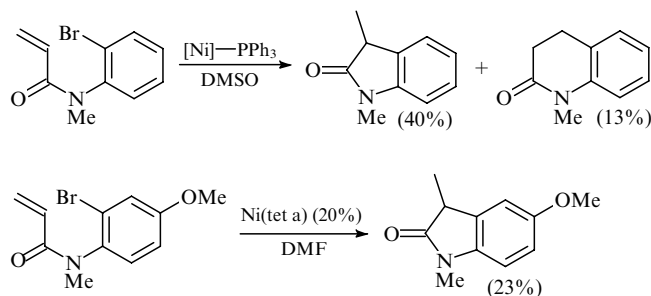
RX	Y	Reaction product	Yield (%)
Me(CH ₂) ₃ Br	NHAc	Me(CH ₂) ₄ CHCO ₂ Me NHAc	70
Me(CH ₂) ₃ Br	H	Me(CH ₂) ₅ CO ₂ Me	75
Ac ₂ O	NHAc	AcCH ₂ CHCO ₂ Me NHAc	67
Ac ₂ O	H	Ac(CH ₂) ₂ CO ₂ Me	70
MeO ₂ C(CH ₂) ₃ Br	NHAc	MeO ₂ C(CH ₂) ₄ CHCO ₂ Me NHAc	72

The nucleophilic addition can be performed in the presence of Ni(II) complexes, which are transformed into Ni(0) complexes upon cathodic reduction. The Ni(0)(bipy) complexes rapidly react with alkyl, alkenyl and aryl halides. However, in this case the organonickel intermediate generated through oxidative addition does not give the corresponding addition product in the presence of activated alkenes. In the presence of a Ni complex with a weaker bound ligand (for example, with pyridine, which prevents activated alkene from being coordinated to the metal atom), the regioselective 1,4-addition of aryl groups to activated alkenes was carried out under very mild conditions (60 °C, an undivided cell with a sacrificial aluminium or iron anode). Arylation products were obtained in 20%–63% yields,¹⁵³ which are comparable with those obtained in reactions using arylcopper or cuprates. The reactions performed in methanol or ethanol instead of DMF gave products in only slightly lower yields [the nickel complex with di(2-bipyridyl)amine as the catalyst].⁵⁵



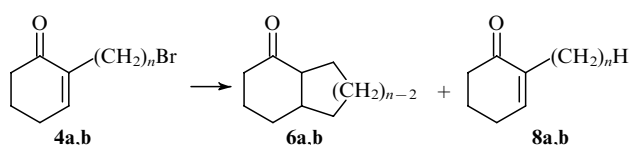
Ar	R ¹	R ²	R ³	Yield (%)
Ph	H	H	CO ₂ Et	63
4-NCC ₆ H ₄	H	H	CO ₂ Et	48
2-Naphthyl	H	H	CO ₂ Et	50
4-MeOC ₆ H ₄	CO ₂ Et	H	CO ₂ Et	46
4-MeCOC ₆ H ₄	CO ₂ Et	H	CO ₂ Et	31
2-Naphthyl	H	Me	CO ₂ Et	27
2-Naphthyl	Me	H	CO ₂ Et	20
2-Naphthyl	H	H	CN	61
2-Naphthyl	(CH ₂) ₄ CO	H		20

Intramolecular nucleophilic addition can follow either the radical or carbanion pathway.^{51, 137, 138, 154} Some examples are given below.^{51, 137, 138}



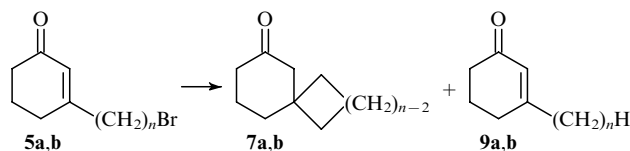
Bicyclic ketones were synthesised in the presence of 5% of vitamin B₁₂.¹²⁷

Some other Co complexes as well as Ni complexes catalysed cyclisation of bromocyclohexenones **4a,b** and **5a,b** to form bicyclic ketones **6a,b** and **7a,b**, respectively,¹⁵⁴ but the numbers of catalytic cycles in these cases were rather small. These reactions afforded open-chain compounds **8a,b** and **9a,b** as by-products. The Ni(cyclam)(ClO₄)₂, Ni(CR)((ClO₄)₂ and Co(bpp)OAc [bpp = C₅H₅NC(O)N[−](CH₂)₃N[−]C(O)C₅H₅N] complexes proved to be most efficient as catalysts.¹⁵⁴



$n = 4$ (a), 5 (b).

Catalyst	Substrate	Yields of products (%)			
		6a	8a	6b	8b
Ni(cyclam)(ClO ₄) ₂	4a	70	6	—	—
	4b	—	—	33	18
Ni(CR)(ClO ₄) ₂	4a	60	1	—	—
	4b	—	—	42	14
Co(bpp)OAc	4a	52	5	—	—
	4b	—	—	28	21

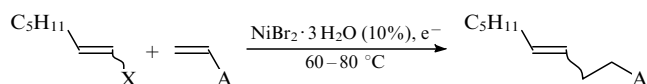


$n = 4$ (a), 5 (b).

Catalyst	Substrate	Yields of products (%)			
		7a	9a	7b	9b
Ni(cyclam)(ClO ₄) ₂	5a	30	4	—	—
	5b	—	—	65	21
Ni(CR)(ClO ₄) ₂	5a	42	4	—	—
	5b	—	—	16	19
Co(bpp)OAc	5a	47	11	—	—
	5b	—	—	40	13

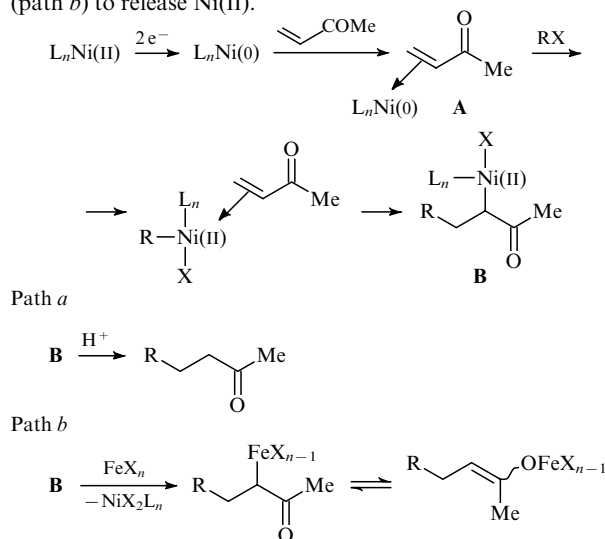
Intramolecular arylation of unsaturated amides gives rise to lactams. These reactions can follow either the radical or carbanion pathway. The carbanion mechanism is realised in the presence of the nickel triphenylphosphine complex to give a mixture of γ - and δ -lactams in a ratio of 3 : 1.⁵¹ The reactions through the radical mechanism [in the presence of the Ni(tet a) complex] proceed selectively to give δ -lactam, although in rather low yield.¹³⁷

The electroreductive addition of (*Z*)- or (*E*)-alkenyl halides to electron-deficient alkenes in the presence of a sacrificial iron anode proceeds in high yields with complete retention of the stereochemistry of the alkenyl fragment. These reactions can be used for functionalisation of isomerically pure (*Z*)- or (*E*)-alkenes.¹⁵⁵

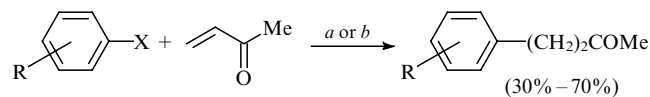


X = Cl, Br, I; A = CO₂Et, COMe, CN.

The conditions were optimised using the model reaction of methyl vinyl ketone (A = COMe) with (*Z*)- or (*E*)-1-halohept-1-enes. It was found that high yields (up to 84%) can be achieved in the presence of 1,2-dibromoethane and an iron anode. The process involves preelectrolysis, *viz.*, oxidation of an iron anode and reduction of 1,2-dibromoethane, followed by electrolysis of a mixture of alkenyl halide and methyl vinyl ketone. The role of iron ions is not understood. Conceivably, they function as Lewis acids, activate electron-deficient alkenes and facilitate the formation of the C–C bond. The reaction mechanism is not entirely known. Presumably, it involves coordination of electron-deficient alkene by electrochemically generated Ni(0) species. Oxidative addition of vinyl halide to the complex **A** affords the organonickel compound **B**, which is either protonated by residual water (path *a*) to form an addition product or transmetalated with iron ions (path *b*) to release Ni(II).



Recently, it was found¹⁵⁶ that cobalt bromide, either in the free form or in the complex with 2,2'-bipyridyl, catalyses the electrochemical addition of aryl halides to activated alkenes in a DMF–pyridine or acetonitrile–pyridine mixture. The reactions proceeded only with the use of a sacrificial iron anode, whereas the addition products were not detected in the reactions performed with other anodes (Zn or Al).



R = 4-CO₂Et, 4-COMe, 4-CF₃, 4-CN, 4-CHO, H, 4-OMe, 2-COMe; X = Br;

(*a*) DMF–PyH, CoBr₂–bipy (1 : 2), Fe anode, Ni cathode, 70 °C;

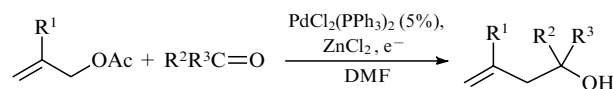
(*b*) MeCN–PyH, CoBr₂, Fe anode, Ni cathode, 60 °C.

2. Addition to carbonyl compounds

Data on electrochemical allylation of carbonyl compounds and the Reformatsky reaction are presently available.

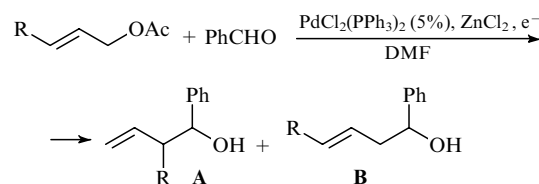
Some carbonyl compounds can be subjected to direct electrochemical allylation; however, coupling reactions catalysed by transition metals are more efficient, particularly, in the case of ketones.

One of procedures involves PdCl₂(PPh₃)₂ as the catalyst in the presence of the zinc salt (ZnCl₂). This procedure allows one to transform allyl acetates into the corresponding tertiary alcohols in good yields.¹⁵⁷



R ¹	R ²	R ³	Yield (%)
H	Ph	H	77
H	4-MeOC ₆ H ₄	H	84
H	4-ClC ₆ H ₄	H	68
H	(CH ₂) ₅	H	40
Me	Ph	H	62

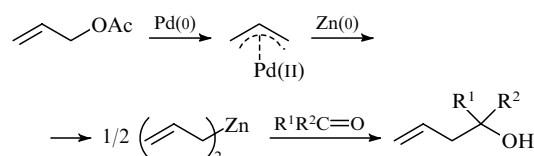
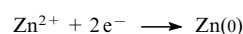
Of two possible isomers, the more branched isomer **A** was obtained as the major reaction product.



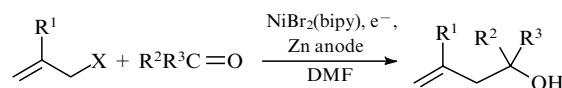
R = Me (56%, **A** : **B** = 91 : 9); Ph (71%, **A** : **B** = 83 : 17).

The reactions with conjugated carbonyl compounds proceed as 1,2-addition.

Exploration into the mechanism of this reaction revealed the key role of ZnCl₂,¹⁵⁸ which is most readily reduced to give Zn(0). The latter is capable of reducing the π-allylpalladium intermediate. The reaction products are formed through addition of diallylzinc to carbonyl compounds.



Carbonyl compounds can be allylated with the use of a nickel catalyst.^{82, 159, 160}

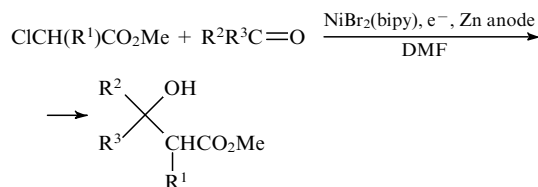


X	R ¹	R ²	R ³	Yield (%)
Cl	Me	Ph	H	85
Cl	Me	Me(CH ₂) ₅	H	70
Cl	Me	Ph	Ph	86
Cl	Me	Bu ^t	Me	60
Cl	Me	CH ₂ =CH	Me	43
OAc	H	Ph	H	80
OAc	H	(CH ₂) ₅	H	83

When employing an undivided cell, this reaction proceeds efficiently only in the presence of a sacrificial zinc anode. The reactions of aromatic and aliphatic aldehydes or ketones give rise to the corresponding homoallylic alcohols in good yields. The reactions of branched ketones, such as diisopropyl ketone, afford products in lower yields. In the case of α,β-unsaturated carbonyl compounds, the addition occurs exclusively at the 1,2-position. The Pd–Zn catalytic system is also efficient in these reactions. It was suggested^{160, 161} that the process is accompanied by transmetalation of the allylnickel complex, which is formed upon the oxidative addition of allyl halide (acetate) to the Ni(0) complex, with anodically generated Zn(II) species.^{160, 161}

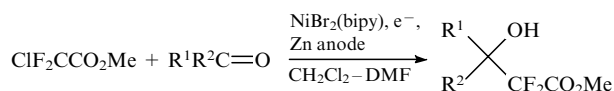
The Reformatsky reaction can also be carried out in an electrochemical mode either directly or with the use of a mediator.

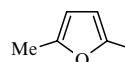
Catalysis by nickel compounds provides an efficient way of transforming the corresponding α -chloro derivatives to β -hydroxy esters or nitriles.¹⁶² These reactions also involve the oxidative addition of cathodically generated Ni(0)(bipy) to a halogen-containing derivative as the first step. In this case, the nature of a sacrificial anode is also of importance although the formation of an organozinc derivative was not unambiguously confirmed.



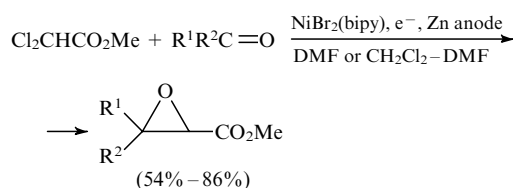
R ¹	R ²	R ³	Yield (%)
H	Et	Et	77
H	(CH ₂) ₅		86
H	Ph	Ph	77
Me	Pr ⁿ	Me	64
Me	Ph	H	80
Me	CH=CH(CH ₂) ₃		50

The reaction of carbonyl compounds with methyl chlorodifluoroacetate,¹⁶³ which cannot be activated by conventional chemical methods, provides an interesting example demonstrating the possibilities of this procedure. The best results were obtained with the use of a CH₂Cl₂–DMF mixture (9 : 1). The ¹⁹F NMR spectroscopic studies demonstrated that the reaction was accompanied by transmetalation.



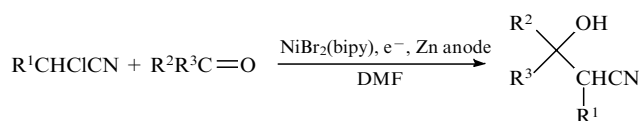
R ¹	R ²	Yield (%)
Ph	Me	72
(CH ₂) ₅		63
Ph	H	70
Me(CH ₂) ₂	H	77
	H	45

Under analogous conditions, the reactions of methyl dichloroacetate with acetophenone or cyclohexanone afforded epoxides in high yields.¹⁶²



R¹ = Ph, n-C₆H₁₃, Bu^t; R² = H, Me, Ph; R¹–R² = (CH₂)₅.

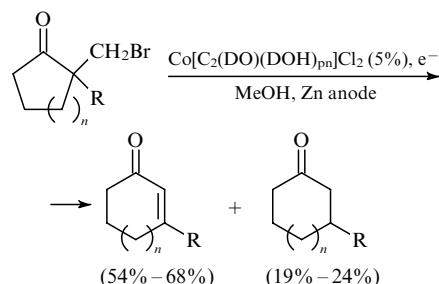
The reactions of chloroacetonitrile and α -chloropropionitrile with ketones proceeded analogously.¹⁶²



R¹ = H, Me; R² = Ph, n-C₆H₁₃, Bu^t; R³ = H, Me, Ph; R²–R³ = (CH₂)₅.

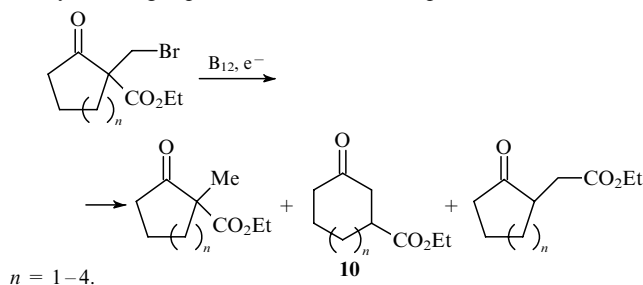
The intramolecular addition to the carbonyl group has not been adequately investigated. Only the ring expansion reactions of α -bromomethylcycloalkanones, which were carried out in the

presence of Co[C₂(DO)(DOH)_{pn}]Cl₂ as the catalyst at 55–60 °C, were reported.^{133, 164} It was assumed that the reaction proceeds *via* the radical pathway in accordance with the usual behaviour of alkylcobalt intermediates. The use of a sacrificial zinc anode in combination with a cobalt catalyst leads to an increase in the number of catalytic cycles and improvement in the yield.¹³³



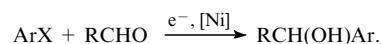
R = Buⁿ, n-C₆H₁₃, n-C₁₁H₂₃; n = 1–4.

Much attention has been given to the use of catalytic systems based on cobalt complexes in the organic synthesis, particularly, in the ring expansion reactions suitable for the preparation of natural compounds. The traditional electrolytic scheme of the synthesis was proposed. Under electrochemical conditions, Co(II) in heptamethyl cobyrinate perchlorate { [Cob(II)₇C₁ester]ClO₄ }, which is a catalyst simulating vitamin B₁₂, is readily reduced to Co(I) to give highly nucleophilic intermediates. The latter react with alkyl halides to form alkylated complexes containing the Co–C bond. The electrochemical reactions or photolysis of these complexes afford the final products. Torii and coworkers¹⁶⁴ studied the ring expansion reactions of 2-(bromomethyl)cyclopenta(hexa)nones with the use of cobaloxime (MeOH, 60 °C) in the galvanostatic mode under irradiation with visible light. Murakami and coworkers¹⁶⁵ used [Cob(II)₇C₁ester]ClO₄ as the catalyst of ring expansion reactions in the potentiostatic mode.



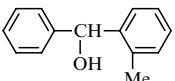
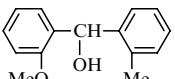
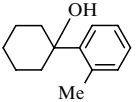
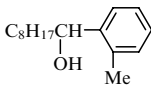
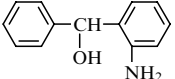
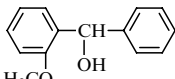
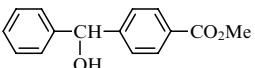
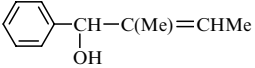
In different electrolytic modes, the ring-expansion product **10** was obtained as the major product (in yields of up to 56%). The course of the reaction was monitored by electronic and ESR spectroscopy, which made it possible to identify intermediates formed at different potentials either in daylight or in the dark. The potentials ≤ -1.5 V (with respect to a saturated calomel electrode) are optimum for electrolysis. The reaction cycle involves electrochemical reduction of the Co(II) complex to supernucleophilic Co(I) species, which react with the substrate to give the corresponding alkylated complex. The latter decomposes upon electrolysis (rather than photochemically) to the final product and the cobalt complex is recycled back to the catalytic cycle as the mediator. The ratio of the reaction products is determined by the strain energy of alicycles. Thus the highest yield of the ring-expansion product was achieved in the transformation of five-membered cyclic ketone to six-membered ketone.¹⁶⁵

Under particular conditions, electroreductive coupling of organic halides with aldehydes catalysed by the nickel(0) complex with 2,2'-bipyridyl proceeds in good yields (Table 10).¹⁶⁶



Alcohols can be obtained in high yields with the use of nickel, iron or stainless steel anodes. Aromatic aldehydes bearing the

Table 10. Coupling of organic halides with carbonyl compounds catalysed by the $\text{NiBr}_2(\text{bipy})$ complex (1 mmol) (see Ref. 166).^a

ArX	$\text{R}^1\text{R}^2\text{CO}$	Reaction product	Anode	Yield (%) (see ^b)
2- $\text{BrC}_6\text{H}_4\text{Me}$	PhCHO		Mg	14 (75) ^c
			Zn	18
			Ni	61
			Fe	63
	2-MeOC ₆ H ₄ CHO		inox ^d	80
			Ni	60
			inox ^d	71
			Ni	50
	$\text{C}_8\text{H}_{17}\text{CHO}$		inox ^d	58
2- $\text{BrC}_6\text{H}_4\text{NH}_2$	PhCHO		inox ^d	42
2- $\text{BrC}_6\text{H}_4\text{OMe}$	PhCHO		Ni	85
4- $\text{ClC}_6\text{H}_4\text{CO}_2\text{Me}$	PhCHO		inox ^d	50 ^e
$\text{MeC}(\text{Br})=\text{CHMe}$	PhCHO		inox ^d	52

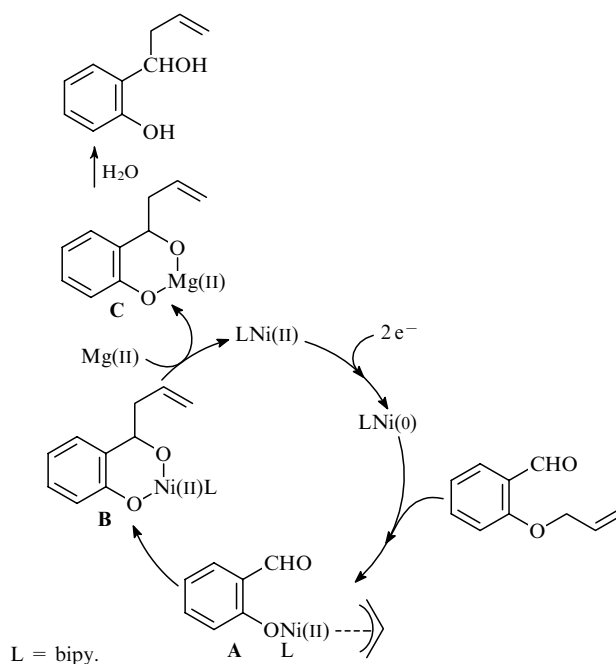
^a Reaction conditions: ArX, 15 mmol; $\text{R}^1\text{R}^2\text{CO}$, 7.5 mmol; Bu_4NBF_4 (10^{-2} mol litre⁻¹) as the supporting electrolyte; $I = 0.1$ A, a nickel cathode, 20 °C.^b The yields are given with respect to the carbonyl compound; ^c $\text{NiBr}_2(\text{bipy})$, 7 mmol; ^d inox is a stainless steel anode; ^e the yield is given with respect to ArCl (ArCl , 7.5 mmol, PhCHO, 30 mmol).

electron-donating groups in the ring, aliphatic aldehydes and cyclohexanone can be involved in these reactions. 2-Bromoaniline and 2-bromoanisole can serve as arylating agents, whereas other isomers cannot perform this function due, apparently, to stability of the arynickel intermediate $\text{ArNi}(\text{I})(\text{bipy})$. The reactions of aryl halides containing substituents at positions 3 and 4 yield predominantly biaryls, whereas the addition at the carbonyl group proceeds to only a small extent. The reaction of benzaldehyde with aryl halide containing the electron-withdrawing methoxycarbonyl group in the ring proceeded in satisfactory yield upon the replacement of Br by Cl. In this case, homocoupling of $\text{ArNi}(\text{I})(\text{bipy})$ with ArX was suppressed but a three- to fourfold excess of the aldehyde was required. The fact that aromatic aldehydes containing electron-withdrawing substituents in the ring, which are favourable for π -bonding, virtually do not enter into the reactions (whereas aliphatic aldehydes can be involved in these reactions) is indicative of the predominant σ -character of the bond between the organonickel complex and the carbonyl group of aldehyde.

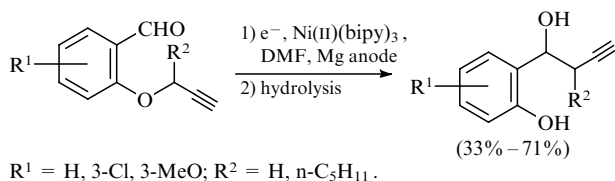
Selective reduction of aryl propargyl ethers to the corresponding phenols in the presence of electrochemically generated nickel complexes proceeds under mild conditions and in good yields. This reaction provides the means of removing the allyl and propargyl protective groups.¹⁶⁷

The carbonyl group in allyl ether of salicylaldehyde was subjected to electrochemical intramolecular allylation [$\text{NiBr}_2(\text{bipy})$, Mg anode, -1.2 V with respect to a saturated calomel electrode] using nickel complexes as the catalyst.¹⁶⁸ It is believed that this process involves electrochemically generated $\text{Ni}(\text{0})$ complexes as active catalytic species capable of reacting with the allyl fragment of the ether to form the π -allyl nickel complex **A**.

The intramolecular transfer of the allyl fragment to the carbonyl group affords intermediate alkoxide, *viz.*, nickel(II) phenoxide **B**. Conceivably, the Ni^{2+} ions in this complex can be replaced by the Mg^{2+} ions to give the intermediate **C**, which is accompanied by liberation of the $\text{Ni}(\text{II})$ complex and completion of the catalytic cycle. Hydrolysis of the alkoxide **C** gives rise to the final product:

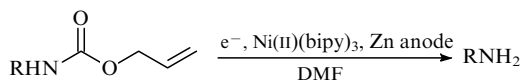


Later on, it was demonstrated¹⁶⁹ that the propargyl fragment in *o*-(propargyloxy)arencarbaldehydes was transferred to the carbonyl group under the action of electrochemically generated nickel complexes to produce homopropargyl alcohols.



It was believed that the C–O bond in propargyl ether was initially cleaved followed by the addition of the propargyl fragment to the carbonyl group. The reactions of ring-unsubstituted propargyl ethers afforded allene isomers as by-products.

Electrochemical reductive deprotection of the amino group in allylcarbamates containing several functional substituents in the presence of catalytic amounts of the Ni(II)(bipy)₃ complex proceeded selectively to give the corresponding amines in 40%–99% yields.¹⁷⁰



$R = \text{Ph, 4-MeO}_2\text{CC}_6\text{H}_4, 4\text{-NCC}_6\text{H}_4, 2\text{-MeCOC}_6\text{H}_4, \text{Bn, cyclo-C}_6\text{H}_{13}, (\text{MeO})_2\text{CHCH}_2.$

The reactions proceed under mild conditions (20 °C) in an undivided cell with a sacrificial zinc anode. The allyl groups in arylcarbamates are selectively removed in 70%–99% yields. Under these conditions, the ether, ketone, acetal and nitrile groups remain intact.

VII. Electrocatalytic reduction of carbon dioxide

The data on electrocatalytic reduction of nitrogen and its oxides, carbon oxides and small molecules containing triple bonds (acetylene, cyanides) were surveyed in the reviews.^{13, 171} All these substrates are electrochemically inactive and contain very strong bonds, which are rather difficult to cleave. Hence, activation of these molecules by inserting them into the coordination sphere of metal followed by (or preceded by) the electrochemical electron transfer is the most promising way for subjecting poorly reactive molecules to various chemical transformations. Besides, electrocatalytic procedures involving metal complexes attract considerable attention because they allow the use of vast biosphere reserves of N₂, CO₂ and O₂ as cheap and accessible starting materials in various chemical processes.

Direct reduction of CO₂ at a metal cathode, for example, at a mercury cathode, requires a high overpotential ($E_{\text{CO}_2/\text{CO}_2^{\cdot-}} = -2.21$ V with respect to a saturated calomel electrode, DMF). Other metal cathodes, for example, copper or gold cathodes, can reduce CO₂ in aqueous solutions at somewhat lower cathodic potentials (from –1.3 to 1.7 V). However, even these values are too high for practical applications because water is reduced at these potentials with hydrogen elimination. In principle, it is possible to use non-aqueous solvents, but these processes require larger energy consumption and are often accompanied by side reactions.

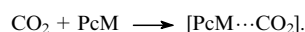
The use of various metal complexes as catalysts has the most promise for selective electroreduction of CO₂. Generally, these processes are carried out using complexes with nitrogen-containing macrocyclic ligands, *viz.*, porphyrins and their analogues, which are well known as biocatalysts.¹⁷² Compared to natural catalysts, artificially synthesised metal complexes with nitrogen-containing macrocyclic ligands (for example, with phthalocyanines) possess even more extended π -conjugated chains, whereas their catalytic activity is highly competitive with that of natural analogues. Metal complexes with phthalocyanines,^{173–185} Co(II)

complexes with porphyrins,⁹⁰ Ni(II) complexes with cyclam,^{186–191} bis- and polypyridyl complexes of Rh(II),¹⁹² Re(I),¹⁹³ Cu(II),¹⁹⁴ Co(II), Fe(II) and Ni(II),^{195–199} iron and cobalt complexes with 4,5-dihydroxybenzo-1,3-disulfonate and 2-hydroxy-1-nitrosonaphthalene-3,6-disulfonate^{200, 201} ligands proved to be catalysts of CO₂ reduction. Most of the above-mentioned complexes act as efficient catalysts of CO₂ reduction only in non-aqueous media because CO₂ reduction in water is preceded by proton reduction. Only the cobalt complex with phthalocyanine (PcCo)^{173, 174, 176–181, 201, 202} and the nickel complex with cyclam^{185, 195, 203, 204} proved to be efficient electrocatalysts of CO₂ reduction in water or aqueous acetonitrile, the latter being active only at a mercury cathode at which the overpotential of hydrogen elimination is higher than that at a platinum cathode. It was suggested^{186, 187} that higher selectivity of electroreduction of CO₂ compared to that of H₂O observed in these processes is associated with the larger size of the macrocyclic ligand and the presence of the NH groups in Ni(cyclam).

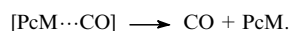
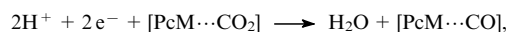
A considerable advantage of metal complexes as catalysts is the possibility of changing their reactivities by modifying the macrocyclic ligand with electron-donating or electron-withdrawing substituents. Thus the nickel(II) complex with a cyclam analogue containing two methyl groups in the macrocycle (3,10-dimethyl-1,3,5,8,10,12-hexaazacyclodecane) exhibits much higher catalytic activity than the nickel(II) complex with unsubstituted cyclam.²⁰⁵ It should be noted that the insertion of σ -acceptor substituents (for example, of fluorine) into the nitrogen-containing ring also leads to improvement in the catalytic activity and selectivity of CO formation (compared to hydrogen elimination). In these cases, the Ni(II) complex with 3,3,10,10-tetrafluorocyclam proved to be most efficient. The further increase in the number of the fluorine atoms in the macrocycle leads to deterioration of activity.²⁰⁶

Metalloporphyrins can also exhibit catalytic activity in reduction of CO₂ to CO in aqueous and non-aqueous media.²⁰⁷ However, porphyrins are rapidly consumed in the course of electrolysis and the catalysis ceases after a rather small number of catalytic cycles. Catalysts are poisoned due to carboxylation and hydrogenation of porphyrins (see Ref. 208).†

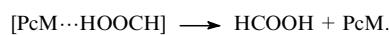
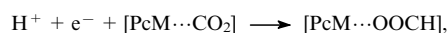
Mechanisms for formation of different products of CO₂ reduction catalysed by metallophthalocyanines have been proposed.^{173, 174}



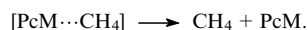
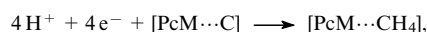
The formation of carbon monoxide



The formation of formic acid



The formation of methane

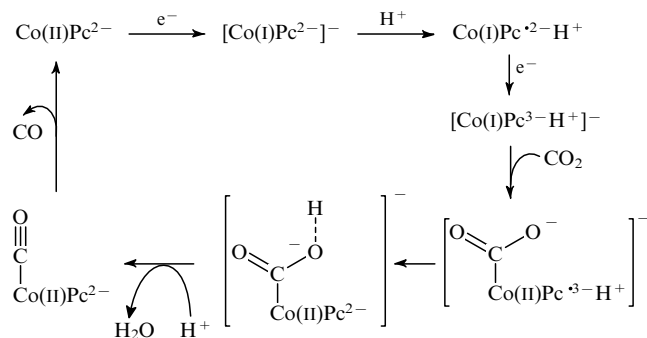


† Undesirable cathodic processes can be prevented performing gas-phase reactions of CO₂ with electroactive films at solid electrolytes.²⁰⁹ In many cases, heterogeneous catalytic reduction of CO₂ was carried out with the use of an active catalyst, for example, metalloporphyrin or metallophthalocyanine, deposited on a solid electrolyte (graphite) and coated with a conducting film (Nafion), which prevents it from passing into solution.^{173, 174, 176–181, 210} However, these systems are beyond the scope of the present review.

It should be noted that the formation of the metal–CO₂ complex was postulated as the key step in virtually all studies devoted to catalytic binding of CO₂ by transition metal complexes.²¹¹ In most cases, this suggestion was supported only by indirect evidence obtained in IR and NMR spectroscopic studies because, first, the lifetime of these intermediates is short and, second, the presence of the solvent molecules, which are also capable of being coordinated, hinders the detailed analysis of the structure of the complex.

The reaction mechanism was investigated also with the use of semiempirical quantum-chemical calculations. For example, an attempt was made to relate the catalytic activity of phthalocyanines to the energy of the frontier orbitals of the complex.²¹¹ It appeared that the catalytic activity of phthalocyanine complexes correlates with the ability of the metal atom to coordinate an additional ligand, which, in turn, depends on the difference between the energy of the *d* orbitals of the metal atom and the energy of the frontier orbitals of the coordinated ligand.

Electrocatalytic reduction of CO₂ was examined in aqueous solutions at a graphite electrode, which was coated with PcCo bound to poly-4-vinylpyridine as a donor axial ligand.^{179, 183, 184} It was demonstrated that the presence of the latter leads to a substantial improvement in the catalytic activity of PcCo due, apparently, to a rise in the electron density on the metal atom. In this catalytic system, the selectivity of CO₂ reduction is much higher than that in the case of pure PcCo in spite of the fact that competitive water reduction persists. This is attributable to an increase in the local concentration of CO₂ in the near-membrane layer through hydrophobic interactions of CO₂ with polyvinylpyridine.¹⁷⁷ The reaction scheme was proposed.^{183, 184}



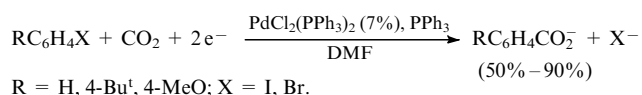
The catalytic process starts only at the second reduction wave of PcCo because the first reduction step is followed by rapid addition of H⁺ to the peripheral nitrogen atoms of the phthalocyanine ring and the active species capable of reducing both H⁺ and CO₂ to form H₂O and CO, respectively, are generated only at the second wave. However, no direct evidence for the formation of the PcCo–CO₂ adduct was obtained.

VIII. Synthesis of carboxylic acids

1. Carboxylation of organic halides

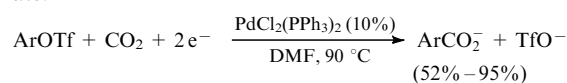
In the early 1980s, it was demonstrated that electroreduction of aryl halides catalysed by nickel complexes with PPh₃ (see Ref. 212) or dppe²¹³ in the presence of CO₂ affords predominantly arenecarboxylates rather than biaryls. Based on the results of electroanalytical investigation of the [Ni]–dppe system, the catalytic cycle was proposed.^{214, 215}

The Pd complex with PPh₃ also catalyses electrocarboxylation of aryl iodides and bromides.²¹⁶



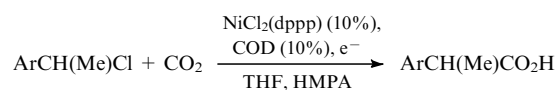
In this reaction, CO₂ was assumed to react as an electrophile with [ArPd(0)(PPh₃)₂][–] generated upon reduction of the aryl-

palladium(II) σ-complex.²¹⁷ Aryl chlorides react with Pd(0) too slowly to ensure efficient carboxylation. Aryl triflate and aryl bromide possess higher reactivities and, hence, arylcarboxylic acids can be synthesised starting from the corresponding aryl triflate.^{57, 58}



Ar = 4-RC₆H₄ (R = Cl, CF₃, CO₂Et, F, Me), 1- or 2-naphthyl.

Nonsteroid anti-inflammatory drugs, *viz.*, α-arylpropionic acids, were prepared from the corresponding benzyl chlorides and CO₂ in the presence of the Ni–dppe or Ni–dppp system [dppp is 1,3-(diphenylphosphino)propane] and cyclooctadiene (COD).²¹⁸ There is no need to use a catalyst in these reactions, but it suppresses homocoupling, which becomes the main reaction at high concentrations of benzyl chloride and lower CO₂ pressure.²¹⁹



HMPA is hexamethylphosphoramide.

Product	Name	Yield (%)
PhCH(Me)CO ₂ H		89
	naproxen	81
	ibuprofen	80
	phenopropfen	76

There is also no need to use a catalyst in electrocarboxylation of aryl halides or various benzyl compounds in an undivided cell in the presence of a sacrificial aluminium²²⁰ or magnesium^{21, 221} anode. Organic halides containing functional groups, which make it impossible to apply direct electrochemical reduction, are subjected to electrocarboxylation using a catalyst simultaneously with a sacrificial anode.

Interest in transition metal complexes with tetraazamacrocyclic ligands as applied to electrocatalysis is associated with the fact that these complexes are similar to natural photosynthetic systems.²²² The mechanism of CO₂ reduction catalysed by tetraazamacrocyclic complexes of Ni(II) and Co(II) was examined by cyclic voltammetry and preparative electrolysis. Reduction affords CO, which then reacts with a Ni(I) complex to form Ni(0) carbonyl compounds, which eventually poison the catalyst.²²²

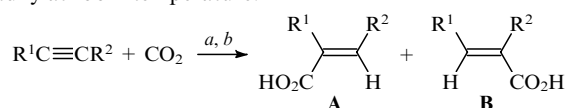
Electrocatalytic reduction of CO₂ under the action of trinuclear nickel cluster radicals was investigated by electrochemical methods and spectroelectrochemistry.²²³

2. Carboxylation of alkenes and alkynes

It is possible to subject unsaturated compounds to direct electrochemical carboxylation.^{18, 224} However, this procedure is of limited usefulness because only arylated or activated alkenes can be used as substrates. For alkynes, only a few examples of the successful application of this reaction have been reported.^{225–229}

Indirect electrochemical reductive coupling of alkynes with CO₂ gives rise to substituted acrylic acids through hydroxycarboxylation.^{60, 225–231} Electrolysis was carried out at 20–80 °C in an undivided cell in DMF containing a catalytic amount of a nickel complex in the presence of a sacrificial magnesium anode at

ambient or slightly elevated (5 atm) CO₂ pressure. Alkynes containing electron-donating groups are more readily subjected to carboxylation at elevated temperatures, whereas carboxylation of alkynes bearing electron-withdrawing groups proceeds more readily at room temperature.



(a) Ni(bipy)₃(BF₄)₂ (10%), e⁻, DMF, Mg anode; (b) hydrolysis.

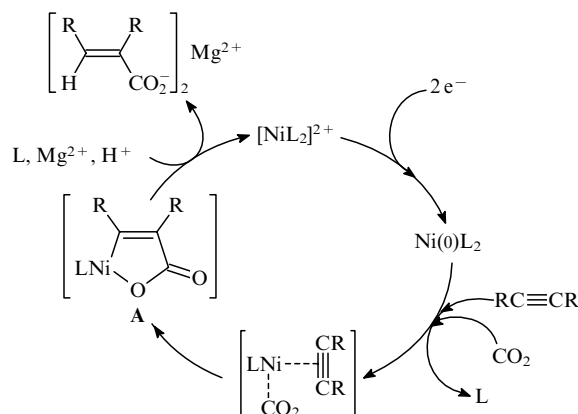
R ¹	R ²	Yield (%)	Ratio A : B
n-C ₆ H ₁₃	H	65	90 : 10
Pr ⁿ	Pr ⁿ	93	
Ph	H	55	71 : 29
Ph	Me	72	38 : 62
Ph	CO ₂ Et	75 ^a	

^a The ratio between the di- and monocarboxylation products was 74 : 26.

The reactions proceed predominantly as the *cis*-addition with good regioselectivity (in the case of terminal alkynes, CO₂ reacts at position 2). Monocarboxylation takes place only in the absence of electron-withdrawing groups.

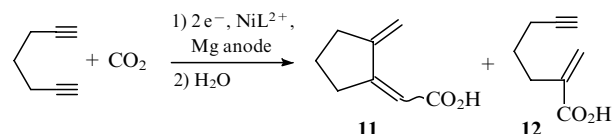
This procedure has advantages over the chemical method devised by Hoberg *et al.*,^{232, 233} which, for the most part, required stoichiometric amounts of air-sensitive Ni(0)(COD)₂; instead, readily accessible Ni(II) complexes are used in the electrochemical procedure.

In these reactions, the advantages of a sacrificial anode are evident, a magnesium anode being most suitable. Oxidation of the latter gives rise to Mg²⁺ ions, which can be involved in the catalytic cycle to decompose nickelacycle **A** thus liberating Ni for further transformations.



The formation of the nickelacycle **A**, which was established by cyclic voltammetry, confirms the proposed mechanism. In the absence of Mg²⁺ ions (the reactions were carried out in a divided cell in the presence of ammonium ions), the nickelacycle was not decomposed and the reaction was terminated once the starting nickel compound has been completely consumed. After the addition of MgBr₂ to a solution of the nickelacycle prepared electrochemically, Ni(II) was regenerated.²³⁴

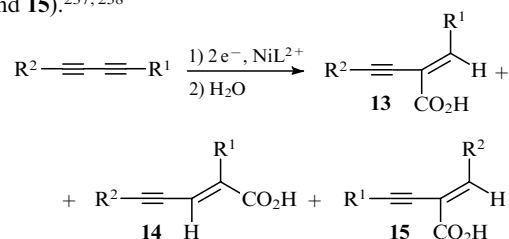
Diacetylenes are used for the construction of polycyclic compounds. Thus bicyclic pyrones were prepared by electrochemical carboxylation in the presence of CO₂ and a stoichiometric amount of a Ni(0) complex.²³⁵ This procedure was also applied to the synthesis of linear and cyclic monocarboxylic acids from nonconjugated diacetylenes.^{236, 237} The composition of the reaction products depends on the nature of the ligand. Thus cyclic compounds **11** were prepared with the use of a nickel complex with bipyridyl at normal CO₂ pressure, whereas linear adducts **12** were obtained with the use of pentamethyldiethylenetriamine (PMDTA) as the ligand and elevated CO₂ pressure (5 atm).



L	Yield (%)	Ratio 11 : 12
bipy	35	59 : 4.5
PMDTA	30	9 : 45

The addition of CO₂ to diacetylenes containing both the terminal and internal triple bonds proceeds predominantly at position 2.

Electrochemical carboxylation of 1,3-diacetylenes in the presence of Ni(PMDTA) as the catalyst proceeded regio- and stereoselectively to give predominantly (*E*)-2-alkylidenealk-3-ynoic acids **13** (sometimes, with an impurity of isomeric products **14** and **15**).^{237, 238}

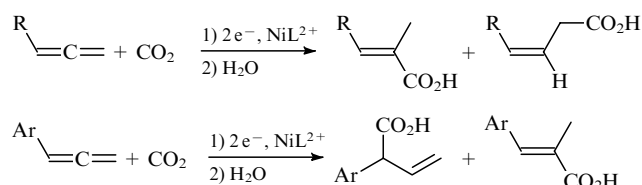


L = PMDTA.

R ¹	R ²	Yield (%)		
		13	14	15
n-C ₅ H ₁₁	n-C ₅ H ₁₁	58	25	—
Ph	Ph	40	0	—
MeOCH ₂	MeOCH ₂	60	1	—
Ph	Bu ⁿ	37	16	3
MeOCH ₂	Ph	50	0	11

In this process, double bonds proved to be less reactive than triple bonds.²³⁹ In nonconjugated as well as in conjugated alkenynes, only the triple bond is carboxylated with regio- and stereoselectivity analogous to those observed for acetylenes.²⁴⁰

According to this procedure, monocarboxylic acids were prepared in good yields starting from 1,2-dienes.²⁴¹ In the case of alkyl- and cycloalkallenes, the addition of CO₂ proceeds predominantly at the C(2) atom. In the case of arylallenes, the addition occurs predominantly at the C(3) atom.



R = n-C₈H₁₇, cyclo-C₆H₁₁; Ar = Ph, 4-MeOC₆H₄;

L = PMDTA; p_{CO₂} = 5 atm.

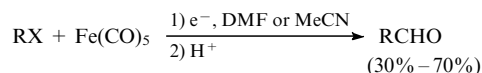
Some other examples of homogeneous electrochemical activation of CO₂ were also described among which are the synthesis of lactones by telomerisation of butadiene and CO₂,²⁴² synthesis of bicyclic lactones using nickel or cobalt complexes,²⁴³ trans-carboxylation²⁴⁴ and insertion of CO₂ into epoxides catalysed by Ni(cyclam)Br₂.²⁴⁵

IX. Carbonylation of organic substrates

Carbonylation of organic substrates is still a complicated problem because the presence of CO leads to deactivation of the catalytic system. The reactions of carbon monoxide with transition metals

in low oxidation states afford different metal carbonyls, which exhibit low reactivity with respect to the carbon–halogen bonds because of strong coordination with CO.

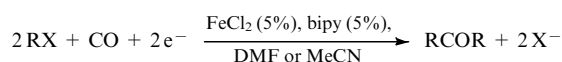
Some metal carbonyls can be activated by electrochemical reduction with generation of active anionic species. For example, aldehydes can be synthesised by electrolysis of a stoichiometric mixture of alkyl halides and iron pentacarbonyl.^{246, 247}



R = n-C₅H₁₁, Et, Bn; X = I, Br.

Carbon dioxide can be used as a CO source. It is well known that complexes of transition metals in low oxidation states catalyse chemical and electrochemical reduction of CO₂ to CO. This approach was applied to the generation of the mixed Ni(0)bipy(CO)₂ complex by electrochemical reduction of Ni(bipy)²⁺ in *N*-methylpyrrolidone or DMF in the presence of CO₂.^{248, 249} The resulting complex can react with alkyl, benzyl and allyl halides to form symmetrical ketones with regeneration of Ni(bipy)²⁺. The proposed two-step procedure for the synthesis of ketones involves electroreduction and chemical coupling.

It was demonstrated²⁵⁰ that carbonylation can also be carried out by electrolysis of a solution of organic halide containing a catalytic amount of bipy under an atmosphere of CO in an undivided cell with a stainless steel anode. This process produces symmetrical ketones in good yields.

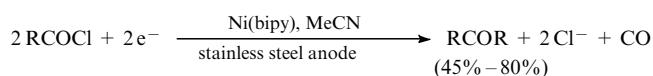


RX	Yield (%)
BnCl	80
2-MeC ₆ H ₄ CH ₂ Br	70
4-MeC ₆ H ₄ CH ₂ Br	62
2-ClC ₆ H ₄ CH ₂ Cl	75
MeCH=CHCH ₂ Cl	65
Me(CH ₂) ₅ Br	62
4-CF ₃ C ₆ H ₄ Br	50

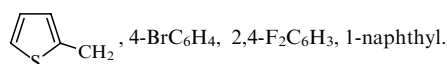
The anodic reactions afford the Ni(II)(bipy) and Fe(II)(bipy) complexes, which are reduced at a cathode to give intermediates catalysing the synthesis of ketones. In these processes, complexes of nickel coordinated both by bipy and CO serve as reactive species. Iron complexes, apparently, exhibit a synergistic effect.

Ketones were successfully prepared by electroreductive coupling of organic halides with CO using the Ni(bipy)²⁺ complex as the catalyst. Either CO entering the solution^{250–252} or metal carbonyls²⁵³ serve as a source of carbonyl groups. Electroreduction of CO₂ proceeded under the action not only of Ni(0)(bipy)^{248, 249} but also of iron porphyrinates in the presence of anodically generated Mg²⁺ ions.²⁵⁴

Ketones can be prepared not only by electrochemical carbonylation of organic halides but also by some other reactions catalysed by nickel complexes. Thus unsymmetrical ketones were obtained by NiBr₂(bipy)-catalysed electroreductive coupling of acyl chlorides with alkyl halides.²⁵⁵ Acid chlorides are transformed into symmetrical ketones in an undivided cell equipped with a nickel or stainless steel anode.



R = Bn, Ph, 3-FC₆H₄, 3-MeC₆H₄, 4-MeC₆H₄, 4-FC₆H₄,



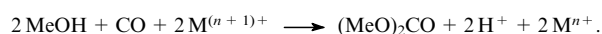
It is believed that the first reaction step gives rise to alkynyl-nickel intermediates through oxidative addition of acid chloride to an electrochemically generated unstable low-valent nickel com-

plex. Regeneration of divalent Ni yields a bisacylnickel complex. Ketone is derived from the bisacylnickel complex by reductive elimination of Ni bound with one CO molecule.²⁵⁶

In the presence of the Ni(bipy) complex, arylzinc compounds, which are electrochemically generated from aryl halides and zinc salts, react with (CF₃CO)₂O to give the corresponding aryl trifluoromethyl ketones.⁷⁹

The reactions involving the electroreductive formation of the carbon–heteroatom bond under the conditions of transition metal catalysis are few in number. For example, mention may be made of electrochemical silylation of allyl acetates in the presence of the Pd–PPh₃ system²⁵⁷ and the electrochemical synthesis of aryl thioethers from thiophenol and aryl halides.²⁵⁸

Based on electrochemical activation of salts and complexes of some transition metals, catalytic systems were designed for carbonylation of methanol to form dimethyl carbonate.²⁵⁹ The reactions are carried out by passing CO through a methanolic suspension or through a solution of a complex under atmospheric pressure at 20 °C in an ion-exchange membrane cell. Metal complexes catalyse oxidative carbonylation of methanol.



The anodic process leads to regeneration of metal in a higher oxidation state.



The redox pairs, which are active in chemical carbonylation promoted by oxygen, viz., Cu(I)/Cu(II), Pd(0)/Pd(II) and Co(II)/Co(III), were tested as catalysts. However, the electrochemical conditions appeared to be milder than those used in conventional chemical reactions. In some cases, the complexes exhibited higher catalytic activity. In these complexes, bipy, salen, acac and PPh₃ were used as ligands. The highest faradaic yields (%) of dimethyl carbonate were achieved with the complexes CuCl(bipy) (84.8), PdCl₂(bipy) (64.0), CoCl₂ (26.0), RhCl₃ (25.0) and AgBF₄(bipy) (10.2). The VCl₃, Mn(salen), Mn(acac)₂, ReCl₃(bipy), Cr(acac)₃, NiCl₂(bipy) and RuCl₂(PPh₃)₂ compounds proved to be either poorly reactive or inactive at all. Only in the presence of the PdCl₂(bipy) complex, did more than one redox cycles occur.

It is known that many transition metals catalyse oxidation of CO to CO₂ in water. It is these transition metals that exhibit the highest activity in oxidative carbonylation of alcohols to form dialkyl carbonates. This reaction mechanism involves the formation of methoxycarbonylmethyl intermediates (MCO₂Me, where M = Cu, Co or Pd) whose stability and reactivity depends substantially on the structure of the complex and the nature of the ligands.^{260, 261} For example, CuCl exhibits activity only at 70 °C, whereas it is active even at 20 °C in the presence of bipy. Electroactivation of CuCl, PdCl₂, PtCl₂ and AgBF₄ occurs only in the presence of bipy. To the contrary, the addition of bipy as well as of acac, salen and PPh₃ to CoCl₂, NiCl₂ and AuCl₃ impairs the efficiency of the process.

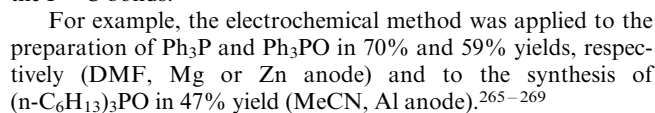
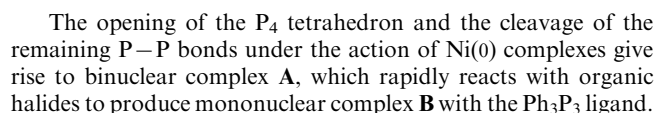
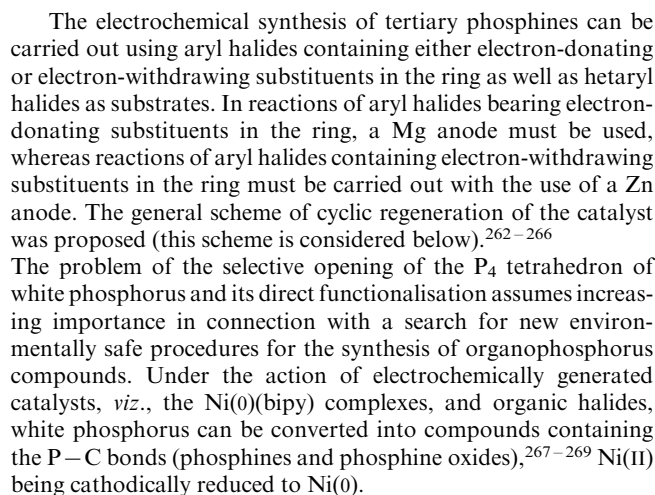
X. Electrochemical synthesis of organophosphorus compounds from chlorophosphines or white phosphorus

The development of synthetic approaches to the preparation of compounds containing P–C bonds based on white phosphorus or phosphorus chlorides is of importance in the preparative chemistry of organophosphorus compounds. Considerable attention is given to the synthesis of tertiary phosphines, which are widely used in organometallic and coordination chemistry.

The promising process^{262–266} for the preparation of tertiary phosphines is based on electrochemical coupling of mono- or dichlorophosphines with aromatic and heteroaromatic halides catalysed by the nickel complex with bipy in an undivided cell using a sacrificial magnesium or zinc anode (Table 11).

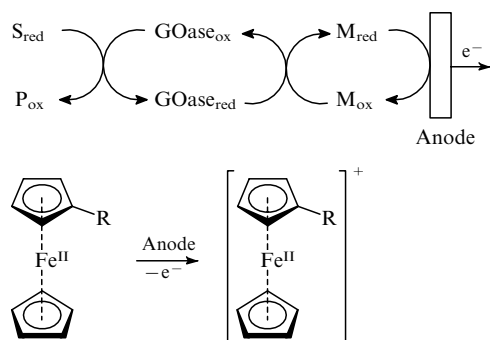
ArX	Product	Yield (%) ^a	Anode
PhBr	Ph ₃ P	87	Mg
2-BrC ₆ H ₄ Me	Ph ₂ PC ₆ H ₄ Me-2	54	Mg
4-BrC ₆ H ₄ Me	Ph ₂ PC ₆ H ₄ Me-4	56	Mg
4-MeOC ₆ H ₄ Br	Ph ₂ PC ₆ H ₄ Me-4	52	Mg
4-Me ₂ NC ₆ H ₄ Br	Ph ₂ PC ₆ H ₄ NMe ₂ -4	70	Mg
4-EtO ₂ CC ₆ H ₄ Br	Ph ₂ PC ₆ H ₄ CO ₂ Et-4	63	Zn
3-EtO ₂ CC ₆ H ₄ Br	Ph ₂ PC ₆ H ₄ CO ₂ Et-3	66	Zn
2-ClC ₅ H ₄ N	Ph ₂ PC ₅ H ₄ N-2	80	Mg
3-ClC ₅ H ₄ N	Ph ₂ PC ₅ H ₄ N-3	63	Mg
2-ClC ₄ H ₃ S	Ph ₂ PC ₄ H ₃ S-2	65	Mg
2-Cl-6-MeOC ₅ H ₃ N	Ph ₂ P(6-MeO-2-C ₅ H ₃ N)	66	Mg
2-ClC ₄ H ₃ N ₂	Ph ₂ PC ₄ H ₃ N ₂ -2	50	Mg
3-NCC ₆ H ₄ Br	Ph ₂ PC ₆ H ₄ CN-3	45	Zn
5-Cl-1,3-Me ₂ C ₃ HN ₂	Ph ₂ P(5-C ₃ HN ₂ -1,3-Me ₂)	25	Mg

^a The preparative yield is given with respect to chlorophosphine.



In recent years, the principles of indirect anaerobic electrochemical regeneration of galactose oxidase (GOase) were developed.²⁷¹ This enzyme oxidises the primary alcohol group of D-galactose to the corresponding aldehyde. The synthetic use of GOase is of interest because it is highly sensitive to the nature of the substrate and can perform selective oxidation of primary hydroxy groups in polyols. Thus xylitol is oxidised to L-xylose. Substituted ferrocenes exhibiting high catalytic activity were used as mediators. The iron(II) and ruthenium(II) complexes with the phenanthroline ligands appeared to be less efficient. For these processes, phosphate buffers with pH 10.8 are the media of choice. Electrochemical regeneration of GOase allows the pre-

vention of the undesirable formation of the enzyme inhibitor (hydrogen peroxide), which is generated under aerobic conditions in reactions involving GOase.



S is a substrate, P is a product, M is a mediator (ferrocene derivative).

XII. Characteristic features and mechanisms of reactions catalysed by nickel and palladium complexes

1. Kinetic regularities

The application of electrochemical methods to generation of complexes of Ni(0) and other metals in low oxidation states makes it possible to use catalytic amounts of complexes generated at an electrode. In addition, electrochemical methods allow one to obtain quantitative estimations of the rates of catalytic reactions and in some cases even to separate the overall process into individual steps and to evaluate the reactivities of intermediates and stability of different forms of metal complexes.

Based on the external morphological traits,^{24, 33, 272–274} in the $Ni(II)L_n-Ni(0)L_n$ system ($L = PPh_3$ or bipy) (Fig. 1). These are an increase in the current of reduction of the starting $Ni(II)L_n$ complex (see Fig. 1 a), the wave corresponding to reduction of the complex involving the substrate as the ligand (see Fig. 1 b) and the wave of catalytic reduction of the organometallic compound, which is a product of the reaction of the reduced form of the starting complex with the substrate (see Fig. 1 c). In all these cases, the observed pattern can be (with some reservations) considered as a classical pattern and, hence, the increase in the current (the ratio of the catalytic to diffusion current, i_c/i_d) can be used for calculating the rate constant of catalyst regeneration (k_{eff}), which describes the overall process.³³

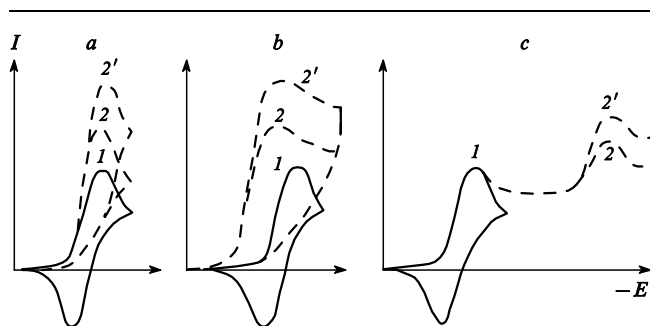
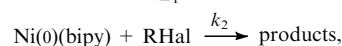
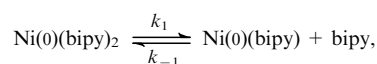


Figure 1. Morphology of catalytic waves in the $Ni(II)L_n-Ni(0)L_n$ system;²⁴

(a) an increase in the current of reduction of the starting complex; (b) the wave corresponding to reduction of the complex with the substrate, (c) the wave of catalytic reduction of the organometallic compounds; (1) the $Ni(II)L$ complex, (2) and (2') the $Ni(II)L$ complex in the presence of increasing amounts of organic halides.



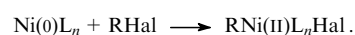
$$k_{eff} = \frac{k_1 k_2}{k_{-1}} \cdot \frac{[RHal]}{[bipy]}.$$

The lower the donor number of the solvent, the higher the efficiency of the catalytic process.³³

The nickel complex with bipy proved to be the most active and versatile catalyst, which exhibits a pronounced catalytic effect in reactions with various substrates containing the C–Hal, P–Cl or Si–Cl bonds.^{24, 33}

2. Relationship between electrochemical redox properties of nickel complexes and their reactivities in dehalogenation

The redox potentials of the complexes were used as the starting characteristics for predicting the reactivities and the reaction mechanisms of organometallic compounds.^{24, 26, 32, 33, 275} For a series of $Ni(II)$ and $Ni(0)$ complexes, the electrochemical gap $G = E_{ox} - E_{red}$, the electrochemical electronegativity $\chi = (E_{ox} + E_{red})/2$ and the degree of charge transfer $\Delta N = \Delta\chi/\Sigma G$ were estimated experimentally.^{24, 26, 32, 33} The G , χ and ΔN parameters can be used for evaluating the reactivities of the complexes in oxidative addition to organic halides.



These parameters are also suitable for estimating interactions between the complex and various ligands and substrates and for obtaining information on the complex-forming properties and donor-acceptor complex–substrate interactions. This is of particular importance in the case of organophosphorus substrates exhibiting both σ -donor and π -acceptor properties in interactions with transition metals. The largest electrochemical gap characterising the degree of ‘hardness’ of the complex was found for $Ni(II)Br_2$.^{24, 25, 32, 33} For phosphine and phosphite complexes of $Ni(II)$, the G values are much smaller. On the contrary, the electrochemical gap increases and, consequently, the donating ability and polarisability decrease in the series of the $Ni(0)$ complexes with bipy (0.60 V), phen (0.72 V) and Ph_3P (1.04 V). Based on these characteristics, the degrees of charge transfer between the complexes and substrates were calculated on the assumption that the $Ni(II)$ or $Ni(0)$ complex and the substrate act as an electron donor and an electron acceptor, respectively.^{24, 25, 32, 33} In the case of $Ni(II)$ complexes, the degrees of charge transfer are small, whereas these values are an order of magnitude higher in the case of $Ni(0)$ complexes. In the latter case, oxidative addition reactions are assumed to proceed. The sign of the degree of charge transfer indicates that the $Ni(0)$ complexes with all substrates exhibit pronounced donor properties ($\Delta N \gg 0$).

The reactivities of nickel complexes in catalytic processes were accounted for based on the data from voltammetric measurements, results of quantum-chemical calculations and estimations of the G , χ and ΔN values.^{24, 25, 32, 33} The reactivities of $Ni(0)$ complexes in reduction reactions of organic halides are determined by a number of factors among which are the electrochemical gap G , the degree of charge transfer ΔN , the strength of the Ni–P bond, the electronic and steric effects of the ligands and the occurrence of the subsequent redox processes. In the series of the $Ni(0)L$, $Ni(0)L^-$, L^- mediators ($L = bipy$ or phen) possessing reducing properties, the energy of stabilisation of the transition state decreases on going from the inner-sphere to outer-sphere reduction processes, which is accompanied by the corresponding decrease in the reaction rate, as compared to the inner-sphere mediator characterised by the same driving force for the process.³⁰

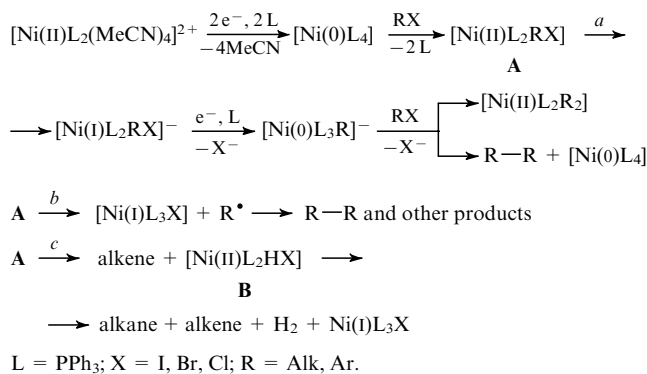
In the studies,^{26, 276–278} the mechanism of two-electron reduction of the complexes was proposed with consideration for competitive homogeneous redox reactions, the evidence for the

An analogous electrocatalytic cycle was suggested for the synthesis of hexa-1,5-diene from allyl bromide in the presence of nickel complexes with 2,2'-bipyridyl²⁹⁸ as well as from allyl

chloride under the action of the electrochemically generated cobalt complex with 2,2'-bipyridyl.³⁰⁵ However, the numbers of the catalytic cycles in these processes were rather low due to rapid decomposition of the catalyst.

Shiavon *et al.*⁴⁸ made an attempt to generalise the notions of the reaction mechanisms of organic halides under the conditions of homogenous catalysis by Ni(0) complexes with phosphine ligands. In this case, the efficient electrochemical process occurs through a lowering of the activation energy of RX reduction and cyclic regeneration of the catalyst. At less negative potentials ($|E_{RX}| > |E_{Ni(II)L}|$), a lowering of the activation energy and RX reduction lead to a change in the reaction pathway compared to that observed in non-catalytic conditions because heterogeneous reduction of RX proceeds at substantial overpotentials and high cathodic potentials. As a consequence, the radical generated upon the transfer of the first electron is reduced to the carbanion and the corresponding hydrocarbon RH and does not give coupling products.

In all cases, reduction can proceed *via* a series of simple steps involving electrochemical reduction of the nickel(II) complex to Ni(0), activation of organic halide through its oxidative addition to the Ni(0) complex and reductive elimination with the cleavage of the metal–carbon bond (either thermal decomposition or further cathodic reduction) as the key steps.⁴⁸



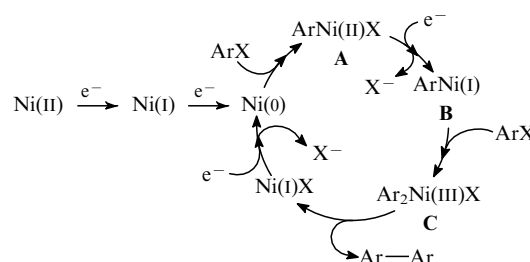
It should be noted that intermediates of the catalytic cycles were neither detected nor isolated.⁴⁸

The path *a* is realised if the σ -organonickel complex **A** is rather stable, as in the case of PhBr and BnCl at low temperature. For the catalytic process involving these halides to occur, the complexes **A** must be reduced. Later on, it was shown^{87, 301, 302, 306} that a Ni(0) complex serves as a reducing agent and the catalytic process takes place at $E_{Ni(II)/Ni(0)}$. The path *b* is typical of neopentyl bromide and benzyl iodide at 25 °C, the coupling product being formed *via* dimerisation of the radicals generated upon the homolytic cleavage of the nickel–carbon bond in the complex **A**. The reaction with butyl bromide follows the path *c*. In the latter case, thermal decomposition of an organonickel intermediate occurs through β -elimination involving the nickel hydride complex **B** as an intermediate. For homocoupling to proceed, the reaction must take the path *a*, which is realised at more negative working potentials, the composition of the products being determined by the ratio between the paths *a* and *c*.

Oxidative addition of organic halide to the Ni(0) complex is the rate-limiting step. An increase in catalytic current allows the comparison of the reaction rates for various halogen-containing derivatives. The reactivity was found to decrease in the series $Bu^tI > Bu^tCH_2I > BnCl > PhBr$ in parallel with the change in dipole moment.

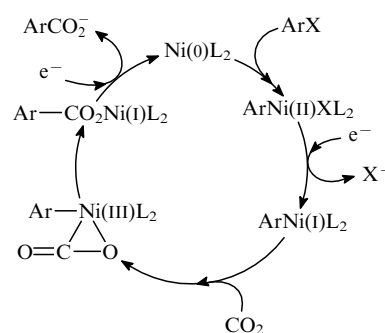
Electroanalytical methods provide information on the reaction mechanisms of coupling of aryl halides. In the general case, a zero-valent nickel or palladium complex is formed at a cathode if PPh_3 , dppe or bipy serve as ligands. The first step of the catalytic cycle involves oxidative addition of aryl halide to a Ni(0) or Pd(0) complex giving rise to a σ -arylnickel or σ -arylpalladium inter-

mediate. Coordinatively unsaturated complexes of the Ni(0)(bipy),²⁷² Ni(0)(dppe)²⁹² or Pd(0)(PPh₃)₂ type²⁹⁵ proved to be much more reactive than the corresponding coordinatively saturated complexes. The reactivities of the Ni(0) or Pd(0) species depend also on the nature and the concentration of halide ions bound to the starting complex or added to the reaction medium.^{218, 238} The formation of biphenyl from bromobenzene catalysed by Ni(dppe) was examined in detail^{292, 293} and the catalytic cycle for this process was proposed. In this catalytic cycle, the σ -arylnickel intermediate **A** is initially reduced to the corresponding Ni(I) complex **B** followed by the transformation into the diarylnickel(III) complex **C**.



The complex **C** is subjected to reductive elimination to form the corresponding product and the Ni(0) complex from which Ni(0) is generated.^{292, 293} Hence, homocoupling proceeds through intermediate paramagnetic [Ni(I) and Ni(III)] and diamagnetic [Ni(0) and Ni(II)] species. The threshold potential (–2 V with respect to a saturated calomel electrode) was demonstrated to exist, which is necessary for the formation of biphenyl. At a less cathodic potential, the reaction affords the phenylnickel derivative PhNi(II)(dppe)Br, which needs to be reduced for the cyclic process to occur. It should be noted that the scheme proposed based on voltammograms^{292, 293} lacked experimental support because none of the postulated intermediates was isolated or identified. Equations describing the kinetic characteristics of the assumed sequence of the reactions were derived and the rate constants of different steps were calculated. It is believed that reductive elimination is the rate-limiting step.

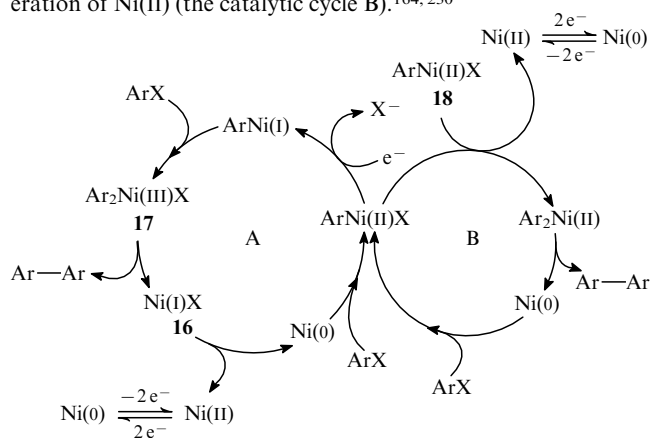
The formation of biphenyl was completely suppressed upon introduction of CO₂ into the reaction system giving rise to a new catalytic cycle to form carboxylation products.



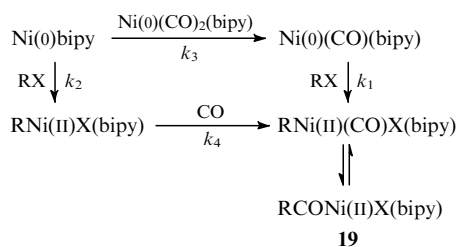
The reaction mechanism was proposed based on the results of an investigation of the reaction products, examination of the voltammetric behaviour of the starting complexes in the presence of the substrate and the behaviour of intermediates and kinetic calculations of individual steps of the process. Since the addition of CO₂ to ArNi(I)L₂ ($k = 1-2 \text{ mol}^{-1} \text{ litre s}^{-1}$) proceeds approximately 100–200 times faster than the addition of ArX, the formation of biaryls in the presence of stoichiometric amounts of CO₂ is completely eliminated.^{215, 294, 307}

By analogy with the reactions catalysed by Ni(dppe), two hypothetical catalytic cycles involving the formation of a σ -arylnickel intermediate were proposed for the reactions in the presence of the Ni(bipy) complex. In the catalytic cycle A, the Ni(I)X

complex (**16**), which is derived from the Ni(III) complex (**17**) in the reductive elimination step, undergoes disproportionation into Ni(0) and Ni(II) followed by reduction of Ni(II).³⁰⁵ An alternative mechanism assumes the formation of biaryl in the course of metathesis of σ -arylnickel(II) complex **18** accompanied by regeneration of Ni(II) (the catalytic cycle B).^{164, 230}



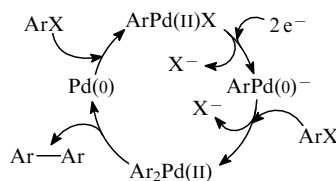
The reactivity of the nickel(0) complex with bipy with respect to carbon monoxide and organic halides under conditions of competitive reactions was examined by electroanalytical methods, which enabled the authors to devise a new procedure for the synthesis of ketones.^{251, 252} Reduction of Ni(bipy)²⁺ in the presence of an excess of CO rapidly afforded the inactive Ni(0)(CO)₂(bipy) complex. It was noted that RX remained intact when electrolysis was carried out with bubbling of CO through the reaction mixture, *i.e.*, when the solution was saturated with CO. Organic halides were efficiently converted into ketones when the concentration of CO was limited and the possibility existed of generating a mixture of Ni(0)(CO)₂(bipy) and Ni(0)(bipy). Based on the kinetic data, two alternative pathways for the formation of acylnickel complex **19** were proposed.



The first pathway involves oxidative addition of RX to Ni(0)(CO)(bipy) (the rate constant k_1), whereas the second pathway includes oxidative addition of RX to Ni(0)(bipy) (the rate constant k_2) followed by addition of CO from the mixed complexes Ni(0)(CO)₂(bipy) or Ni(0)(CO)(bipy) or from CO present in the solution (the rate constant k_4). The reactions of highly reactive organic halides (for which $k_2 > k_3$), such as aryl iodides, follow the second pathway. In contrast, benzyl chlorides, aryl bromides and alkyl halides are moderately reactive with respect to Ni(0)(bipy) ($k_2 \ll k_3$) and their reactions follow the first pathway.

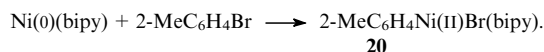
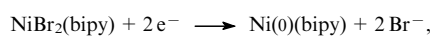
The preparative synthesis of ketones was carried out in the presence of catalytic amounts of Ni(bipy)²⁺ (5% with respect to RX).²⁵⁰ Under these conditions, the constants k_2 and k_3 have similar values and the two pathways for formation of the acylnickel complex **19** compete with each other.²²⁸

The Pd-PPh₃ system is characterised by two-electron reduction of the σ -arylpalladium intermediate⁷⁷ analogous to reduction of the corresponding intermediate in the Ni-PPh₃-ArX system studied earlier.^{48, 231} In the presence of the Pd-PPh₃ system, the biaryl is formed, apparently, through reductive elimination from diarylpalladium(II) followed by regeneration of Pd(0).

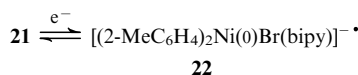
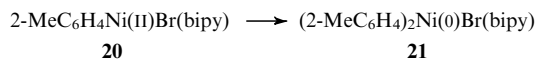
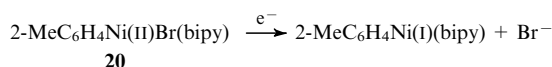


Many key steps of the mechanisms of reactions catalysed by Ni(0) complexes were suggested without sufficient substantiation. In some cases,³⁰¹ the catalytic waves in voltammograms were incorrectly interpreted and the calculated rates of particular steps were in error.

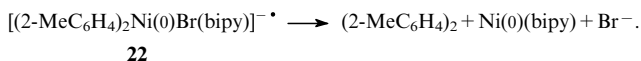
The reaction mechanism of coupling of organic halides under the action of the electrochemically generated Ni(0)(bipy) complexes was investigated.³⁰³ *o*-Bromotoluene was chosen as a model aryl halide. Its reaction with Ni(0)(bipy) afforded the stable σ -complex 2-MeC₆H₄Ni(II)Br(bipy) (**20**) through oxidative addition.



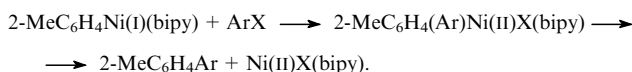
Reduction of the complex **20** gave rise to a new complex, *viz.*, (2-MeC₆H₄)₂Ni(0)Br(bipy) (**21**), which was isolated and characterised. The stability of arylnickel σ -complexes containing the methyl group in the ortho position of the aromatic nucleus is attributed to the steric factors, which hinder the rotation about the Ar-Ni σ -bond and the axial attack of the reagents on the nickel atom.^{53, 308} The complex **21** was reversibly reduced to radical-anionic intermediate **22**.



As the outer-sphere electron carrier, the complex **22** can reduce 2-bromotoluene to toluene, which was confirmed by chromatography. Slow decomposition of [(2-MeC₆H₄)₂NiBr(0)(bipy)]^{-•} (**22**) in solution to form a biphenyl derivative was a competitive reaction. This reductive elimination was induced by electron transfer.



The mechanism of Ni(0)(bipy)-catalysed cross-coupling of aryl and hetaryl halides was investigated taking into account the notion of the mechanism of homocoupling reported earlier.³⁰³ It was demonstrated that a Ni(I) complex serves as the active form in cross-coupling.



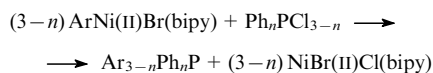
A particular complex can either serve as an efficient catalyst of homocoupling of organic halides or be poorly active or even inactive in cross-coupling of two different RX. In the general case, the efficiency of the catalyst depends on the following factors.

1. The possibility of rapid regeneration of the catalyst, *i.e.*, the number of catalytic cycles.

2. The reaction rate of reductive addition of the arylnickel intermediate to aryl halide must be higher than the rates of its competitive decomposition, protonation, *etc.*

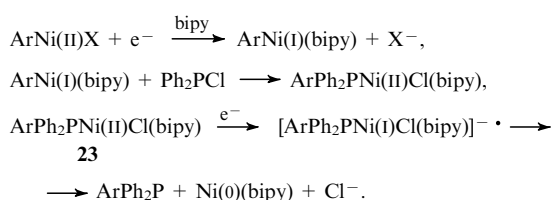
3. The reaction rate of reductive elimination of the $\text{Ar}^1\text{Ar}^2\text{NiX}$ complex must be rather high for regeneration of the catalyst (conceivably, promoted by the electron transfer) to be successful.

The electrochemically synthesised stable σ -complex $2\text{-MeC}_6\text{H}_4\text{Ni(II)Br(bipy)}$ (**20**) proved to be a convenient model for studying the mechanism of formation of tertiary phosphines.^{304–306} Thus it was demonstrated that the cross-coupling product containing the P–C bond was generated in the substitution reaction

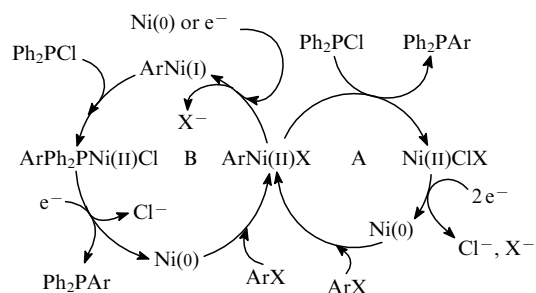


$n = 0-3$.

The competitive pathway through nickel phosphides is not realised. Phosphines are generated primarily according to the following sequence of reactions



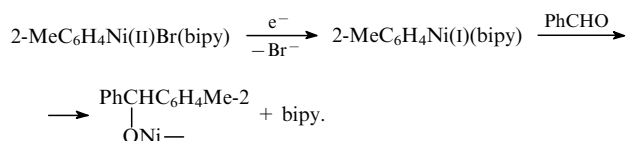
Reductive elimination of the (triarylphosphine)nickel complex $\text{ArPh}_2\text{PNi(II)Cl(bipy)}$ (**23**) affords the target compounds.



$\text{X} = \text{Cl}, \text{Br}$.

In the initial steps of electrolysis, products are formed through the reactions of the catalytic cycle A, whereas the reactions of the catalytic cycle B become dominant as the catalyst is consumed.

The use of the complex **20** as a model compound made it possible to follow the pathway of formation of secondary alcohols in electroreductive coupling reactions of organic halides with aldehydes catalysed by the nickel complex with 2,2'-bipyridyl.¹⁶⁶ The yield of the product was found to be proportional to the concentration of $\text{NiBr}_2(\text{bipy})$ in solution. It was suggested that nickel ions were involved in the corresponding nickel alkoxide thus being removed from the catalytic cycle. In addition, it was shown that alcohol was not generated at a potential of Ni(II)/Ni(0) reduction (-1.2 V with respect to a saturated calomel electrode). Cross-coupling proceeded only at more cathodic potentials corresponding to further reduction of the σ -complex $2\text{-MeC}_6\text{H}_4\text{Ni(II)Br}$ (-1.35 V).



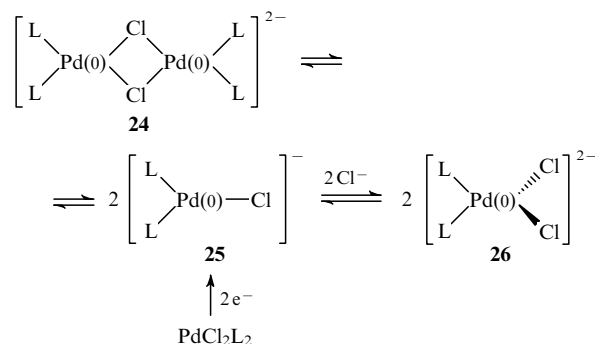
4. Mechanisms and kinetics of reactions in the presence of palladium catalytic systems

Palladium serves as the most versatile catalyst because of its high efficiency in reactions of aryl halides, vinyl halides (triflates) and

allyl derivatives with nucleophiles (cross-coupling, Stille coupling, Suzuki coupling, Heck reaction, Tsuji–Trost reaction) to form the C–C, C–H, C–N, C–O, C–P, C–S and C–C(O)–C bonds.³⁰⁹ In the presence of an electron source, the reactions of these substrates with electrophiles can give rise to the C–C, C–H and C–CO₂ bonds.^{310,311}

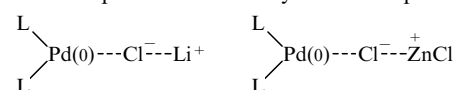
The efficiency of palladium is associated with the fact that zero-valent palladium is capable of activating C–X bonds ($\text{X} = \text{I},^{312,313} \text{Br},^{313} \text{Cl},^{313} \text{O}^{314}$) by oxidative addition yielding organopalladium(II) complexes, which are able to react with nucleophiles.^{315–318} The nucleophilic reaction affords a new organopalladium(II) complex from which the final product is generated in one or several steps.³⁰⁹

The recent data published in the literature (see the review³⁰⁸ and references cited therein) allowed revision of the commonly accepted mechanisms of palladium-catalysed reactions. It appeared that the reactivity of the low-coordinate 14-electron Pd(0)L_2 complex, which serves as an active species initiating the catalytic cycle, depends not only on the nature of the ligand at the Pd atom but also on the precursor of the Pd(0) complex. With the aim of revealing the reasons for this specificity, the structures and reactivities of different Pd(0) complexes prepared by oxidative addition were studied. It was found that the oxidative addition to aryl halides afforded various arylpalladium(II) complexes (neutral, anionic or cationic).³⁰⁹ For example, the oxidative addition of aryl triflates to $\text{Pd(0)(PPh}_3)_4$ gave rise to the cationic $\text{ArPd(II)(PPh}_3)_2^+$ complexes, whereas the neutral $\text{ArPd(II)Cl(PPh}_3)_2$ complexes were obtained in the presence of chloride ions. These complexes can be related by the dynamical equilibrium. The structures of arylpalladium(II) complexes depend substantially on the structure of the efficient Pd(0) complex involved in the oxidative addition and on the nature of the anions bound to Pd(0) . Earlier, it was assumed^{295,309,312,313} that two-electron reduction of $\text{PdCl}_2(\text{PPh}_3)_2$ afforded the $\text{Pd(0)(PPh}_3)_2$ complex. However, the ³¹P NMR spectrum of this complex after its exhaustive electrolysis has three signals²⁹⁵ belonging to three different anionic complexes (**24–26**), which are at dynamical equilibrium.



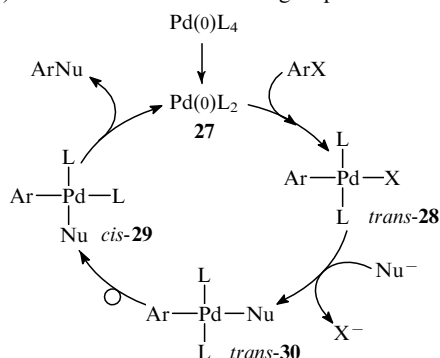
$\text{L} = \text{PPh}_3$.

The dimer **24** is the most reactive species. Hence, the $\text{Pd(0)(PPh}_3)_2$ complex does not exist in solution. When generated in the presence of halide ions, this complex gives anionic Pd(0) complexes. Oxidative addition proceeds more rapidly in the presence of cations (Li^+ or Zn^{2+}).³⁰⁹ The reactions of the cations with the chloride anions bound to palladium(0) produce ionic pairs and improve the reactivity of the complex.

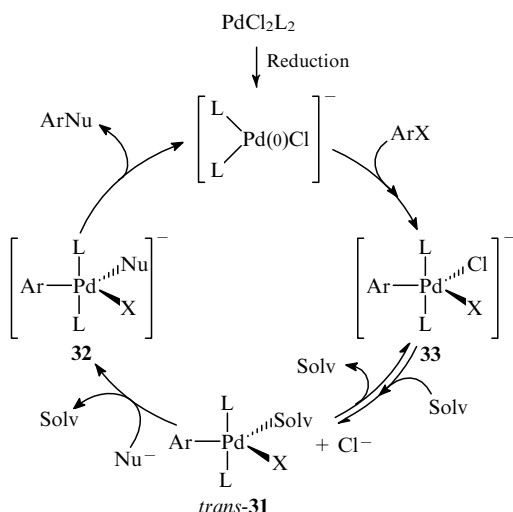


In the reactions with poorly reactive aryl bromides, the oxidative addition of aryl bromide to zero-valent palladium complex **27** is conceivably the rate-limiting step.^{315–317} For more reactive aryl halides, transmetalation [the nucleophilic attack on trans-ArPdXL_2 (**28**)] was considered as the rate-limiting step.^{318,319} Reductive elimination from cis-ArPdNuL_2 (**29**) gen-

erated upon the rearrangement of the *trans*-ArPdNuL₂ complexes (**30**) can also be the rate-limiting step.^{318, 320, 321}



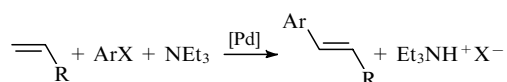
The results of the study³²² provided convincing evidence that reduction of PdCl₂(PPh₃)₂ yielded the anionic palladium(0) complex Pd(0)(PPh₃)₂Cl⁻ and that the oxidative addition afforded the anionic five-coordinate arylpalladium(II) complex ArPdXCl(PPh₃)₂⁻, which was slowly transformed into *trans*-ArPdX(PPh₃)₂.³²² Under these conditions, the Cl⁻ anion was the best nucleophile and simultaneously the best leaving group. Hence, this rapid equilibrium is the degenerate S_N1 nucleophilic substitution. Based on the above-mentioned results, the new catalytic cycle was suggested.



L = PPh₃.

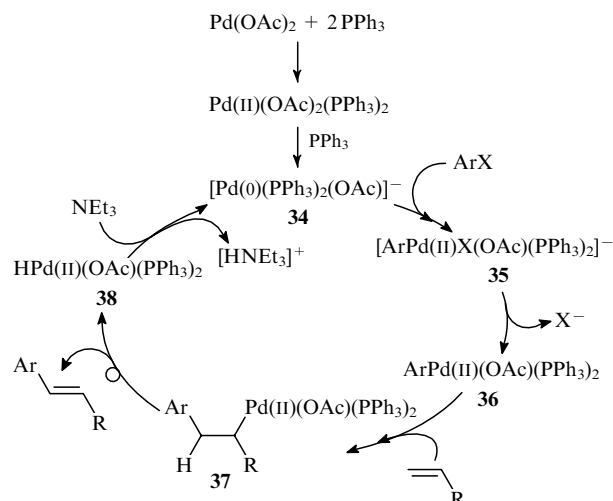
The nucleophile attacks the intermediate five-coordinate neutral arylpalladium(II) complex (**31**) to give the anionic five-coordinate complex [ArPd(II)XNuL₂]⁻ (**32**) in which the aryl group and the nucleophile are arranged in such a way as to provide rapid reductive elimination. Hence, the *trans*-ArPdXL₂ complex (**28**) may be ignored as an intermediate of PdCl₂(PPh₃)₂-catalysed cross-coupling. In the absence of nucleophiles, the formation of *trans*-PhPdI(PPh₃)₂ was demonstrated to be accelerated by cations³²² because the equilibrium **31** ⇌ **33** was shifted toward the complex **31**. In the presence of a rather strong nucleophile, the reaction follows the above-described scheme. Evidently, its mechanism can be changed in the catalytic cycle depending on the reaction conditions.

The reaction of alkenes with aryl halides catalysed by palladium complexes was discovered by Heck in 1968 (see the review³²³). In the presence of chiral ligands, enantioselective reactions can be carried out.^{323, 324}



[Pd] = Pd(OAc)₂ + nL.

The Heck reaction is performed in the presence of a base and, generally, in DMF. Of the catalytic systems, which were empirically chosen for the Heck reaction, mixtures of Pd(OAc)₂ and phosphines exhibit the highest efficiency. The catalytic cycle proposed for the Heck reaction in the study³⁰⁹ differs from that postulated earlier^{315–317} by the reduction of Pd(II) to Pd(0) under the action of phosphine^{325–327} and by the presence of the anionic Pd(0)(PPh₃)₂(OAc)⁻ complexes (**34**) generated *in situ*. The latter undergo oxidative addition to aryl halides yielding the short-lived five-coordinate arylpalladium (II) complex (**35**). Then the ArPd(II)(OAc)(PPh₃)₂ complex (**36**) is subjected to the nucleophilic attack by alkene. Reductive elimination of complex **37** affords the reaction product and hydride complex **38** from which the catalyst **34** is regenerated under the action of triethylamine.



The results of the cited studies provide evidence that the anionic complexes generated from precursors of zero-valent palladium complexes play a key role and account for the empirical data concerning the characteristic features of catalytic palladium systems.^{328–333}

XIII. Conclusion

To summarise, many interesting synthetic applications combining electroreduction with transition metal complexes were reported in the last 15 years. Electrochemical equipment and procedures for electrosynthesis become increasingly simple due to which many electrochemical methods compete with conventional chemical methods. Presently, some reactions, which have been previously described as catalytic processes, for example, carboxylation of organic halides or homocoupling of alkyl halides, can be carried out by direct electroreductive coupling in the presence of a sacrificial anode. However, electrochemical transition metal catalysis is often more selective. In recent studies, considerable attention has been given to the synergism between transition metal atoms of the catalyst and metal ions obtained upon dissolution of the anode.

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Sorption mechanism and prediction of sorbents' behaviour in physicochemical systems

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Abstract. The possibility of quantitative and semiquantitative prediction of sorbents' behaviour in various physicochemical systems is discussed. The attention is primarily devoted to the investigation of elementary processes at different surface areas of a sorbent grain. It is noted that the achieved level of the description of sorption processes based on semiquantitative estimations provides sufficient information to predict sorption kinetics and equilibrium *a posteriori*. The possibility of sorption by both a separate sorbent grain and grain agglomerates is analysed. The peculiarities of sorption processes on biosorbents are considered. Steps in the search for an optimum sorbent for a given system are described. The bibliography includes 242 references.

I. Introduction

In the present review, sorption implies the transfer of a substance onto the surface or into the bulk of solids or liquids from the environment without formation of a separate phase of the substance. Such a viewpoint corresponds to a common sorption definition (see Ref. 1, for instance), though it is much broader than the interpretation of the process as the uptake of a substance from the medium by a specially prepared sorbent only. In real systems, any solid or liquid phase of a substance is a sorbent for the other substances being present in the environment. The character of such a sorption differs from that on a specially prepared sorbent in terms of quantity only.

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The sorption accompanies any processes occurring in heterogeneous systems, and so researchers from almost all laboratories over the world deal with it to a greater or lesser extent. Information about sorption is mainly an incidental result of laboratories' work, although a vast number of studies specially cover the study of sorption and sorbents every year. The scope of sorption phenomena under investigation has significantly been extended^{2–11} during the last decade. Methods for the detailed and express analysis of sorbents' and sorbates' state have gained ground, efficient methods for the mathematical simulation of sorption processes have become available. Yet the main thing is that the possibility of observing the behaviour of separate adsorbed atoms and molecules *in situ* has arisen. The first observations of adsorbed atoms were made as early as 1958.¹² However, such observations became widespread as late as the present time. As a result, a transition to a new stage of sorption investigation is possible, which can be called the stage of visualisation of sorbed molecules.

A change in direction of many sorption investigations can be considered as the first indication of the advent of the new stage. If previously one aimed to create a macrokinetic model of sorption first and then make conclusions about molecules' motion, at present, one aims to obtain experimental data about behaviour of separate molecules first and, based on this, interpret macrokinetic sorption characteristics.¹³

The second indication is the introduction of a new research methodology avoiding application of *a priori* conceptions of the character of elementary processes. This methodology includes successive alternate implementation of laboratory, computing and, further, pilot experiments, based on the data obtained from observations *in situ* on connection of molecular motion with sorption macrokinetics.¹⁴

The fact that there is a tendency to predict the behaviour of sorbing bodies quantitatively by solution of kinetic equations describing the state change of these bodies and the medium during sorption can be considered as the third indication. The prediction can be incorrect if the kinetic equations employed ignore a number of necessary factors. However, methods for composing and solving kinetic equations of sorption are presently being improved rapidly.

This review considers only new studies giving an idea of the recent achievements in the investigation of elementary processes

with an emphasis on the data obtained by visualisation of molecular motion. The matter of the synthesis and usage of sorbents to solve applied problems is not concerned here.

II. General pattern of sorption

Consider a system which consists of sorbing bodies and a liquid or gaseous environment containing a sorbate. The 'bodies' can be represented by single crystals; microcrystals' agglomerates accreted so that the medium can penetrate into pores remaining between them; aggregates of particles of the amorphous substance; globules of polymeric molecules; pieces of tissue from sorbing fibres, *etc.* The bodies can form dense layers, localise in certain parts of the system or move freely in its bulk.

The sorbate molecules (ions) migrate from the bulk of the medium to the surface of each body and transfer into its adsorption layer during sorption. The adsorbed molecules migrate in this layer, diffuse into the bulk of the body or desorb. Molecules in the adsorption layer interact with each other and with the sorbent atoms located in the near-surface monoatomic layer of the bodies (Fig. 1). If the interaction of sorbate molecules with each other is sufficiently strong, they assemble into two-dimensional clusters that can grow over the surface until they contact neighbouring clusters. The two-dimensional clusters do not form on weak interaction of absorbed molecules with each other, while the influence of surface atomic relief on adsorption increases.

Migrating over the surface, molecules stay on an adsorption centre for some time, then jump to an adjacent centre. Molecule's dwell times on vertices, edges or steps of single crystal faces can differ by factor of tens in this process. This difference is the case for molecules' dwell times on adsorption centres located at different crystal faces with different atomic relief. Therefore, faces with an unequal number of steps have different sorbing abilities. Each face is characterised by its own local adsorption factor and sorptive capacity.¹⁵

The difference in sorbing properties of different faces is levelled if a body represents an agglomerate of microcrystals with pores between them. In that case, the sorbate first gets into pores between the microcrystals and subsequently adsorbs on their surfaces and diffuses into the bulk. Microcrystals have usually various habits and differ in composition, defectiveness, faces' relief and mutual arrangement. Hence, agglomerate properties can vary significantly.¹⁶ Considerable distinctions in properties are observed for aggregates of amorphous particles, globules of polymeric molecules, *etc.*^{17, 18}

Taking into consideration the discussion above, one should operate with a distribution function of sorbing bodies (sorbent particles) over properties (state parameters) to describe sorption

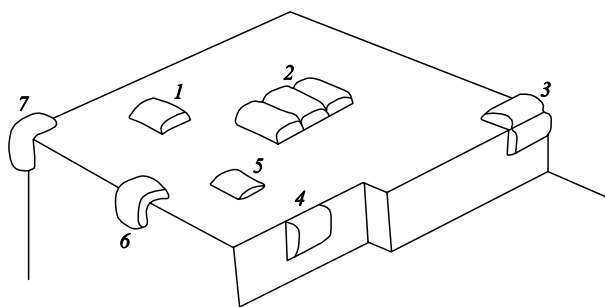


Figure 1. Scheme of the arrangement of adsorbed molecules on the surface of the sorbent crystal.

(1) Single molecule, (2) two-dimensional cluster on a face, (3) cluster at the vertex, (4) molecule at the adsorption site on the step end, (5) molecule that passed to the near-surface monolayer, (6) molecule at the edge, (7) single molecule at the vertex.

$$\varphi(\{x_i\}, t) = \frac{\partial^p N}{\partial x_1 \cdots \partial x_i \cdots \partial x_p},$$

where x_i ($i = 1, 2, \dots, p$) is one of the state parameters of the particles at the moment t , p is the number of the state parameters considered, N is the number of particles in a volume unit of the system, which have values of state parameters not exceeding $\{x_i\}$.

The state of each body is being changed during sorption: they undergo Ostwald curing and structural ordering,^{19–21} the bodies dissolve partly and sorb extraneous agents.^{21, 22} If bodies are in a stirred medium, they are partly destroyed upon collisions with each other and with walls of the system (vessel) and decompose at high temperature.²³ Bearing this in mind, one should define the state of each body with external parameters, among which are the spatial coordinates of its centre of gravity $\{X_i\}$, the velocity of movement relative to the walls ($\vec{v}_k$) and the mass m_k , and with internal parameters, the habit, characteristics of surface relief, and the phase and elemental composition. Each sorbing body can be presented as an aggregate of several species of structural elements. The structural element implies an aggregate of similar sorbing centres, and the sorbing centre is a group of atoms in the bulk or on the surface of a body, which can hold one molecule of the sorbate. Hence,

$$\{x_i\} = X_i, \vec{v}_k, m_k, \{n_j\}, \{\theta_j\},$$

where n_j is the number of adsorbing centres in the same state, which is determined by the centre's location in the body, the composition and configuration of molecules forming it, θ_j is the fraction of centres of a given sort occupied by the sorbate.

A conservation condition for the number of sorbent particles and all species of adsorbing centres can be written in the form^{24–26} (taking into account the continuous change of their states)

$$-\frac{\partial \varphi}{\partial t} = \sum_{i=1}^p \frac{\partial}{\partial x_i} \left[G_i \varphi - \sum_{j=1}^p \frac{\partial}{\partial x_j} (D_{ij} \varphi) \right] + Q(x_i, \varphi), \quad (1)$$

where

$$G_i = \lim_{\Delta t \rightarrow 0} \frac{\langle \Delta x_i \rangle}{\Delta t}, \quad (2)$$

$$D_{ij} = \frac{1}{2} \lim_{\Delta t \rightarrow 0} \frac{\langle \Delta x_i \Delta x_j \rangle}{\Delta t}.$$

In these equations, G_i is the rate of the change of parameter x_i for particles with approximately the same properties, D_{ij} is the fluctuation factor of the rate G_i upon the influence of random changes of the parameter x_j ; $Q(x_i, \varphi)$ is the frequency of particles' dissociation upon collisions with each other, thermal decomposition or phase transitions in the particles' bulk; Δx_i is the increment of x_i over the interval Δt ; averaging is performed for an ensemble of particles.

Equation (1) reflects the concept that every particle can with a certain probability move from one state to another, which is consistent with the conservation laws. The probability of some transitions is negligibly small, but they must be taken into account within the framework of a general pattern of sorption.

Another conservation condition has the form

$$-\frac{\partial(\varepsilon c)}{\partial t} = \text{div}[\varepsilon(\vec{v}_L c - D \text{grad} c)] + \frac{dM}{dt}, \quad (3)$$

where M is the number of moles of a substance extracted by the sorbent from a volume unit of the medium,

$$M = \int_{-\infty}^{+\infty} q \varphi dx_i,$$

$$\varepsilon = 1 - \int_{-\infty}^{+\infty} V_k \varphi dx_i,$$

ε , c and $\vec{v}_L$ stand correspondingly for the local porosity, the concentration of the sorbate, and the velocity of medium movement in the interval where particles have distribution $\varphi(x_i, t)$, D is the molecular diffusion constant for the sorbate in the medium, q is the sorbate quantity in a particle with parameters $\{x_i\}$, V_k is the volume of the particle, integration is performed over all parameters x_i .

Variable q is usually represented as a sum of sorbate quantities in the near-surface layer of a body

$$q_s = \sum_j q_{sj}$$

and in its bulk

$$q_v = \sum_j q_{vj},$$

where index j belongs to the adsorption centres of the j th species. If a body is a single crystal, then the layer of adsorbed molecules (sometimes along with one or two additional monolayers of crystal atoms) is regarded as a near-surface one.²⁷

If a body is composed of accreted microcrystals, then one includes both those which have at least one facet contacting the medium and the pores between them in the near-surface layer.

For the near-surface layer which is homogeneous along a normal to the surface, we have

$$\frac{dq_s}{dt} = \sum_j [\omega_j a S c - (\lambda_j + v_j) q_{sj}], \quad (4)$$

$$\frac{dq_v}{dt} = \sum_j \lambda_j q_{sj},$$

where ω_j , v_j are correspondingly the probabilities of the sorbate intake from the medium into the near-surface monolayer through sorption centres of the j th species and its leaving from these centres for the medium in a time unit, a is the normalising factor (effective width of the layer, from which sorbate molecules can get into the near-surface layer as a result of unit translation), S is the surface area, λ_j is the probability of a sorbate molecule transfer from the adsorption centre of the near-surface layer into the bulk of the body in a time unit.

Terms in the second member of Eqn (4) can differ in the order of magnitude, which will reveal itself in the stepwise character of sorption.²⁸

If a body is homogeneous, a transition of a sorbate from the near-surface layer into the bulk can approximately be described as a convective transfer with the effective diffusion constant D_v upon ordered motion of sorbate particles relative gravity centre of the body with velocity $\vec{v}_v$. The velocity $\vec{v}_v$ rides on the shift of the near-surface boundary due to dissolution and swell (compression) of the body upon sorption. If a body is highly porous, $\vec{v}_v$ is associated with the flow in pores caused by external pressure or phase transitions in the body.²⁹

The change with time of the sorbate concentration c_v in each region of the body in which the position is fixed relative to the body's surface is described by the equation

$$-\frac{\partial c_v}{\partial t} = \text{div}(\vec{v}_v c_v - D_v \text{grad} c_v) + W(t), \quad (5)$$

where $W(t)$ is the rate of a sorbate transition into a motionless state in the bulk of the body.

In terms of D_v , $\vec{v}_v$, c_v quantities, we have

$$\sum_j \lambda_j q_{sj} = \lim_{r \rightarrow 0} \oint_S \left(v_v c_v - D_v \frac{\partial c_v}{\partial r} \right) dS, \quad (6)$$

where r stands for the distance from the near-surface layer to the point where the sorbate concentration is equal to c_v , v_v is the normal component for the velocity of a surface shift to the centre of the body over the area dS .

Quantities included in Eqns (1)–(6) are functions of medium properties $\{y_i\}$, from which the following are usually defined:

$$\{y_i\} = T, c_i, \vec{v}_L, H_i, \rho_L, \mu_L,$$

where c_i is the concentration of the system components in the medium, $\vec{v}_L$ is the medium velocity, H_i is the field strength for an external field, ρ_L and μ_L are the medium density and viscosity, respectively.

Equations (1)–(6) are applied in a simplified form. For example, one assumes that $D_{ij} = 0$ (considering sorption as a purely determinate process) and $\vec{v}_v = 0$. If one takes into account the fluctuations of bodies' properties, then one assumes that $D_{ij} = \text{const}$, and changes in state parameters $\{x_i\}$ are independent of each other.^{30–32} This makes the solution easier, but excludes 'cross effects' reflecting the mutual influence of the body's state parameters and the medium's ones^{33,34} from the consideration. The cross effects are indirectly taken into account by the introduction of functions $G_i(x_i, y_i)$ and $D_{ij}(x_i, y_i)$ reflecting all the elementary processes.

III. Sorption gas dynamics and hydrodynamics

Velocities $\vec{v}_k$ and $\vec{v}_L$ determine the bodies' positions in the system. The sorption systems are heterogeneous as a rule, therefore, the position of a body is its most important state parameter.

1. Motion of an individual body in the flow of the medium

Any component of the instantaneous velocity of a body's movement can be represented as a sum of the velocities of the ordered motion $G_i = v_{ki}$ and the random fluctuations characterised by coefficient $D_{ij} = D_{ki}$, i.e.

$$\frac{dZ_i}{dt} = v_{ki} + D_{ki} \xi_{ki}(t), \quad (7)$$

where Z_i is the coordinate of the gravity centre of the body, $\xi_{ki}(t)$ is a random function of time,

$$D_{ki} = D_B + v_{ki} p_{ki},$$

v_{ki} is a component of the velocity $\vec{v}_k$, averaged over time, D_B is the diffusion constant when $v_{ki} \rightarrow 0$, and p_{ki} is the characteristic scale for fluctuations of the body's position.

Velocity v_{ki} is formed from the velocities of the body sedimentation in the field of terrestrial gravity, the approach of the bodies under the action of molecular interaction forces, the bodies' shifts in electric and magnetic fields, the thermo- and diffusiophoresis, the drift caused by the flow of medium and the chemoreactive movement. These kinds of motion are investigated with regard the sorbing bodies of simple form with little internal porosity.^{35–38} The movement of the bodies of complex forms has not been adequately studied.

Quantity D_B is determined by the Brownian motion. Functions $\xi_{ki}(t)$ and $p_{ki}(x_i, y_i)$ have different shapes. Theoretical approaches to their determination have been developed for the movement of particles in homogeneous suspensions.^{38–41}

The experiment has repeatedly been confirming the propriety of using correlation (7). As a result of the observations of trajectories of particles with dimensions of 1–5 μm in a liquid medium, it was established in recent time that the motion of the particles is really the sum of the ordered sedimentation in the field of terrestrial gravity and the random fluctuations characterised by coefficient D_B invariable with time.^{42,43}

2. Liquid flow near the surface of a body

The motion of a liquid near the surface of a solid determines in many respects the mass transfer to the surface of the solid.^{35, 42–46} The motion of a liquid whose molecules' interaction with each other and with molecules of the body is described by the Lennard–Jones potential, has been calculated by the molecular dynamics method^{47, 48}

$$v(r') = 4\varepsilon_i \left[\left(\frac{\sigma_i}{r'} \right)^{12} - \left(\frac{\sigma_i}{r'} \right)^6 - \left(\frac{\sigma_i}{r_{0i}} \right)^{12} + \left(\frac{\sigma_i}{r_{0i}} \right)^6 \right], \quad (8)$$

where r' is the distance between the gravity centres of the molecules, ε_i , σ_i are correspondingly the energy parameter and the dimension parameters of the potential of the interaction of molecules of the liquid with each other ($i = 1$) and with molecules of the solid ($i = 2$), r_{0i} is the boundary of the potential action area.

It was assumed in calculations that the body's surface is molecular smooth, and the molecules of the liquid move chaotically with a resulting shift along the direction of the stationary flow.

The calculations showed that in a broad interval of flow velocities, when $\varepsilon_2/\varepsilon_1 > 0.6$ and $\sigma_1 = \sigma_2$, the liquid moves along the surface so as the liquid's molecules in the layer of width σ practically do not move along the flow, and so this layer is motionless. The molecules which are more remote from the body surface move in accordance with the velocity gradient of the shear flow. Provided that $\varepsilon_2/\varepsilon_1 \leq 0.6$ and $\sigma_2 < \sigma_1$, a jump in the flow velocity takes place at a distance σ from the surface, in other words, the liquid 'slides' over the body's surface. This result means that numerous considerations of the near-surface motion of the liquid that do not take into account the slide motion and the existence of a 'motionless' layer need refinement.

When motion velocity increases, 'vortexes' are produced near the surface, which, multiplying, form wave structures disintegrating into chaotic vortexes in velocity flows l .⁴⁹ The most important peculiarity of the liquid's motion relative to a body is the anisotropy of motion velocity that leads to an unequal accessibility of different surface areas to the sorbate.^{35, 50, 51} Figure 2 illustrates the results of the calculations of velocities of medium motion near a body of size d at different flow velocities $\vec{v}_L$.⁵² In this case, there are several critical values of the Reynolds numbers

$$Re = \frac{1.6d |\vec{v}_L|}{\mu_L},$$

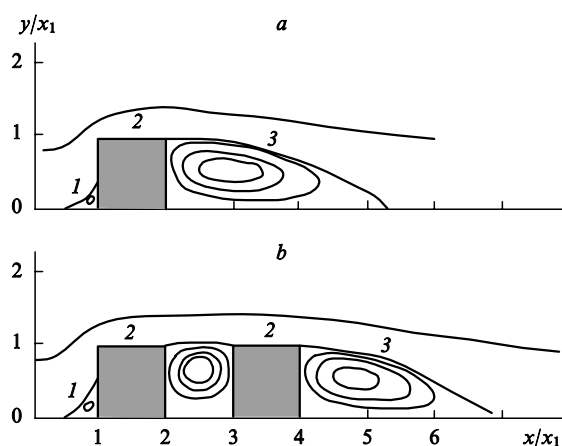


Figure 2. Results of calculations for solution streams flowing around a single grain of the sorbent (a) or a group of grains fixed on the support (b) by numerical solution of the Navier–Stokes equation for $Re = 10$.⁵² (1) Frontal vortex, (2) grain, (3) rear vortex; y and x are the spatial coordinates, x_1 is the size of the body.

changing the character of the velocity distribution of medium motion near them. If $Re < 0.1$, the flux flows around a body without producing vortexes; a stationary 'rear' vortex is produced near each body in the interval of $0.1 < Re < 100$; provided that $Re > 100$, vortexes break periodically away from the body. [An analogous vortex forming occurs for a body being in an ascending current (the Karman track) and for other motion regimes.⁵³]

Vortexes magnify anisotropy of the sorbate concentration field around the body and, therefore, increase unequal accessibility of its surface areas. If a body is fixed, its surface is unequally accessible at any Re values; if not, the difference in the area accessibility is substantial upon the laminar medium motion. In the latter case, the body orients in the flow in such a way that the medium makes a minimum resistance to the motion. The body retains such orientation (if we neglect re-orientation shifts caused by the rotary diffusion).⁵⁴ Thereby, the body retains unequal accessibility of its surface. It chaotically migrates and rotates in a turbulent flow so that its surface becomes equally accessible on average.

The concept of accessibility of different surface areas of bodies is fundamental to describe the external-diffusion regime of sorption. The consideration of this regime requires the determination of velocities of bodies' motion and medium flows around the bodies with high accuracy.

3. Chemoreactive movement

Chemoreactive movement is added to the common forms of the body's motion if the surface of a body is sorptively heterogeneous, in other words, if there are active sites distributed irregularly over the surface.^{55–60} Such a movement was discovered, for example, for sorbing water vapour on Al_2O_3 grains. The bodies' movement was investigated in a release reactor of which a scheme is shown in Fig. 3. Sorbent grains are introduced into section 1 for sorbent preparation, then they are blown in pre-reactor 2. A portion of the grains gets over channel 3 into adsorber 4, where they fall freely down in a sorbate gas. Flying through the adsorber, the grains deflect from the vertical trajectory if their velocity has a horizontal component.

The bodies were of size $d = 30 \pm 5$ microns and represented agglomerates of microcrystals. They were one by one introduced into the reactor filled with a mixture of water vapour and air. The agglomerates fell freely down reaching the bottom in several seconds. After that, distribution functions of agglomerates were determined with respect to motion velocities in the horizontal direction over the falling time. The measurements demonstrated that the distribution of the bodies over the velocities was the same as in the case of a dry sorbent in dry air if the bodies were brought to an equilibrium with water vapour before introduction into the reactor. If the bodies contained a non-equilibrium amount of water and fell in a humid medium, the velocity of their motion was considerably higher (Fig. 4). There were areas with a high rate of adsorption of water on the bodies' surfaces, which was caused by the capillary condensation started to proceed there. These sites adsorbed water vapour at the same rate as the other sites did, but desorbed it to a lesser degree, since a portion of the adsorbed water

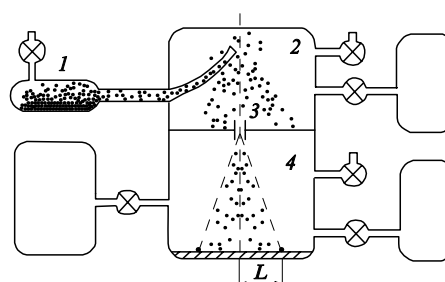


Figure 3. Scheme of the release reactor.⁵⁵

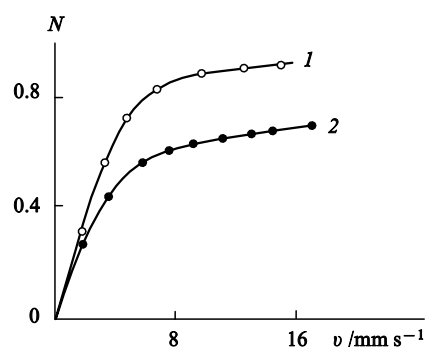


Figure 4. Distribution of Al_2O_3 grains according to the movement velocities in water vapour (from Refs 55 and 56). N is the fraction of grains that move in the horizontal direction at a rate lower than v . Partial vapour pressure, kPa: (1) 2.0, (2) 3.0.

was removed as a condensate. As a result, the momentum flux of recoil from desorbed water molecules over such sites was less than the momentum flux over the other areas, and this caused the bodies' movement.

4. Motion in an ensemble of sorbing bodies

The motion of bodies in an ensemble of them is affected by the superposition of fields of velocities in the environment around the bodies and by direct contacts of different bodies. Interaction in the vortex medium furthers the approach and coordinated movement of bodies. For instance, if a homogeneous suspension of glass balls of diameter $\sim 50 \mu\text{m}$ in a water–glycerol medium ($\mu_L = 5 \times 10^{-2} \text{ Pa s}$, $\varepsilon = 0.5\text{--}0.9$) is poured into an empty vessel, the coordinated motion of aggregates of hundreds of balls will take place in different directions against a background of slow sedimentation after the cessation of the motion caused by pouring.^{61,62} The bodies can stick together, undergo a plastic deformation and even be destroyed if the velocity of their approach is great.^{63–65}

The dimensions and shapes of the aggregates produced in ensembles of moving bodies depend on the flow velocity, the medium composition, the sizes, shapes, and relief of the bodies' surfaces. Any suspension flow is characterised by its own distribution function of aggregates over dimension and shape parameters. This function shifts to smaller dimensions of the aggregates on increasing the flow velocity and decreasing the concentration of particles in the flow. In contrast, the function shifts to large aggregates on increasing the concentration of the particles, and the aggregates can change their shapes from fractal ones to colloid crystals depending on the movement regime. All these results follow from the observations of moving suspensions with an optical or atomic force microscope *in situ*, and also from the observations of 'preserved' suspensions with an electronic microscope (see Refs 66–69, for example).

The force of resistance to the flow changes upon aggregation of particles and, therefore, so does the regime of their motion. One can make conclusions about the scale of such changes from data on effective viscosities μ_{ef} of sorbent–medium suspensions. Thus, the effective viscosity of a suspension of polystyrene spherical particles with sizes of $d = 70 \text{ nm}$ in an aqueous solution of gelatin (1 mass %) with particles' concentration $q_0 = 2.7 \times 10^{20} \text{ m}^{-3}$ and shearing strain $p_s = 0.1 \text{ Pa}$ in the shearing strain of the suspension is 500 times greater than in the absence of the particles.⁶⁷ The dependence $\mu_{\text{ef}}(p_s)$ shows that the suspension is a single 'loose' aggregate which moves as a whole at the indicated concentration q_0 and $p_s < 0.3 \text{ Pa}$. This aggregate dissociates into smaller fragments upon increasing p_s , and most particles move at $p_s > 30 \text{ Pa}$ almost independently from each other. The value of μ_{ef} keeps at the level of 10^8 Pa s in the shearing flow of SiO_2 particles in an ester ($T = 300 \text{ K}$, $d = 14 \text{ nm}$, $q_0 = 1.7 \times 10^{20} \text{ m}^{-3}$) at $p_s < 10 \text{ Pa}$,

while at $p_s \rightarrow 10 \text{ Pa}$ it undergoes a jump until $\sim 0.1 \text{ Pa s}$, at which it stays in the interval of $p_s = 10\text{--}100 \text{ Pa}$ (see Refs 67 and 68). This jump indicates a mechanically stimulated rearrangement of the suspension, resembling a first-order phase transition. The accessibility of the surface of bodies to a sorbate on such a rearrangement changes with a jump too.

The possibility of aggregation of bodies in an ensemble depends on the composition of the adsorption layer. The sorption can both accelerate and suppress the aggregation.^{67,70} This dependence becomes of particular significance in the presence of a sorbate whose molecules can adsorb on two close particles at once, producing 'molecular bridges' between them.⁷⁰ Such sorbates are employed to control the aggregation.

These facts highlight the change in the velocity of a stationary flow of a suspension due to a change in its effective viscosity caused by the adsorption-induced acceleration or the deceleration of aggregation. It seems that such 'adsorption-dependent destabilisation' of a flow is more intensive for concentrated suspensions of small particles.

Dissipative structures reflecting cooperative interactions of bodies arise in moving suspensions.^{71–73} For example, if a mixture of glass balls of diameter of $\sim 0.27 \text{ mm}$ and sucrose crystals of size $\sim 0.80 \text{ mm}$ is discharged to an empty vessel with the form of a rectangular parallelepiped with dimensions of $5 \times 200 \times 300 \text{ mm}$ along one of the long edges, a texture is formed of inclined layers of the glass balls alternating with layers of the sucrose crystals. The widths of the layers and their angles of inclination relative to the bottom of the vessel will depend on the form and subtle peculiarities of the surface relief of sucrose crystals.⁷³ Separation of the initial mixture of particles with the formation of a spatially dissipative structure occurs at a comparatively low input of mechanical energy in the system. The grounds of such separation could be explained after a considerable specification of conditions of particles' contacts in the flow.

The examples above indicate that the variety of hydrodynamic phenomena accompanying sorption increases nonlinearly with an increasing number of bodies in the system. Each of these phenomena can influence or depend on sorption under certain conditions as it takes place for the adsorption destabilisation of a suspension flow. The phenomena in question can be described by the motion equation of solids in the flow and by Navier–Stokes equation by detailed accounting of the forces affecting the sorbing bodies.

5. Prediction possibilities

A complete *a priori* prediction of the hydrodynamic behaviour of a system of sorbing bodies in the medium is still impossible in the general case (although it can be made with an acceptable accuracy under some sorption conditions^{74,75}). To make the complete prediction, one needs to have methods to calculate the parameters of Eqns (5)–(7) based on data on molecular motion as well as methods to solve the equations specified by accounting for the variety of hydrodynamic behaviour of an ensemble of bodies in the medium. However, no universal methods for such a calculation exist so far.

The methods of molecular dynamics allow prediction of properties of flows of bodies based on data on potentials of interatomic interactions. However, specification of the kind of interatomic potentials is necessary to apply these methods widely to describe flows of particles and the medium. Observations of adatoms of gold in the contact area of two crystals in a tunnelling microscope has shown that atoms' behaviour cannot be explained by using the Lennard–Jones potential [see Eqn (8) or other known potentials].^{76,77} Therefore, the contemporary conceptions of the potentials of interatomic interactions are approximate. Nevertheless, this does not exclude successful semi-empirical prediction of motion of particles and a medium in narrow intervals of sorption conditions, for instance, upon sedimentation in reactors of different shapes^{78,79} or in shearing flows of concentrated suspensions.⁶⁷ However, such calculations require expenses which are commensurable to those for experimental

work. Hence, one has to restrict oneself to the estimations obtained using various models, *e.g.* the cell model,^{80,81} if the geometry of a system is complex.

IV. Adsorption kinetics

It is convenient to present the velocity of sorption in the form

$$\frac{dM}{dt} = \sum_j \int_{-\infty}^{+\infty} (\omega_j a S c - v_j q_{sj}) \varphi dx_i, \quad (9)$$

where

$$v_j = \frac{kT}{h} \chi_j \exp\left(-\frac{E_j \beta_j}{kT}\right). \quad (10)$$

Here k and h are the Boltzmann and Planck's constants, respectively, χ_j is the frequency factor, E_j is the detachment energy of a sorbate molecule from an adsorption centre, β_j is the ratio of an excess of the activation energy of desorption to the detachment energy. Correlations (9) and (10) demonstrate that it is necessary to take adsorption centres of all sorts into account, although adsorption centres do not always differ by values of v_j as sharply as, for example, for the sorption of antimony by the faces (001) of a GaAs crystal. (Three forms of the antimony are discovered in this case with $E_j \beta_j$ values differing by almost 1 eV.⁸²) Nevertheless, three species of adsorbed molecules were also found upon an exploration⁸³ of the sorption of a 5,10,15,20-tetrakis[3,5-di-*tert*-butylphenyl]porphyrin complex of copper onto the surface of a gold crystal at 420 K from a gaseous environment by scanning tunnelling microscopy *in situ*. The central porphyrin part of the molecule was not observable in the microscope against a background of the substrate while the *tert*-butyl groups manifested themselves as bright spots. The conformations of molecules of all species could be judged from the location and the intensity of the spots. The kinetics of mutual conversions of the forms could be deduced from the change in the number of the images. It turned out that one form localised on the steps, the second one on the breaks of rectangular terraces, the third on the terraces. The *tert*-butylphenyl groups of the second form localised at an angle of 65° to the plane of the porphyrin part of the molecule, and those of the third form at an angle of 45°. Heating the substrate till 520 K over 12 min led to the disappearance of the second form from the substrate without any observable desorption of the third form. In this case, the energy of gold atoms on the breaks of the terraces and far from them differed by a few millielectronvolts only.⁸⁴ However, such a difference causes a noticeably distinct behaviour of the second and the third forms of the mentioned molecules.

Therefore, an estimation of the role of the centres of all sorts is necessary in any case. Yet it is hard to measure the values of $\omega_j = \omega_j(\bar{v}_L, D)$ for the centres of all sorts, and an *a priori* calculation of these quantities is only possible after a specification of the form of interaction potential.

Specification can be achieved by a search for quantities which are independent of the form of the potential. Such invariants will restrict the possibility of changes in the potential. One of these invariants can be connected with the diffusion constant, D , of the sorbate in the medium and, hence, with ω_j .^{85,86} Indeed, D along with self-diffusion constant D_s characterises thermal motion of molecules

$$D = \gamma(y_i) D_s,$$

where $\gamma(y_i)$ is a function that does not depend on D_s explicitly. The coefficient D_s calculated by the method of molecular dynamics for 1.6×10^4 atoms at different forms of a potential of molecules' interactions can be presented in the following form for a dense monoatomic liquid:^{85,86}

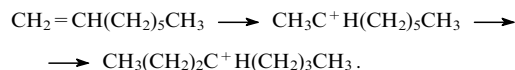
$$D_s = \frac{B \exp(S_0)}{g_0 r_0^4},$$

where B is a coefficient that does not depend on the form of a potential, S_0 is the difference between the entropy of a liquid and a gas of the same composition, and g_0 is the value of radial distribution function of liquid's atoms at the point of the first maximum of the distribution for which the interatomic distance is equal to r_0 .

This correlation indicates the possibility of searching a correlation of coefficient D and, therefore, frequency ω_j with the potential of the interaction of medium molecules through the invariants resembling coefficient B .

Functions $q_{sj} = q_{sj}(y_i, t)$ and $\chi_j = \chi_j(y_i, t)$ reflect the kinetics of all the elementary surface processes leading to sorbate migration between centres of different sorts, chemical transformations of adsorbed molecules and a sorption change of the state of the surface. Rates of elementary processes usually differ significantly, and so functions q_{sj} change with time stepwise. Some steps can be slow in this case.

For instance, a three-step process proceeds during adsorption of oct-1-ene by crystals of aluminosilicate zeolite H-ZSM-5 at 290 K over $10^2 - 2 \times 10^5$ s. A transfer of the oct-1-ene into the adlayer occurs at the first step, the adsorbed oct-1-ene reacts with hydroxy groups of the zeolite, producing carbenium ions at the second step, and at the third step, the carbenium ions undergo a rearrangement



These steps were identified by observing ¹³C NMR spectra *in situ* (in magnetic fields up to 18 T with the sample spinning at a 2–5 kHz frequency at a magic angle, using cross-polarisation). It follows from the intensities of lines in the NMR spectrum at 14.3 ppm which correspond to the terminal groups ¹³CH₃ and are given in the study⁸⁷ that the third step is determined by the relation

$$\left(\frac{q_{sj}}{q_{0sj}}\right) = 0.31 + 0.69 \exp(-\sqrt{\omega_q t}),$$

where q_{0sj} and q_{sj} stand for the amount of cabenium ions in the adlayer at the beginning of the third step and at moment t , correspondingly, $\omega_q = 4.5 \times 10^{-5} \text{ s}^{-1}$ stands for the characteristic frequency of rearrangements.

The three-step nature of the process in question can be explained by the fact that centres of three sorts exist on the surface of the zeolite that differ in composition and mutual location of atoms. The centres of the first sort have a much larger value of ω_j than the other centres, thus, sorption mainly starts with transition of molecules onto these centres. At the second step, the molecules move to the centres of the second sort, which have hydroxy groups reacting with the oct-1-ene. The carbenium ions rearrange in the slow third step, remaining on the centres of the first sort or moving to the centres of the third sort.

The surface processes are so varied that one has to consider their peculiarities at a qualitative level. This has been done below using the sorption by single crystals as an illustration and the level of details of description achieved to date is also presented.

1. Accommodation of sorbate molecules

Different sorbing centres have different probabilities of accommodation, so that

$$\omega_j = \alpha_j \frac{S_j}{S} \xi_j, \quad (11)$$

where α_j is the local factor of accommodation at centres of the j th sort, S_j is the area of the body's surface containing these centres, S is the total area of the body's surface, ξ_j is the probability that a sorbate molecule contacts the surface in a unit time as a result of transition of molecules from a gas or a liquid.

A sorbate molecule is promoted to an excited state upon collision with the surface.⁸⁸ The promotion proceeds in a period τ_0

in the order of 10 fs. It is accompanied by deformation of electron density and activation of vibrational motion of both the molecule and the body in the contact point and sometimes by a configuration change of the molecule.^{89,90} Then the relaxation of the electronic excitement of the molecule proceeds in 10–100 fs, and the relaxation of the vibrations in $\tau_s = 1–10$ ps. Vibrations of atoms of a body can accidentally synchronise giving a molecule sufficient momentum to break it away from the surface. Molecules dwell at the surface of a body for different time τ owing to the accidental character of the synchronisation process and

$$\alpha_j = 1 - \int_0^{\tau_s} \bar{\varphi}_j(\tau) d\tau,$$

where $\bar{\varphi}_j(\tau)$ is the density of the distribution of molecules occupying centres of the j th sort over τ .

Function $\bar{\varphi}_j(\tau)$ implicitly characterises the dependence of τ on molecule's velocity and orientation at the beginning of the contact. An elastic reflection of the molecules from the surface is observed and $\alpha_j \rightarrow 0$, if all the molecules have the velocity and the orientation at which function $\bar{\varphi}_j(\tau)$ is localised in the region of $\tau \approx \tau_0 < \tau_s$. If most molecules have $\tau \approx \tau_s$, then almost complete accommodation takes place and $\alpha_j \rightarrow 1$. Coefficient α_j can be determined for the adsorption of a rarefied gas on a homogeneous surface with high accuracy based on the data on a molecular beam reflected from a body. When considering sorption from a liquid medium, one has to content oneself with rough values of α_j . It is of some use to determine the function $\bar{\varphi}_j(\tau)$ characterising the first step of sorption by methods of femtochemistry.⁹¹

2. Migration on the surface

The sorbate molecules fixed on the surface jump from one adsorbing centre to another. The frequency of the long distance jumps which are accompanied by re-orientation of the molecules increases with increasing temperature. It is established by observation with the tunnelling microscope that the jumps of acetylene molecules on faces (111) of a lead crystal occur with a change of orientation at $T > 70$ K, and all six orientations are realised.⁹²

Superficial mobility of molecules depends on their configuration.^{93,94} Molecules can move from one centre to another due to conformational changes. Increasing the number and the strength of bonds of a molecule with an adsorbing centre weakens the tendency to such changes. This results, for instance, in sorption of a dendritic DNA on a graphite crystal, where DNA molecules can bind to the crystal through numerous guanidine bridges.⁹⁵ In the case of adsorption of 1,4-bis[β -(2-pyridyl)vinyl]benzene on face (100) of a silicon crystal, the sorbate molecules that are sufficiently strongly bound to silicon atoms migrate with low velocity so that their motion cannot be detected even on a sufficiently long observation in a tunnelling microscope. Molecules of this sorbate exist as four conformational species on the surface, however, motion with an observable velocity is not a specific feature for any of them. The migration proceeds much faster if it occurs at the face (100) of silicon where every near-surface silicon atom is blocked by a hydrogen atom.⁹⁶

Cooperative effects reveal themselves upon increasing the fraction θ_j of the surface occupied by the sorbate. The mobility gets smaller with the rise of θ_j if the attraction dominates in lateral interaction of sorbate molecules. The mobility increases first and then diminishes if the repulsion dominates.⁹⁷

Thus, the detailed description of molecules' motion over the surface requires that possible changes in their configuration upon jumping from one centre to another and their collective motions be taken into account.

Migration is quantitatively characterised by quantity D_j

$$D_j = \frac{kT}{h} \sum_i \chi_{ji} \exp \left[-\frac{(E_j - E_i)\beta_{ji}}{kT} \right], \quad (12)$$

where χ_{ji} is the frequency function for the transition of a molecule from the j th sorbing centre to the i th one, E_j and E_i are the energies of interaction of the molecule with the crystal on the j th and the i th sorbing centres, respectively, and β_{ji} is the correction function reflecting cooperative effects of activation.

It is assumed while calculating D_j that the shifts to the nearest vacant sorbing centre dominate among jumps of each molecule, and $E_j = n_j E_{j2}$ and $E_i = n_i E_{i2}$, where n_j and n_i are the number of the crystal's atoms in the nearest neighbourhood of the molecules on the j th and the i th sorbing centres, correspondingly, E_{j2} and E_{i2} are the average energies of the pairwise interaction of the molecules with the nearest neighbours.⁹⁸ It is also taken that $\beta_{ji} = 1$ and $\chi_{ji} = \text{const}$.⁹⁹ The calculation of E_j and χ_{ji} is attempted based on 'the first principles', but it is a success for the simple sorbates only.¹⁰⁰ It was possible to calculate these quantities for the migration of H_2 on the face (001) of a nickel crystal with a 10% discrepancy with the experimental data. However, one failed to explain the absence of an observable isotope effect in the superficial diffusion of hydrogen at low temperatures.¹⁰¹

If the energy of adsorption is sufficiently high, the near-surface layers of a crystal get disordered, molecules come to the surface from these layers, which leads to acceleration of superficial migration.¹⁰² One can get an idea of the scale of such acceleration based on the data on superficial migration of atoms during the adsorption of hydrogen and benzene on the crystals of iron and nickel. For instance, the hydrogenation of the adsorbed benzene is accompanied by a 10^4 – 10^5 -fold increase in the intensity of the superficial migration of iron and nickel atoms.

3. Formation of superficial clusters

Adsorbed molecules can join into clusters that grow up to the size of a whole face for large θ_j .^{103–105} The rate of the formation of the clusters increases quickly if the concentration of the sorbate in the medium achieves a critical value, which is substantially different in the case of the weak and strong bonds of the sorbate molecules with the crystal and with each other.

For example, the clusters can be observed in the sorption of hexadecyltrimethylammonium bromide by the surface of clinoptilolite crystals only at the concentration for which $\theta_j \rightarrow 0.25$. In the case of a lesser extent of the adlayer filling, the sorbate exists on the surface as separate molecules, which are observed as oblong knobs of 0.4 nm height in the atomic force microscope.¹⁰⁶ The heights of some knobs double at $\theta_j \rightarrow 0.25$, which can be interpreted as the formation of clusters.

The probability of their formation and growing up depends on the extent of conformity between the structures of the sorbate molecules and the near-surface monolayer of the body. In the case of the adsorption of simple molecules, this probability is higher for the sorbates whose crystal lattices have planes with an arrangement of atoms close to that in the near-surface monolayer of the body. The formation of clusters is facilitated in the case of the adsorption of complex molecules at certain configuration of the sorbate molecules.^{107,108} This is confirmed by the observation of the adsorption of oligosaccharide polymers on the face (100) of a graphite crystal from an aqueous solution in atomic force microscopy *in situ*.^{109,110} The molecule of the polymer, representing a polyvinylamide backbone with numerous dextran and hexanoyl branches, adsorbs so that its backbone is stretched along the surface. The hexanoyl chains contact the carbon atoms of graphite, and the dextran ones are directed outwards.

The orientation of molecules on the surface of a body depends on the ratio between the numbers of the hexanoyl chains and the dextran ones (q_m). The majority of molecules orients along one of two crystallographic directions of the crystal lattice at $q_m = 1/5$. In the case of a sufficiently high concentration of oligosaccharides in solution, a number of molecules successively attach to each molecule fixed on a free surface area, producing a two-dimensional cluster. The clusters spread out over the surface until they merge into a continuous monolayer of 0.7–1.2 nm width. The

orientation of molecules is arbitrary, and no two-dimensional clusters form at $q_m = 1$.

The two-dimensional clusters, enlarging, can turn into three-dimensional formations. For example, the clusters turn with time into epitaxial incrustations¹¹¹ upon adsorption of cadmium arachidonate $\text{Cd}[\text{CH}_3(\text{CH}_2)_{12}\text{CO}_2]_2$ from the vapour on the face (001) of a crystal of KCl.

Clusters can change their compositions and structures,^{112, 113} and successive monolayers of an adsorbed substance can be deposited over the produced ones¹¹⁴ at certain values of θ_j . Such a phenomenon was *in situ* observed in tunnelling and atomic force microscopies. The conclusions from the observations were confirmed by calculations using the methods of molecular dynamics.^{115, 116} In particular, it was established that multi-layer crystals arise, which can have different structures varying in the mutual orientation of molecules, upon the adsorption of H_2O on the face (100) of a crystal of MgO at $\theta_j \rightarrow 1$. One of the orientations dominates at $T < 200$ K, and the other one at higher temperatures.¹¹⁶ Structural transitions occur in the monolayer of lead on the face (100) of a copper crystal: the first one at $\theta_j \rightarrow 0.38$, the second, at $\theta_j \rightarrow 0.5$, and the third, at $\theta_j \rightarrow 0.6$. In this case, each of the structures undergoes 'two-dimensional' fusion¹¹⁷ on heating. The structural rearrangement of monolayers is accompanied by significant acceleration of adsorption over the adsorption of dodecanethiol and butanethiol on the face (111) of a gold crystal at 298 K.¹¹⁸

4. Two-dimensional solid solutions

Adsorbed atoms can be incorporated into near-surface interstices or occupy vacancies in the near-surface monolayer of crystal atoms, *i.e.* form two-dimensional interstitial solid solutions or substitutional ones.²⁷ This could be observed directly in the case of the sorption of InAs from its vapour on the faces (100) of a crystal of InP by atomic force microscopy.¹¹⁹ The sorption of vanadium oxide on the face (001) of a crystal of TiO_2 was detected by emergence of an additional component in the band $\text{V}2P_{3/2}$ of the photoelectronic spectrum at 623 K. (This band is caused by the transition of a vanadium atom into the lattice of TiO_2 .¹²⁰) It was possible not only to detect solid solutions, but also to determine their structures by means of X-ray diffraction analysis while studying the sorption of bismuth from its vapour on the face (001) of a copper crystal.¹²¹ It turned out that the bismuth atoms substitute the copper ones at small θ_j chaotically, and each bismuth atom transferred into the near-surface monolayer is shifted towards the vapour with respect to the copper atoms by 0.06 nm. The sorbed atoms of bismuth form a two-dimensional structure of the type $C(2 \times 2)$ at $\theta_j \rightarrow 0.35$, their radius is equal to 0.163 nm, which is considerably smaller than that of a bismuth atom in the bulk of its crystal (0.182 nm). Thus, the structure of two-dimensional solutions can change with increasing θ_j .

The mobility of molecules in the near-surface monolayer of the crystal is far lower than that in the adlayer.^{27, 122} Hence, the sorbate transfers to the adlayer at the first stage rather rapidly and forms a two-dimensional solid solution at the second stage slowly. The third stage arises after large periods of sorption, which consists of the transfer of the sorbate to the bulk of the sorbent.

5. Change in the properties of a sorbing body

All properties $\{x_i\}$ of the body change during sorption, and the scale of these changes is nonlinearly connected with the body's state and can be great in a narrow interval of sorption conditions. For example, a change in velocity of the body's motion under the influence of sorption becomes detectable if the body can freely move in the sorbed gas for a long time and the sorption is localised on a portion of the body's surface.⁶⁰ The change in temperature is considerable if the medium is characterised by the low thermal conductivity and the great heat of sorption. Sorptive changes in electroconductivity, magnetic, thermophysical and optical properties can turn out to be substantial for porous bodies, which is employed in sensor devices.¹²³

There can exist both positive and negative feedback between the sorption and the properties of a sorbing body. For instance, the feedback of the quantity of an adsorbed substance q with the velocity of chemoreactive movement $\vec{v}_k$ is positive since increasing $\vec{v}_k$ leads to growth in ω_j , and growth in ω_j facilitates the acceleration of the movement.⁵⁵ The feedback between q and T is usually negative since increasing the temperature leads to growth in the rate of desorption dominating over increasing α_j .¹²⁴

The character of the feedback between q and parameters $\{x_i\}$ is of great significance in the development of sensors.^{123, 124}

6. The possibilities of computational experiment

The direct observations of the motion of adsorbed molecules encouraged the application of the methods of molecular dynamics and Monte Carlo for the simulation of elementary processes of sorption under the quantum-chemical interpretation of interatomic interactions or the usage of atom-atomic potentials of the type (8). Simultaneously, the computational methods of chemical kinetics based on differential equations of the type (4) become more widely applied in investigating the sorption processes. As a result, separate elementary processes of sorption could approximately be described for some of the simplest molecules, based on the 'first principles'. It has become clear at the same time that some elementary processes can *a priori* be excluded from the consideration only in the case if we limit ourselves to a narrow set of conditions when modelling sorption. A complete kinetic model of sorption which is applicable for a broad set of conditions must take into account all the details of elementary superficial processes. However, the complexity of the model does not allow making computational experiments *in corpore*.

V. Sorbate migration into the bulk of a body

1. Diffusion into the bulk of crystals

Sorbate migration into the bulk of a body is usually characterised by coefficient D_v reflecting all elementary processes leading to the translation movement of sorbate molecules (ions).¹²⁵ Function $W(t)$ can be excluded from Eqn (5) while the sorption at the crystals is described. Coefficient D_v can be considered as a tensor taking into account the anisotropy of crystals' properties in this case. To solve Eqn (5), one should reflect the polyhedral form of crystals and the possibility of their formation with different faces in edge conditions. One also has to take into consideration the fact that the sorbent crystals have 'biographical' structural defects affecting D_v . Besides, the crystals acquire new defects during sorption that are distributed irregularly in their bulk. For example, the defects are localised at the periphery of each crystal for the crystals of K_2SO_4 or NaCl being in an intensely agitated aqueous solution. In this case, the sorbate accumulates significantly faster at the defect areas than at the other ones.^{63, 64} The values in the order of D_v of $10^{-25} \text{ m}^2 \text{ s}^{-1}$ are a characteristic of the perfect crystals of BaSO_4 with an ion-covalent bond of atoms at 300 K; for the sorption of SrSO_4 , in particular, by the crystals of BaSO_4 with high defectiveness of growing, $D_v = 10^{-16} \text{ m}^2 \text{ s}^{-1}$ (see Refs 126 and 127).

The molecules of sodium ethylenediaminetetraacetate and trinitrophenol diffuse into interlayer spaces of the crystals of hydrotalcite $\text{Mg}_3[\text{Al}(\text{OH})_8][\text{CO}_3]_{0.5}$, which have a lamellar structure with the ion-covalent bond of atoms within the layers and the van der Waals one between the layers, with the diffusion constant $D_v \approx 10^{-16} \text{ m}^2 \text{ s}^{-1}$ at 300 K.¹²⁸

Diffusion rate is especially high for sorption by the organic analogues of zeolites. The crystals of organic zeolites consist of groups of covalently bound atoms producing ring-shaped formations (blocks).¹²⁹ Closing each other up, the blocks produce channels whose width can reach several nanometres. Atoms of the crystal occupy not less than half volume of a channel, the rest space is occupied by molecular pores. Sorbate molecules can migrate along the channels with high values of D_v , which, for example, takes place in the crystals of $\text{C}_{72}\text{H}_{98}\text{N}_{12}\text{O}_{40}\text{Zn}_3$ with a

trigonal lattice (the diameter of a channel ~ 1 nm, the channels orient along axis c).¹³⁰ The channels accounting for 47% of the crystals' volume are filled with water molecules in an aqueous medium. Migration, for instance, of Na^+ ions over the channels proceeds at 300 K with the diffusion constant $D_v \approx 10^{-14} \text{ m}^2 \text{ s}^{-1}$, which was estimated from the data on the rate of ion exchange between the crystals and the solution.

One can judge elementary acts of sorbate migration in molecular crystals by the results of calculations made by the molecular dynamics method.^{131–133} The calculations showed a sharp change in the frequency of jumps of sorbate molecules over the channel and the number of molecules in the channel at small changes of the potential of interactions with atoms of the channel's 'walls'. The motions of sorbate molecules lead to significant fluctuations of the number of the molecules localised per length unit of the channel. The scale of such fluctuations also depends on the potential of interaction of molecules with atoms of the channel's walls. Thus, if a carbon nanotube with a diameter of 0.81 nm and a length of $l = 1.34$ nm is placed in a medium containing 10^3 molecules of H_2O , these molecules get into the nanotube and move inside it. If the interaction potential is of the type (8) and $\varepsilon_i = 0.549 \text{ kJ mol}^{-1}$ and $\sigma_i = 0.328 \text{ nm}$, the molecules of H_2O , having passed through the channel, get out of the tube with the frequency $\omega_e = 2 \times 10^{10} \text{ s}^{-1}$ (see Ref. 133), which corresponds to the coefficient D_v of the order $l^2 \omega_e = 3.6 \times 10^{-8} \text{ m}^2 \text{ s}^{-1}$. Frequency ω_e proves to be lower by several times if $\varepsilon_i = 0.272 \text{ kJ mol}^{-1}$ and $\sigma_i = 0.341 \text{ nm}$. In the channel of the nanotube, H_2O molecules form a monomolecular chain of 2–7 molecules arranged with higher order than in the medium. The molecules of the chain approach each other to a distance at which the hydrogen bond forms much more frequently, existing in such a state for $\tau_e = 5.6 \text{ ps}$ ($\tau_e = 1.0 \text{ ps}$ in water) on average. In addition, the H_2O molecules possess not only the axial mobility but also the radial one (less frequently). In this case, the average number of molecules in a chain varies from 4 to 6 when $\varepsilon_i = 0.549 \text{ kJ mol}^{-1}$ and $\sigma_i = 0.328 \text{ nm}$, and from 1 to 2 for $\varepsilon_i = 0.272 \text{ kJ mol}^{-1}$ and $\sigma_i = 0.341 \text{ nm}$. This example demonstrates the possibility of a sufficiently detailed description of the movement of a sorbate in channels when data on interaction potential of atoms are available.

2. Migration into polymeric grains

Coefficient D_v of the polymeric sorbents has as a rule a complex dependence on their structure, values of θ_j , T , composition of the medium and preliminary swelling of the grains, and this dependence is difficult to predict. For example, $D_v = 3.4 \times 10^{-10} \text{ m}^2 \text{ s}^{-1}$ at pH = 1.0 and $D_v = 1.65 \times 10^{-10} \text{ m}^2 \text{ s}^{-1}$ at pH = 2.0 for the sorption of CdCl_2 by grains of formaldehyde resin from an aqueous solution at 300 K.¹³⁴ The value of D_v grows with increasing θ_j first, and then diminishes during the sorption of LiCl by a resin containing sulfo groups.¹³⁵ Sorbents based on dendrimers and hydrogels have been obtained in recent years. Their coefficient D_v is almost the same as in the medium surrounding a body.¹³⁶ Two models are usually employed to describe sorption by polymeric grains.^{137, 138} The first model implies that all grains are quasi-homogeneous and isotropic, *i.e.*, characterised by a unique value of D_v when $\bar{v}_v = 0$ and $W(t) = 0$; the second one assumes a grain to be a population of small polymeric globules jointed by rare molecular bridges. In this model, a grain is characterised by the constants of the sorbate diffusion over the interglobule bulk (the channels) and from the interglobule space into the bulk of a globule. In this case, function $W(t)$ is determined as a total diffusion flux through surfaces of all the globules being in a volume unit, into their bulk. Both models reproduce basic features of the process only approximately.

The calculations³⁰ have shown that if sorbing bodies are homogeneous and have a Gaussian size distribution, then the time $\tau_{0.9}$ for which they capture 90% of an equilibrium quantity of the sorbate, is

$$\tau_{0.9} = \frac{(0.182 + 0.255\sigma_0 - 0.190\sigma_0^2)\bar{l}^2}{D_v}, \quad (13)$$

where σ_0 is the ratio of the root-mean-square deviation of distribution of particles' sizes to their average size $\bar{l}$. The deviation varies in the interval from 0 to 0.45.

For the lognormal distribution over sizes, we have

$$\tau_{0.9} = \frac{(0.1943 + 0.057\sigma_0)\bar{l}^2}{D_v}. \quad (14)$$

Correlations (13) and (14) characterise reversible sorption (Fig. 5). It follows from these correlations that it takes sufficiently great time to achieve the sorption equilibrium. One has to restrict oneself to the adsorption if it is required to perform the sorption sufficiently rapidly, *i.e.* within the time $t_k \ll t_{0.9}$. At small t_k , the adsorption behaves as a process with a slight deviation from the reversibility, which is related to the transfer of the sorbate into the bulk of grains. Such a deviation is often revealed in practice.^{139, 140}

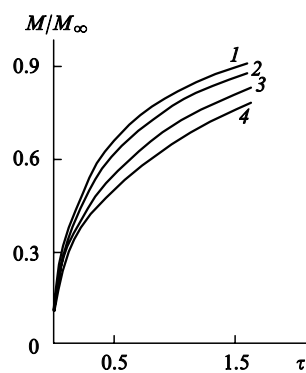


Figure 5. Results of the numerical experiment on sorption by a sorbent with different size distributions of grains.³⁰ Normal distribution at $\sigma_0 = 0$ (1), 0.1 (2), 0.2 (3), 0.3 (4). $\tau = \pi^2 D_v t / \bar{l}^2$ is dimensionless time, M_∞ is the equilibrium amount of the sorbate in grains.

3. Sorption by the agglomerates of microparticles

If a body consists of accreted microparticles, coefficient D_v depends on their shape, size, and the character of their packing.^{141, 142} The relief of the surface of the particles also affects the value of D_v , which was demonstrated with the use of the molecular dynamics method, employing the diffusion of N_2 and isobutane in a cylindrical space between microparticles of 0.4–1.4 nm size at 200–800 K as an illustration.¹⁴³ In addition, the value of D_v can be reduced by infilling the space by the sorbate.

All this suggests that the description of sorption by the agglomerates with the use of coefficient D_v provides little information and shows a necessity to work Eqn (5) out, taking into account the structures of the agglomerates.

Bodies consisting of multiple accrete macroparticles retaining free spaces (macropores) between them are widespread among the agglomerates. In this case, each of the macroparticles is a combination of microparticles divided by the micropores provided that

$$V_k \gg \bar{V}_{k1} \gg \bar{V}_{k2}, \quad (15)$$

where $\bar{V}_{k1}$ and $\bar{V}_{k2}$ are the average volumes of macro- and micro-particles, respectively.

If the state of every particle in an agglomerate is characterised by its size l_i and the volume (V_{pi}) of pores surrounding it, then one can write condition (15) in a continuum approximation

$$c_v = \varepsilon_1 c_{v1} + \int_0^\infty \int_0^\infty m_1 \varphi(l_1, V_{p1}) dl_1 dV_{p1}, \quad (16)$$

$$m_1 = \int_{V_{k1}} \left[\varepsilon_2 c_{v2} + \int_0^\infty \int_0^\infty m_2 \varphi(l_2, V_{p2}) dl_2 dV_{p2} \right] dV,$$

where ε_1 is the total volume of macropores in a volume unit of a body, c_{v1} and c_{v2} are the bulk concentrations of the sorbate in macro- and micropores, m_1 and m_2 are the quantities of the sorbate in a macroparticle in state $\{l_1, V_{p1}\}$ and in a microparticle in state $\{l_2, V_{p2}\}$, ε_2 is the porosity of the microparticles, $\varphi(l_1, V_{p1})$ and $\varphi(l_2, V_{p2})$ are the distribution functions of the particles over their states.

Concentrations c_{vi} ($i = 1, 2$) change during sorption according to a transfer equation, which is analogous with relation (5)

$$\frac{\partial c_{vi}}{\partial t} = \text{div} [\varepsilon_i (D_i \text{grad } c_{vi} - \vec{v}_i c_{vi})] - \int_0^\infty \int_0^\infty \beta_i l_i^2 J_i \varphi(l_i, V_{pi}) dl_i dV_{pi}, \quad (17)$$

where D_i is the diffusion constant of the sorbate diffusion into the bulk of pores, $\vec{v}_i$ is the velocity of ordered motion of a liquid or a gas filling the pores, β_i is the shape factor for the particles, J_i is the sorbate flux from the pores through the surface of a particle.

In relations (16) and (17),

$$m_2 = \beta_2 l_2^2 \int_0^t (J_2 + J_{2s}) dt, \quad (18a)$$

$$J_1 = (\omega_{l1} c_{v1} - v_{l1} c_{a1}) a (1 - \varepsilon_2) + D_2 \varepsilon_2 \left(\frac{\partial c_{v2}}{\partial r} \right)_{l_1}, \quad (18b)$$

$$J_2 = (\omega_{l1} c_{v2} - v_{l1} c_{a2}) a, \quad (18c)$$

where J_{2s} is the intensity of the sorbate transfer into the bulk of microparticles, ω_i and v_{li} are the specific frequencies of the adsorption and desorption, respectively, c_{a1} and c_{a2} are the concentrations of the sorbate in the adsorption layer of microparticles localised on the surface of a macroparticle and in its bulk, $(\partial c_{v2}/\partial r)_{l_1}$ is the normal component of the gradient of sorbate concentration in pores near the surface of the macroparticle, and r is the distance from the centre of the macroparticle to the point where the sorbate concentration is equal to c_{v2} , a is the effective width of the adsorption layer.

Equations (17)–(18a–c) contain only those parameters which can be measured by experiment. Thus, $\varphi(l_i, V_{pi})$, ε_i and β_i can be determined by sectioning the bodies and measuring the sizes of particles and pores on the cuts with the use of optical and electronic microscopy. Frequencies ω_{li} and v_{li} can be measured upon adsorption by the microparticles which are not assembled into agglomerates. The intensity of sorbate transfer J_{2s} can be determined by the use of single crystals with the same molecular relief that the microparticles have. In addition, quantity J_{2s} can be measured directly observing the motion of adsorbed molecules in atomic force or tunnelling microscopy. The motion of individual molecules and atoms could repeatedly be observed in the tunnelling microscopy.^{144, 145} To tell the truth, their trajectories were determined by the electric field of the microscope to a great extent, but there are all reasons to consider that the influence of the field on the surface movement of molecules can be taken into account.

It is not difficult to determine the coefficient D_1 , while to determine D_2 is more complicated. This can be made by the conductometric method in the case where the size of sorbate molecules is not more than 0.5 nm. The current strength fluctuates at limits that are proportional to D_2 if two conductive microparticles of size 5–10 nm are approached so as to retain a space of 1–10 nm width between them, and the space is filled up with a sorbate solution containing NaCl, and the current is passed through the electric circuit formed.^{146, 147} The volume of the solution determining the electrical resistance of the circuit is very

low at the given size of microparticles. Thus, if even one molecule of the sorbate gets into the space, this results in a jump of the electrical conductivity and, therefore, the fluctuation of the current. It appears that a way to conductometric determination of the rate of sorbate accumulation in the bulk and on the walls of an individual micropore was suggested by Bezrukov *et al.*^{146, 147} Therefore, a way to the direct measurements of ω_{li} , v_{li} and coefficient D_2 for molecules of an arbitrary size is also open. It was shown¹⁴⁸ that the value of D_2 amounts to $(1-2) \times 10^{-11} \text{ m}^2 \text{ s}^{-1}$ at 300 K for the diffusion of polyethylene glycol of a mass of 200–10³ a.u. over a channel filled with an aqueous solution of NaCl in the lipid–peptide membrane with a channel radius of 1 nm. This value is lower than that in a free solution by an order of magnitude. This fact confirms the necessity to describe the sorption with Eqns (16)–(18a–b) taking into account possible differences in the values of D , D_1 , and D_2 .

The use of the functions contained in the indicated equations is complicated by the fact that some of them are unknown even for the most common sorbents. Simplifying assumptions are made for these functions, hence, the description of the sorption kinetics becomes semi-quantitative even if it agrees with the experimental data. The following assumptions are the most widespread:

$$\vec{v}_i = 0,$$

$$\varphi(l_i, V_{pi}) = \text{const} \cdot \varphi(V_{pi}) \delta(\bar{l}_i),$$

$$D_i \neq D_i(\bar{l}_i),$$

$$\beta_i \neq \beta_i(\bar{l}_i),$$

$$\omega_{li} = v_{li} = 0,$$

$$c_{a2} = B_a c_{v2},$$

where $\varphi(V_{pi})$ is the distribution function of pores over the bulk, $\delta(\bar{l}_i)$ is the Dirac function, and B_a is the equilibrium coefficient of adsorption. As can be seen, the number of *a priori* assumptions is large. Nevertheless, one has to employ most of them even in the most consistent descriptions.^{149, 150}

4. Possibilities of prediction

Quantum-chemical methods and correlative empirical dependences give an opportunity to estimate coefficient D , *a priori* with a relatively small error for the bodies whose structure is near-equilibrium. But the acting sorbents are non-equilibrium as a rule. The structures of their particles depend on the ‘biography’ of the sorbent. Therefore, the problem of the estimation becomes complicated, and one has to solve it experimentally. Some peculiarities of the migration into the bulk of a body can be predicted by the molecular dynamics method. However, the predicting possibilities of this method are restricted to nanoparticles and small periods of sorption.

VI. Equilibrium sorption

The equilibrium sorption is usually characterised by a distribution coefficient

$$K = (V_f c N_A)^{-1} \sum_j \int_{-\infty}^{+\infty} \theta_j n_j \varphi(x_f, t) dx_f,$$

where V_f is the volume of the sorbing phase, and N_A is the Avogadro constant.

Approaching the equilibrium, function $\varphi(x_f, t)$ converges, and parameters θ_j and n_j become independent from $\{x_j\}$, the number of all the centres except the most stable diminishes, and coefficient K tends to a value

$$K_e = \theta_1 N_1 (c N_A)^{-1} = K_0 \exp\left(-\frac{\Delta F}{kT}\right), \quad (19)$$

where θ_1 is the fraction of the most stable filled centres, N_1 is the number of such centres in a volume unit of the sorbent phase, K_0 is

the ratio between the coefficients of thermodynamic activity of the sorbent in the sorbent phase and in the medium, ΔF is the standard change in the free energy of the sorbent during sorption.

A dynamical quasi-equilibrium is achieved between the centres sorbing most rapidly and the medium in the system upon completion of the first step if the sorption proceeds in several steps and adsorption centres of only one type are involved in the process at each step. Many examples of adsorptive quasi-equilibrium on the 'external' surfaces of bodies or on the surfaces of micro-particles in the bulk of bodies with a successive transition to the equilibrium in the bulk have been described.

Equilibrium coefficients K_e are determined for several thousands of systems (though often without proof of their equilibrium). K_0 and ΔF are calculated for many systems by the methods of statistical mechanics and molecular dynamics. The matter connected with the differentiation of the partial and total equilibrium and the identification of centres that are responsible for the quasi-equilibria still remains unclear.

Functions $\Delta F(\theta_j, y_i)$ and $K_0(\theta_j, y_i)$ that can be converted into isotherms of sorption are diverse.^{151–154} The Langmuir, Freundlich, Frumkin, Totte, Dubinin–Serpinsky isotherms describing a variety of experimental results are applicable in a narrow range of conditions, as a rule. They are special cases of more complex isotherms. Systems are widespread both with a small entropy contribution in ΔF and with a great one.^{155, 156} The great contribution of entropy has been found upon investigation of the sorption of bovine serum albumin and ovalbumin on a series of ion-exchangers.¹⁵⁵ The sorption process of these proteins is endothermic, and coefficients K_e are great.

1. The variety of equilibrium forms

Sorptive centres of several sorts can retain commensurable quantities of a sorbate at the quasi-equilibrium. For instance, it has been proved by the methods of scanning electronic and tunnelling microscopy and also by the diffraction of slow electrons that CO molecules are retained on centres of two sorts on the face (111) of a platinum crystal. In this case, the adsorption on both centres is commensurable if θ_j is high, and the adsorption on one of them dominates if θ_j is low.¹⁵⁷

Four forms of the sorbate, being present in commensurable quantities and manifesting themselves in its magnetic properties, were discovered in the study of the adsorption of Cu(II) salts at TiO₂ single crystals.¹⁵⁸ Three forms of the sorbate with the adsorption heat of 101.6, 112.4, 178.1 kJ mol⁻¹, respectively, were observed upon the adsorption of NH₃ on crystals of CdSO₄·0.66H₂O.²³ The presence of these forms can be interpreted as a result of sorbate localisation at the centres of different type. The presence of several adsorptive forms can be related to the different orientation of molecules on the surface in the case of the adsorption of complex molecules.

The forms whose orientations are favourable to produce the largest number of bonds with the surface dominate over the others. This was demonstrated by Diaz *et al.*,¹⁵⁹ for instance, who compared the sorption ability of the SiO₂ surface covered with an alkyl monolayer with respect to eight polyacrylate specimens (sorbates) to which different number of dodecyl radicals was grafted.

2. The role of complex formation

Coefficient K_e increases if centres arise on the surface and in the bulk of a body which act according to the laws of complex formation: the more stable sorptive complexes, the greater values of K_e .¹⁶⁰ This was cogently shown for the sorption of actinides by sorbents containing organophosphorus substances¹⁶¹ and for the sorbent intended to remove bilirubin from the blood plasma.¹⁶² This fact makes possible the use of ideas of the chemistry of coordination compounds for the interpretation of the sorption, taking into account the fact that the stability of complexes in the bulk or on the surface of the body differs from that in the environment.

Sorbents with centres forming complexes can be selective. For example, the selective adsorption of a lanthanum salt at tetracycline centres is observed if tetracycline hydrochloride is sorbed at zirconium phosphate, and then the resulting sorbent is introduced into a solution of lanthanum, cerium, barium, and thorium salts.¹⁶³ If functional groups based on ethylenediamine or diethylenetriamine are grafted to a matrix of mesoporous molecular sieve MCM-41, a possibility will arise to extract Co²⁺ from its aqueous solution selectively due to the formation of amino complexes in the bulk of grains.¹⁵⁹ The selectivity of sorption depends on the difference in the stability of sorptive complexes. The mechanisms of the processes leading to different stability are similar to those determining the selectivities of homogeneous reactions.

3. Deformation of the electronic structure over adsorption

The electronic structures of sorbate molecules change upon sorption of any type, and the changes can be as substantial as for the formation of chemical compounds.^{140–145} Thus, the deformation of electronic structure of potassium atoms upon the adsorption of the potassium vapour on the face (110) of a GaP crystal is so strong that lines 2p(P) and 3d(Ga) in X-ray electron spectra shift by 1.6 eV at $\theta_j \rightarrow 0.1$.¹⁶⁴

Changes of electronic structure over adsorption affect all atoms of an adsorbed molecule to a greater or lesser extent. However, they are mainly localised on one or several atoms. As a result, some atoms can have great mobility, remaining within a molecule or breaking away from it. In particular, the change of electronic structure affects several atoms connecting the sorbate to the surface over the adsorption of the H₈Si₈O₁₂ clusters at the face (100) of a silicon crystal. The evidence for this is the coincidence of a measured reflection IR spectrum and a calculated one (by the method of density functional).¹⁶⁵

Calculations have shown that an H₂O molecule changes its configuration insignificantly upon its transition on regular adsorption centres localised at the faces (100) of NaCl crystals. But if a molecule of H₂O gets near an anion vacancy in the near-surface monolayer of the crystal, its electronic density changes so much that the molecule dissociates.¹⁶⁶

It has also been shown by the method of density functional that the electronic structure of a thiophene molecule changes to the configuration η^5 upon the sorption on the (010) surface of a crystal of MoS₂.¹⁶⁷ A cleavage of the C–S bond and the hydrogenation take place in this case. It was established by the same method that a hydrogen bond is formed between hydrogen atoms of the molecule of H₂O and any oxygen atoms of the near-surface monolayer (mostly the oxygen atoms of the vanadyl group) upon the adsorption of H₂O molecules on the face (010) of a perfect crystal of V₂O₅. If the sorbent is non-stoichiometric, the electronic structures of H₂O molecules are deformed so that some of adsorbed molecules dissociate.¹⁶⁸ It was shown by the X-ray electron spectroscopy and temperature-programmed desorption that the adsorption of H₂S on the face (100) of a crystal of FeS₂ at 500 K is accompanied by a strong deformation of electron shells of atoms and dissociation of the sorbate molecules. The hydrogen comes further into the bulk of the crystal and sulfur localises near the vacancies of the near-surface monolayer.¹⁵² The molecules of water adsorbed at the surface containing silicon and aluminium oxygen tetrahedra, are deformed to a lesser extent so that one of the protons of H₂O has an increased mobility without the dissociation of the molecules. Such a conclusion was made as a result of the calculation of configuration and normal vibrations of the molecule of water by the Hartree–Fock method.¹⁶⁹

The changes of the electronic structure of the sorbate are specific for the centres of a different sort. This manifests itself, for instance, in the adsorption of CO on the surface of crystals with the composition Cs₂HPW₁₂O₄₈, where the electronic structure of CO changes in different ways depending on whether it is localised on the atoms of cesium or hydrogen. Adsorption bands with maxima at 2165 and 2145 cm⁻¹ emerge in the IR spectra of the sorbate.

The intensity of the former band increases if some of the cesium atoms are replaced with hydrogen ones by changing the conditions of the synthesis of the sorbent.¹⁷⁰

The examples considered above indicate the variety of the forms of adsorption-induced deformation of the electronic structures of sorbate molecules. Information of such deformation is accumulated rapidly, though the general regularities of the response of an electronic structure to the adsorption are not defined concretely.¹⁵⁴

It is worth noting that the observation of $R^1-NHCONH-R^2-NHCONH-R^1$ molecules adsorbed on the graphite by scanning tunnelling microscopy revealed that the contrast in the images of carbamide groups is the same if the hydrocarbon chain contains an odd number of carbon atoms. If the number of the atoms is even, the contrast of these images is different.¹⁷¹ The contrast of the images of the carbonyl group is directly connected with its electronic structure. Therefore, one can conclude that the electronic structure of the sorbate's molecule becomes unsymmetrical with an even number of carbon atoms in the chain. This observation indicates the possibility of a direct microscopic study of some of the peculiarities of the intramolecular distribution of the electronic densities of adsorbed molecules.

4. The relationship between the distribution coefficient and the properties of a body to be sorbed

Experiments have demonstrated that the following condition holds true for some series of sorbates¹⁷²

$$K_e = K_1 \left(\frac{P_s}{P} \right)^m + K_2, \quad (20)$$

where K_1 , K_2 , and m are the characteristic parameters of a series of sorbates, P_s and P are the solubilities (for the sorption from a liquid) or the pressures of saturated vapour (for the sorption from a gas) of the sorbent and sorbate, respectively.

As a rule, $m > 1$ and $K_2 = 0$ in the investigated series. Nevertheless, $m = 1$ and $K_2 > 0$, for instance, for the sorption of α -naphthylamine by the crystals of naphthalene from solutions in various solvents.¹⁷³ Series for which $m = -1$ have appeared in the literature, but this can only be explained by the absence of the equilibrium in the system.¹⁷² Correlation (20) reflects a general tendency for substances with low solubility or pressure of saturated vapour to be sorbed predominantly. The results of quantum-chemical calculations do not conflict with such a tendency, though they show that one can expect a monotonic dependence of coefficient K_e on quantities P_s and P in the case of similar properties of sorbed substances only.^{174, 175}

Numerous facts indicate the importance of the similarity of sorbate's and sorbent's properties. For example, substances whose crystal lattice is similar to the sorbent one for at least one crystallographic direction adsorb better owing to favourable conditions created for the formation and growth of two-dimensional clusters in this case.¹⁷⁶

Inert gases dissolved in water are sorbed by the crystal solvate $SO_2 \cdot 6H_2O$ at $T = 268$ K. In this case, coefficient K_e is monotonically reduced by increasing the difference between the molecular mass of SO_2 and the atomic mass of a gas — Ar, Kr, Xe, and Rn (Fig. 6).¹⁷⁷

A number of admixtures are sorbed by the crystals of germanium and silicon from a melt at the melting point. The smaller the difference in sublimation enthalpy between the sorbed substance and the sorbent, the greater K_e for the formation of solid solutions.¹⁷⁸

Summarising the results of studies,^{172–178} one should note the absence of a determining property, which would uniquely characterise coefficient K_e , among the investigated properties of the sorbate and sorbent. Ratio P_s/P can be considered as such a property as a first approximation. This is indicated by the prevalence of correlation (20). However, the connection of K_e with this correlation is not always unequivocal.

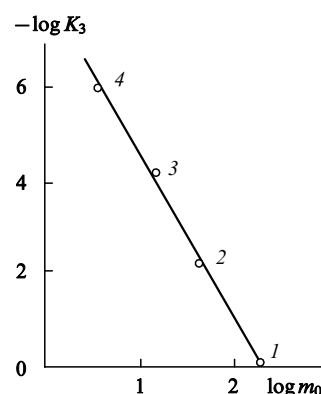


Figure 6. Coefficients of equilibrium sorption by the $SO_2 \cdot 6H_2O$ crystals at 268 K of radon (1), xenon (2), krypton (3) and argon (4) vs. the sorbate atomic mass;¹⁷⁷

m_0 is the atomic mass /a.u.; K_3 is co-crystallisation coefficient.

5. Ways of prediction

The qualitative prediction of function $K_e(y_i, \theta_j)$ is possible based on the regularities of equilibrium sorption mentioned above. The semi-quantitative prediction is performed by analogy, using correlation dependences that are similar to Eqn (20). Another way is to employ approximate calculations of functions $\Delta F(y_i, \theta_j)$ and $K_0(y_i, \theta_j)$ with subsequent application of correlations of the type (19). The calculations are performed with the use of statistical thermodynamics and quantum chemistry.^{179–181}

One aims to determine the values ΔF regarding the resulting interaction of the sorbate and sorbent as a sum of interactions of different types, by considering their influence to be additive.¹⁸² For example, the dispersion, dipole, and pairwise electronic interactions are discriminated while describing sorption.¹⁸³ However, more precise information about the interaction potentials of atoms is required in such a method.

Especially great attention is paid to the calculation of function $K_e(y_i, \theta_j)$ for porous grains.^{184–187} Pores of different diameters and configurations have different sorptive capacities usually. In other words, each of them represents a specific sorbing centre. The assumption that pores and adsorbing centres are distributed over the free energy of sorption continuously could be used without a loss of accuracy if there exist many pores.^{188–190}

The calculations of sorption are carried out for many systems. Nevertheless, some of them deviate from the experimental results sharply.¹⁹¹ Other calculations allowed quantitative explanation of the existing experimental results only, but the new data could be explained at the qualitative level only.

VII. Accompanying phenomena

1. Cosorption on the surface and in the bulk

If a sorbent takes several sorbates up simultaneously, the sorption of each sorbate is rarely additive.^{15, 192} Sorbate particles usually not simply compete with each other for sorbing centres, but also change the sorptive capacity of these centres with respect to their competitors.¹⁹³ If these changes are great, one can speak about negative or positive cosorption of substances. Each cosorption type can be divided into a kinetic one, at which competitors speed up or slow down the sorption of each other, and an equilibrium one, at which they affect not only the rate, but also significantly change the value of K_e .

The range of the kinetic cosorptive effect can be considerable. For example, the rate of the formation of mixed adsorptive layers of $Cu(ClO_4)_2$ and KBr on the faces (100) of a copper crystal in the aqueous medium is so much greater than the rate of the formation of the pure layers of $Cu(ClO_4)_2$ that the adsorption proceeds from the kinetic regime to the diffusion one under the influence of KBr.¹⁹⁴ A powerful negative kinetic effect has been revealed⁹⁰ for

the cosorption of H_2 and Cl_2 on the rearranged (2×1) (001) surface of silicon at 300–1500 K, the initial temperature being 300 K. The molecules of HCl are produced in such an excited state upon the reaction of chlorine and hydrogen adatoms that most of them desorb in picoseconds after the beginning of the contact of the adatoms. The probability of desorption increases to 0.18 in a temperature range from 300 to 1000 K. After that, the probability remains constant, which indicates complex forms of functions $\chi_j(T)$ and $\beta_j(T)$ in formula (10). These functions point out the possibility of cleaning the surface from molecules of one sorbate by the molecules of another one owing to the interaction of the sorbates.

The equilibrium cosorption takes place in different systems. Thus, the sorption of strontium from a hydrothermal solution by Montmorillonite increases by 30% if the Sr^{2+} ions sorb together with Li^+ ions.¹⁹⁵ An analogous positive cosorption of these elements by soils was described by Chitra *et al.*¹⁹⁶

The adsorption of carbon monoxide on SiO_2 from a gaseous phase is negligible under ordinary conditions if the sorbent is not doped with a silver salt. The adsorption is enhanced if the sorbent contains silver. A band at 2169 cm^{-1} has appeared in the IR spectra of the system, which is a characteristic of the Ag–CO bond.¹⁹⁷

The adsorption of polyvinylpyrrolidone on the crystals of $\alpha\text{-Al}_2O_3$ from an aqueous solution at pH 5–7 is enhanced in the presence of polyacrylic acid.¹⁹⁸ The adsorbed molecules of the acid form hydrogen bonds with the polyvinylpyrrolidone. This results in a positive coadsorption. Such a bond changes the conformations of sorbate molecules, which was proved for samples with a spin label by ESR.

At the same time, the biomass of pine bark sorbs substances from a mixture of aqueous solutions of cadmium, copper, and nickel worse than from an individual solution of each salt.¹⁹⁹ A sterilised soil suppresses the sorption of phenanthrene if the soil contains pyrene in a concentration of $5 \times 10^{-4}\text{ mol g}^{-1}$. The pyrene affects the rate of adsorption slightly, but increases the rate of desorption sharply.²⁰⁰

Some sorbents interact with the sorbates, producing microcrystals. This is the case, for instance, for the sorption of $AgNO_3$ from an aqueous solution by copper hexacyanoferrate $Cu_2[Fe(CN)_6]$ (see Ref. 201) or for the sorption of SeO_2 from a gaseous flow by calcium hydroxide.²⁰² An abnormally strong sorption is observed in the latter case in the interval 770–970 K owing to the formation of $CaSeO_4$.

Thus, cosorption is a consequence of chemical reactions between the sorbates in the bulk or on the surface of sorbing bodies where the conditions of reactions of molecules differ from those in the medium surrounding the bodies. Investigating sorption, one can obtain information about the specificity of the interactions of the sorbate molecules in a force field of the sorbent molecules, which is necessary for a directed search for sorbents.

2. Specific features of biosorbents

Biosorbents consist of plant biomass or microbial cells immobilised on supports.^{203–210} Formally, the behaviour of biosorbent grains or separate cells does not differ from that of particles of inorganic sorbents. For example, Madrid *et al.*²⁰⁵ properly predicted the variation of the concentrations of a number of sorbates in a well-stirred reactor containing algae as sorbents. It was found that biosorbents can be characterised by particular diffusion coefficients D_v and by sorption isotherms and that the surface and volume sorption processes can be simulated in the usual way. If the sorbent is a set of identical cells, the membrane, cytoplasm and internal cell organelles should be regarded as its structural units.^{209,210} Sorbate accumulation by cell membrane can be treated as adsorption, while migration of the sorbate inside the cell, as bulk sorption.

Many biosorbents demonstrate selective sorption by separate structural units.²¹¹ For example, redwood bark and moss cells accumulate cadmium, copper and nickel ions from aqueous

solutions by membranes almost without involvement of the cytoplasm.²¹²

The sorption capacities of cells depend on their physiological state but, generally, their 'preferences' do not change.^{213–215} For example, the sorption sequence $Au^{3+} > Cu^{2+} > Ag^+$ always holds for the *Chlorella vulgaris* cells in aqueous solutions. Inside the cells, the sorbed substance undergoes chemical transformations and passes to the colloidal state.

In a study of sorption of various compounds by seeds of legume crops, it was found⁵² that the coefficient K decreases along the series of chromates, molybdates and tungstates: $Cr(VI) > W(V) > Mo(VI)$.

However, no general relationship between the nature of the biosorbent and the D_v or K values has been found so far. Elucidation of this relationship is complicated by strong influence of sorbates on one another^{204,208} and by changes in the sorbate state in the cells or in the physiological state of the cells themselves. The cells or destroyed biomass are to be regarded as 'black boxes'; thus, prediction of sorption becomes groundless, although formally it can provide some results.²⁰⁷

3. Structural memory of sorbents

If sorbate molecules are introduced into particles of a sorbent during its synthesis so that the former can escape to the medium, 'imprints' of the sorbate molecules can be retained in the sorbent structure and may play a role of specific sorption sites for this particular sorbate. The sorbent can 'remember' that the sorbate was present in the system during its synthesis. The 'memory' of inorganic sorbents was discovered long ago.²¹⁶ It has now been proved that organic polymeric sorbents also possess 'memory'; this fact is used successfully for selective and complete removal of side products of organic syntheses.²¹⁷

4. The influence of external fields on sorbents

Recent studies showed that the sensitivity of a sorbent with respect to an electric field can be increased to a practically significant level without deterioration of their sorption properties. For example, sorbents based on titanium phosphate have been developed the sorption capacity of which changes dramatically upon application of an electric field; these sorbents absorb a number of metal ions from aqueous solutions by the ion exchange mechanism and, after that, desorption can be accomplished by merely changing the potential sign.²¹⁸ The application of an electric field accelerates sorbate diffusion inside the bulk of grains.²¹⁹ The field also influences the surface mobilities of atoms; this has been demonstrated, for example, by direct observation in a tunnelling microscope of the behaviour of potassium and sodium atoms on the (100) surface of aluminium.²²⁰

Multiphase sorbents sensitive to acoustic fields have been prepared.^{221,222} The sorbent grains consist of a heat-sensitive polymeric hydrogel, which can undergo a structural phase transition at some temperature T_0 . Microcrystals of a poorly soluble substance with high density are introduced in the polymeric matrix, together with particles of a sorption-active phase. When $T < T_0$, the polymer molecules form a three-dimensional network with large cells, which ensures fast diffusion of the sorbate into the grains.

If the acoustic power is relatively low, the properties of the polymer network do not change on direct exposure to an acoustic field but the microcrystals inside the matrix are heated. They absorb most of the field energy and function as 'internal heaters' for the grains. If the grain temperature increases to T_0 , the polymer molecules are compacted to form denser stacks and the grain permeability decreases abruptly. Once the sound has been switched off and the grain has been cooled to $T < T_0$, the permeability increases again. Thus, the grain responds to acoustic treatment by a triggered transition from one permeability level to another.

New magnetite-containing sorbents have also been prepared. Particles of such a sorbent can move on exposure to a magnetic field.²²³

5. Phase antagonism and synergism in multiphase sorbents

If a sorbent grain contains several phases, they can compete for a sorbate. In this respect, sorbent phases are antagonists. The points where particles of different phases contact with one another can give rise to specific sorption sites with increased K_e values. If this effect predominates over the antagonistic effect, these phases exhibit a synergistic effect.^{224–227} For example, synergism was attained in the synthesis of a fibrous sorbent based on cellulose and zinc or copper ferrocyanide.²²⁴ This sorbent proved to be especially efficient for extraction of cesium salts from aqueous solutions and was recommended for deactivation of natural and technological waters contaminated by ^{137}Cs .

A sorbent based on CuO and $\gamma\text{-Al}_2\text{O}_3$ phases with a large internal surface area of microparticles and a high porosity of grains having a narrow size distribution was prepared by the sol–gel procedure.²²⁷ At 790 K, this sorbent showed a sorptive capacity toward sulfur dioxide of no less than 22.5 mass %, which is much greater than the values observed for other sorbents.

6. The molecular electrical conductivity of adsorbed species

If an adsorbed molecule (a two-dimensional cluster) occurs in a flow of electrons coming to the surface from the bulk, then, with some probability, the electrons adhere to a molecule, remain in contact with it for some period, and then pass to the substrate. Thus, the adsorbed molecule influences the electron flow. This influence can be described by attributing to each molecule an individual electrical conductivity. This parameter can be found by observing separate adsorbed molecules through a tunnelling microscope or by measuring the electric current between electrodes bridged by individual adsorbed molecules. For example, by applying a dilute solution of DNA (the length of the molecule is 10.4 nm) onto two platinum nanoelectrodes located at a distance of up to 8 nm using a special application procedure, one can ensure that one end of the molecule is adsorbed to the cathode and the other, to the anode, thus forming a ‘bridge’ across the gap between the nanoelectrodes.²²⁸ When the electrodes have been dried in a nitrogen flow and the voltage $U = 1\text{--}5\text{ V}$ has been applied, the cathode–DNA–anode circuit carries the current

$$I(U) = \sigma(U - U_\omega), \quad U > U_\omega, \quad (21a)$$

$$I(U) = 0, \quad U < U_\omega, \quad (21b)$$

where $\sigma = 5.3 \times 10^{-10} \Omega^{-1}$ is the molecular electrical conductivity at voltages higher than the threshold value $U_\omega = 1\text{ V}$.²²⁹

The electrical conductivity σ of the DNA molecule is due to tunnelling of electrons through the contact surface between the molecule and the anode and to their one-dimensional diffusion along the molecule.^{228, 230} However, it is not clear yet what are the contributions of these processes to the DNA conductivity.

Relations (21a) and (21b) reflect the threshold character of the molecular electrical conductivity of DNA. Apparently, this is a typical character of the electrical conductivity of molecules of different nature, as follows from the data on the interaction of adsorbed molecules with a flow of tunnelling electrons.

If a molecule is located on the surface of the substrate electrode, a second electrode represented by a spike with a ‘monoatomic’ tip is placed at a distance $R = 1\text{--}5\text{ nm}$, and the voltage U is applied to the spike, then current would flow from the spike to the substrate.^{231–233} The current intensity can be expressed by the relation

$$I(U) = \omega \rho_0 \varepsilon(\rho_0, U, R) [U \eta_1 + (U - U_\omega) \eta_2],$$

where ω is the probability for an electron to pass from the spike to the molecule per unit time, ρ_0 is the electron density of the substrate under the spike before application of the field, $\varepsilon(\rho_0, U, R)$ is the function characterising transition of electrons from the molecule to the substrate, U_ω is the voltage corresponding to the change in the η_1 and η_2 values from $\eta_1 = 1$ and $\eta_2 = 0$ for $U < U_\omega$ to $\eta_1 = 0$ and $\eta_2 = 1$ for $U > U_\omega$.

The threshold voltages U_ω were found for C_2H_2 , CO , benzene and pyridine molecules adsorbed on the surface of copper crystals.^{233–235}

The ω value usually depends slightly on ρ_0 and in the $kT < Ue < \varphi_e$ range (e and φ_e are the charge and the work function of an electron), it can be described by the exponent

$$\omega = \exp\left(-\frac{U_0}{U}\right),$$

where $U_0 = 10\text{--}100\text{ V}$ is the characteristic voltage of the tunnelling field emission.²³⁶ The $\varepsilon(\rho_0, U, R)$ function has a discontinuity at $U = U_\omega$. For $U > U_\omega$, it has several maxima; the $\{U_i\}$ values corresponding to these maxima comply with the condition

$$eU_i \rightarrow \omega_{hi} h,$$

where ω_{hi} is the frequency of a vibrational transition of the molecule or of the substrate below the molecule. This implies that the tunnelling electrons provide a resonance stimulation of vibrations of atoms in the adsorbed molecule, and the vibrations excited by the electrons are synchronised in such a way as to increase the probability of electron transition onto the substrate. The resonance excitation of intramolecular vibrations was found, for example, in the H_2O molecules adsorbed from vapour at 300 K on the surface of titanium oxidised in air.^{231–233} In this case, prior to H_2O adsorption, the $I(U)$ function exhibited maxima corresponding to the stretching vibrations in TiO_2 ($\omega_{hi} h \approx 0.1\text{ eV}$). After adsorption, this function acquired large-scale maxima at

$$e(U_2 - U_1) \approx 0.2\text{ eV},$$

$$e(U_3 - U_1) \approx 0.5\text{ eV},$$

$$e(U_4 - U_1) \approx 0.7\text{ eV},$$

$$e(U_5 - U_1) \approx 1.0\text{ eV}.$$

The first two of these values are close to the quantum energies of bending (0.2 eV) and stretching (0.46 eV) vibrations of adsorbed water molecules (from IR-spectroscopic data). Hence, the other maxima can be attributed to two-quanta and combined vibration transitions.²³³

When H_2O is replaced by D_2O , the positions of the $I(U)$ maxima shift in conformity with the expected isotope effect. This attests unambiguously to the stimulation of intramolecular vibrations by the tunnelling electrons.

VIII. Sorbent degradation

The properties of a sorbent change inevitably during operation as sorbent bodies are gradually dissolved and destroyed upon collisions and chemical reactions with admixtures. The mass of each grain m varies at the rate

$$\frac{dm}{dt} = \beta_{k0} S(c - P_s) - \gamma_k \omega_k m_f + G_k, \quad (22)$$

where β_{k0} is the kinetic coefficient of dissolution, γ_k is the probability of grain fragmentation, ω_k is the frequency of collisions of the grain with other grains or with reinforcing structures, m_f is the average mass of the chopped-off fragments, G_k is the rate of mass variation caused by chemical reactions between the sorbate and the reagents present in the system as impurities.

Each of the above-mentioned paths of the change in the sorbent properties is characterised by the proper time τ_i :

$$\tau_1 = \frac{\bar{m}}{\beta_{k0} S(c - P_s)},$$

$$\tau_2 = \frac{\bar{m}}{\gamma_k \omega_k m_f},$$

$$\tau_3 = \frac{\bar{m}}{G_k},$$

where $\bar{m}$ is the average mass of grains.

The τ_i values can be predicted;^{237, 238} however, the β_{k0} coefficients are unknown for most substances. They should be determined experimentally.

The γ_k value can be estimated using the theory of contact plastic deformation, the frequency ω_k can be determined using the collision theory and m_f is found from the model of fracture of solids.^{239, 240} These values can be appreciably different, depending on the reactor shape and the method of stirring of the suspension. If one deals with a block crystal, chopping-off of blocks is the most probable way of destruction. As a result, the m_f value is similar to the average mass of blocks. If the particle is an agglomerate, the points of accretion of microcrystals are the first to be destroyed upon collisions, thus, m_f becomes equal to the average mass of the separate microcrystal.

IX. The search for an optimum sorbent

The quest for the optimal sorbent is carried out more and more often according to the principle: 'a specific sorbent for each system.' An individual system is characterised by a unique set of $K_e(y_i)$, $\tau_{0.9}(y_i)$ and $\tau_1(y_i)$ functions. The sorbent of choice is one ensuring the specified values of these functions. The best sorbent for a given system is usually selected by searching through the sorbents optimum for similar systems.^{241, 242} If none of these materials is appropriate, the following multistep procedure is executed.

1. Identification of the substance to form the basis of the desired sorbent

At the stage of looking for the substance that would form the basis of the desired sorbent, correlations such as relation (20) are used and the array of materials with rather high K values and low solubility P_s is identified. The K values for each of these materials are determined experimentally and the material with the greatest K is chosen. This material would form the basis of the optimum sorbent.

2. Study of the kinetics of sorption by the disperse phase of the chosen material

When investigating the kinetics of sorption by the disperse phase of the material chosen as the basis for the optimum sorbent, the kinetics of sorbate absorption by the material particles moving freely in the medium should be measured over a broad range of conditions $\{y_i\}$. Using kinetic equations such as Eqns (3)–(11), the $\alpha_j(y_i)$, $v_j(y_i)$, $\lambda_j(y_i)$, and $\tau_{0.9}(y_i)$ functions are determined, while relations of type (13) and (14) are used to determine the $D_v(y_i)$ function. The $\mu_L(y_i)$ and $\rho_L(y_i)$ functions are also found. Using experimental data on sorption for long sorption times and high concentrations of the sorbate and relations of the type (19) and (20), the $K(\theta_j)$ and $\Delta F(\theta_j)$ values are determined and the isotherms of sorption $\theta_j(y_i)$ by the disperse phase are elucidated. The results of measurements are summarised as $G_i(x_i, y_i)$ and $D_{ij}(x_i, y_i)$ dependences [see relations (1) and (2)]. This stage results in quantitative descriptions of the adsorption and desorption, the formation of two-dimensional solid solutions and surface clusters, the formation of multiautomic layers and particles of the sorbate phase on the surface of freely moving sorbent particles, and migration of the sorbate inside the bulk of the chosen sorbent.

3. Study of the role of agglomeration

Agglomerates of particles differing in porosity are studied to identify the effects of contacts between the particles, capillary condensation and crystallisation in the pores on the $K(\theta_j)$, $\Delta F(\theta_j)$ and $\theta_j(y_i)$ functions. By simulating the sorbate interaction with pore walls, the $D_v(x_i, y_i)$ and $K_e(y_i, \theta_j)$ values for agglomerates can be determined.

The results of investigation of the kinetics of sorption by the disperse phase of the material chosen as the basis of the optimum sorbent and study of the role of agglomeration are generalised as kinetic equations of sorption of the type (1)–(13) devoid of arbitrary assumptions concerning the parameters of elementary steps in the sorption by separate particles and their agglomerates.

4. Determination of the rate of sorbent degradation

The rates of dissolution, fragmentation and chemical degradation of the sorbent for the most drastic operation conditions are determined using Eqn (22), and the $\beta_{k0}(y_i)$, $\gamma_k(y_i)$ and $G_k(y_i)$ functions are found. The ways of sorbent modification aimed at increasing its chemical and mechanical stability are developed.

5. Numerical experiment

The kinetic equations of sorption supplemented by edge conditions for the whole range of $\{y_i\}$ parameters formulated as a closed boundary problem are usually solved by numerical methods. The results are presented as the following functions:

$$K_e(x_{0i}, y_i, t_k), \tau_{0.9}(x_{0i}, y_i, t_k), \tau_i(x_{0i}, y_i, t_k),$$

where x_{0i} are parameters for the state of sorbent grains before use, t_k is the time period during which operation of the sorbent is planned.

These functions allow one to answer the question what properties are demanded of the initial sorbent for this sorbent to be regarded as optimal. At the stage of numerical experiment, the $\{x_{0i}\}$ values are found.

6. The nearest goal of the search

The stepwise procedure outlined above has been implemented thus far only for systems that are most important for practical purposes. Most often, in choosing the sorbents, the material that provides the most complete, fast and selective sorption and can be recovered from the medium over the shortest period of time is assumed to be the sorbent of choice.

These conditions are met by a sorbent with dendrite-shaped grains consisting of accreted filamentary nanocrystals forming a highly porous texture. The surface of nanocrystals bears functional groups capable of forming complexes as stable as possible with the given sorbate. The structure of nanocrystals allows the sorbate molecules to be inserted into interstices with a high K coefficient. Judging by the experimental results presented above, grains of such a sorbent would form highly porous filter layers characterised by low fluid-flow resistance, high velocity $\vec{v}_L$ and approximately equal accessibilities of grain surfaces for a sorbate and would ensure favourable conditions for adsorption of sorbate molecules on nanocrystals and diffusion of molecules into their bulk.

X. Conclusion

Analysis of the published data shows that the research into sorption is approaching a new stage of development which can be termed as the molecule visualisation stage. There are grounds to expect that the gap between macroscopic and molecular description of sorption would be filled. By the beginning of this stage, conditions have been created for experimental investigation of all elementary processes taking place on the surface and in the bulk of sorbent bodies. To date, these opportunities have not been exploited to a degree sufficient for the elaboration of a theory of sorption able to describe the whole set of elementary processes. Therefore, it is still impossible to predict quantitatively the behaviour of sorbents over a broad range of sorption conditions.

The current level of detail in the description of sorption makes it possible to compose a particular plan for the accumulation of data sufficient for quantitative prediction of the sorbent behaviour under various sorption conditions on the basis of *a priori* semiquantitative estimates ('by analogy').

This plan should include theoretical analysis of the possible variants of implementation of sorption processes and accumulation of missing experimental results. Theoretical analysis implies the solution of evolution equations that describe the variation of the sorbent state during the synthesis and operation, while experimental studies are aimed at 'information loading' of the evolution equations.

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Polyurethane foams in chemical analysis: sorption of various substances and its analytical applications

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Abstract. Data on the sorption properties of polyurethane foams including their modified forms are surveyed. Examples of application of polyurethane foams for the separation and preconcentration of inorganic and organic compounds are given. The mechanisms of sorption on polyurethane foams described in the literature are analysed. Advances in the development of combined and hybrid methods of analysis with the use of these sorbents are discussed. The bibliography includes 259 references.

I. Introduction

Polyurethane foams (PUF), or foamed polyurethanes, represent an extensive class of synthetic materials prepared from polyurethanes — heterochain polymers that contain urea, amide, ether, ester, or other groups in addition to urethane groups. Polyurethanes were first synthesised by Bayer and co-workers in 1937.¹

Later, industrial production of PUF was started on the basis of these polymers and polyesters or their analogues (Germany, 1944) and, subsequently, on the basis of cheaper polyethers (USA, 1957). Currently, PUF are produced in large amounts (millions of tons a year) in many countries all over the world. Polyurethane foams (in the household, these materials are called foam-rubbers) are widely used for domestic purposes: to produce soft furniture, car seats, mats, sponges, toys, and so on. In industry, PUF are employed as damping and heat insulating materials. Some similarity between the characteristic functional groups present in polyurethane molecules and in macromolecules forming living tissues provides grounds for assuming that PUF-based materials would be promising for use in medicine, all the more so, because polyurethane fibres have long been used in surgical practice as sutures and for the manufacture of vessel prostheses.

The possibility of using PUF as sorbents for extraction of metal ions and organic compounds from water and air was first established by Bowen in 1970.² Two years later, Braun and Farag

proposed the use of PUF as solid polymer matrices for immobilisation of various organic reagents.^{3,4} Since the mid-1970s, PUF have been used in analytical chemistry for preconcentration of inorganic and organic compounds from aqueous solutions or air and for the development of combined or hybrid analytical techniques. During the elapsed time, vast amounts of experimental information dealing with sorption by means of unloaded and loaded PUF has been accumulated and data on sorption mechanisms have been gained. The following practical applications of PUF have become traditional and most important: separation of mixtures in which elements and compounds are present in comparable amounts; isolation of components for preconcentration and subsequent determination directly in the sorbent phase using neutron-activation analysis, X-ray fluorescence, photometry, or another method; and isolation of components for preconcentration and subsequent determination in the eluate phase using chromatography, spectroscopy, or some other analytical technique.

The application of PUF in analytical chemistry is the subject of a monograph⁵ (difficult to access for a Russian reader) and several reviews,^{6–10} which, however, do not cover all applications of this class of sorbent. In addition, after the publication of the latest of the above-mentioned works (1992), the number of studies dealing with this topic has substantially increased and new trends in the use of PUF in chemical analysis have taken shape. This has stipulated the need for generalisation of the accumulated data at a qualitatively new level taking into account, first of all, the modern views on the mechanisms of sorption on PUF and the properties of these sorbents.

II. General characteristics of polyurethane foams

Polyurethane foams are prepared by polycondensation of isocyanates with polyols (glycols, triols, polyethers, or polyesters) followed by foaming of the polymer bulk by carbon dioxide. Polyether and polyester foams can be distinguished. In the industrial synthesis, polyethers with terminal OH groups and molecular masses of 400–6000 are used most often as the initial compounds, together with mixtures of 2,4- and 2,6-toluylene diisocyanates in 65:35 or 80:20 ratio. In the one-step process, diisocyanate, polyether resin, water, catalysts, stabilisers, and emulsifiers are mixed simultaneously. The reaction takes place immediately; foaming starts several seconds after mixing and is over after 1–2 min. Toluylene diisocyanates play an especially important role in the synthesis of PUF. The reaction between

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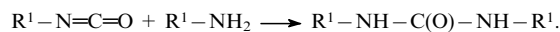
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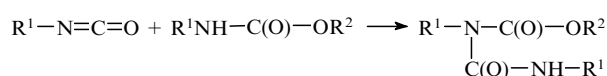
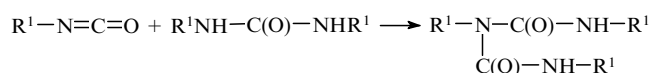
polyhydric alcohol and isocyanate is a chain propagation reaction, resulting in urethane derivatives



The reaction of isocyanate with water yields amine and carbon dioxide, which foams the polymer. Amine can react with excess isocyanate to give substituted urea derivatives



Isocyanate can also react with urea and urethane derivatives giving rise to allophanate and biuret, which induce additional cross-linking of the polymer:



Depending on the number of cross-links, flexible and rigid PUF are distinguished. The materials with low cross-linking density are called flexible PUF, while rigid polymers are characterised by high cross-linking density. Flexible PUF are usually synthesised from polyhydric alcohols with not very high molecular mass and low degrees of branching, while rigid ones are prepared from highly branched alcohols with low molecular mass. Detailed information on the synthesis of PUF can be found in monograph.¹

Foamed polyurethanes contain different functional groups, namely, urethane [$-NHC(O)O-$], ether ($-O-$), ester [$-C(O)-O-$], amide [$-C(O)-NH-$], urea [$-NH-C(O)-NH-$], and terminal toluidine [$-C_6H_3(CH_3)NH_2$] groups and also both aromatic ($-C_6H_4-$) and aliphatic ($-CH_2-$) groups. The diversity of functional groups in the flexible polymer chains of PUF creates favourable conditions for the formation of intermolecular (secondary) bonds of various chemical natures and with different energies (ranging from van der Waals to hydrogen bonds), which has a substantial influence on the physicochemical properties of the materials.^{11, 12} The hydrogen bonds arising upon the interaction of hydrogens of the proton-donating urethane groups with oxygens of the proton-withdrawing ether, ester or carbonyl groups play an especially important role. The type of hydrogen bond depends on many factors, in particular, on the proton-donating and proton-withdrawing capacity of groups, their concentrations and distribution along the polymer chain and on the steric conditions of the formation of the H-bonds. Exhaustive information on the types of hydrogen bonding has been obtained by IR spectroscopy.¹³ Study of IR absorption of polyurethanes of different chemical structures in the region of NH stretching frequencies showed that most of the NH groups in polyurethanes are involved in hydrogen bonds. The vibration frequencies of NH groups perturbed by hydrogen bonding are different in the spectra of PUF based on polyethers and polyesters. This may be due to different types of H-bonding in these systems. From analysis of the IR spectra, it was concluded that the major type of hydrogen bond in polyester-based polymers is that between the hydrogen atom of the urethane group and the carbonyl oxygen of the ester group, while in the polyether foams, this is the bond between the urethane-group hydrogen and oxygen of the polyether chain; the hydrogen bond involving ether oxygen is stronger.¹³

Due to the strong hydrogen bonds which form in PUF a continuous three-dimensional network, in certain cases, linear polyurethanes, cross-linked only through physical bonding exhibit properties normally typical of chemically cross-linked linear chains.¹³ Yet another structural feature of the three-dimensional network formed in PUF is lability. The ability of the

network to be destroyed and reconstructed on heating, treatment with solvents or mechanical stresses suggests that this network can be likened to thixotropic structures, well-known in colloid chemistry. The presence of the labile structural network accounts for many specific properties of PUF. For example, the tensile and compression strengths of PUF are believed to be mainly due to the presence of intermolecular interaction. In the case of pronounced deformations (bending, stretching, *etc.*), the secondary bonds are destroyed, while the primary (chemical) bonds remain intact. Evidently, the ability of polyurethanes to 'heal' the defects arising upon deformations can be explained by the relative ease of network destruction and subsequent restoration. Therefore, after multiple compression, PUF is softened and its initial strength is restored after a certain 'rest'.¹¹

Polyurethane foams are foamed plastics in which some of the solid has been replaced by gas, usually air, which exists in the polymer as numerous bubbles (cells). Depending on the relationship between the rate of the macromolecule growth and the rate of gas evolution at the foaming stage, the cell walls are either broken (ruptured) or not; this gives rise to polymers with open-cellular or closed-cellular structure, respectively. As a rule, flexible PUF have an open-cellular structure and rigid ones are characterised by a closed-cellular structure. If the volume occupied by gas bubbles is less than 76% of the total volume of the specimen, the bubbles can be spherical; if this volume is greater than 76%, the bubbles are shaped most likely as quasi-spherical polyhedra, mainly, pentagonal dodecahedra.^{5, 6, 9} The polymer itself forms the walls of the bubbles, which are actually polyurethane membranes. In open-cellular PUF, at least two membranes (faces of the pentagonal dodecahedron) are ruptured.

Among the properties of PUF, one should mention the lightness (the apparent density is $0.015-0.045 \text{ g cm}^{-3}$), enhanced stability against thermooxidative destruction ($180-220^\circ\text{C}$), and chemical and radiation stability. The properties of PUF do not change (not counting the reversible swelling) on contact with hydrochloric (up to 6 M), sulfuric (up to 4 M), nitric (up to 2 M), or glacial acetic acid, solutions of sodium hydroxide or ammonia (up to 2 M), and many organic solvents such as benzene, tetrachloromethane, chloroform, diethyl ether, other ethers or esters, methyl isobutyl ketone, alcohols. Polyurethane foams based on esters are less stable in acidic or alkaline media than those based on ethers because the former are more susceptible to hydrolysis. Both types of PUF are soluble in concentrated sulfuric acid or a hot solution of arsenic(III) chloride; they are destroyed on treatment with concentrated nitric acid and oxidised by an alkaline solution of $KMnO_4$.²

Estimation of the purity of PUF of various brands showed that the content of inorganic impurities in them is comparable with or even less than that in other sorbents such as active (activated) carbons, synthetic ion exchange resins or chelating sorbents.⁵ It was found by neutron activation analysis that the major impurity in PUF is tin, its content being substantially lower in polyester PUF.¹⁴ This may be due to the fact that organotin catalysts are used in the synthesis of PUF based on ethers. In addition, small amounts of Na, Mg, Al, Mn, V, Cl, Br and I have been found in PUF.

The organic impurities extracted from industrial PUF specimens by various methods, namely, on treatment with solvents,^{15, 16} by thermodesorption^{17, 18} or by supercritical fluid extraction¹⁹ have been identified by a combination of gas chromatography and mass-spectrometry techniques. The impurities were mainly toluylene diisocyanates,¹⁵ various aliphatic and aromatic amines^{16, 18} and fluorocarbons (Freons).^{17, 19} The composition of the impurities depends on the solvent used and on the features of the PUF manufacturing process.[†]

[†] It is known¹ that amines and Freons are used as catalysts and as additional foaming agents, respectively, in the production of some sorts of PUF.

The specific surface area of PUF can be determined from isotherms of low-temperature adsorption of nitrogen^{20, 21} or carboxy-¹⁴C-stearic acid.²² The specific surface areas of the PUF specimens studied were 0.007–0.035 m² g^{−1}, which is much smaller than the values found in sorbents such as Tenax GC (6.4–25 m² g^{−1}) or XAD-2 (300–360 m² g^{−1}).

As applied to PUF, a method for the estimation of the microenvironment hydrophobicity, based on the interfacial partition of pyrene between water and the medium to be tested, has been developed.²³ The partition coefficient of pyrene between the sorbent and water, aqueous acetonitrile or aqueous ethanol is used as a measure of hydrophobicity. A comparative estimate of the surface hydrophobicities for six industrially manufactured specimens of PUF based on ethers and esters and for other sorbents such as Diasorbs C₄, C₈, C₁₆, phenyl and carboxyl, XAD-8, cellulose, cellulose triacetate and activated carbon AX-21 showed that the PUF specimens studied are characterised by approximately equal surface hydrophobicities and that, regarding this parameter, they should be placed between Diasorb C₁₆ and activated carbon AX-21.

Fluorescence spectroscopy has been demonstrated to provide extensive possibilities in investigations of the properties of polyurethane foam membranes.^{24, 25} Using pyrene as the fluorescence probe, the polarity of the pyrene microenvironment (ϵ_{ef}) in the matrix of various PUF has been estimated.²⁴ For low degrees of filling of the sorbent phase (0.3–0.9 $\mu\text{mol g}^{-1}$), the ϵ_{ef} value ranges from 24 to 39, polyether PUF being less polar than polyester PUF; for high degrees of filling of the sorbent phase (4.2–5.6 $\mu\text{mol g}^{-1}$), the polarity of the pyrene microenvironment decreases, the ϵ_{ef} values being 10–19 for polyester PUF and ~ 2 for polyether PUF. The polarity of the pyrene microenvironment in the matrices of protonated PUF proved to be higher than those for the initial PUF. The data on quenching of the fluorescence of pyrene sorbed on PUF by quenchers of different natures, namely, potassium iodide and bromoform, gave rise to the suggestion that solid-phase foamed polyurethane membranes contain polar and hydrophobic microregions characterised by different physical properties.²⁵ Lower values for the calculated Stern–Volmer constants for pyrene in the PUF matrix compared to the values for aqueous solutions point to a decrease in the mobility of pyrene and quencher molecules, related, first to the their transition to a thicker medium and, second, to the rigid fixing of these molecules at particular sections of the polymer chain. The fact that the pyrene molecule is rigidly fixed in the PUF matrix is also indicated by the absence of the excimer band in the fluorescence spectra of pyrene sorbates, even when it is sorbed from suspended media.²⁵

In a study of the protolytic properties of PUF, it was shown that stepwise protonation of PUF takes place in aqueous solutions of mineral acids (pH < 3).^{25, 26} The protonation constants were calculated; it was suggested that the terminal toluidine groups in the PUF molecules are the first to be protonated.

Thus, PUF are foamed plastics with a ‘membrane-like structure’ characterised by a relatively low specific surface area and high chemical stability and purity.

III. Sorption of elements and organic compounds on unloaded polyurethane foams

1. Sorption of elements

At present, the sorption of ~ 50 elements on unloaded PUF has been studied. Most often, PUF adsorb elements as metal acido complexes,[‡] more rarely, as heteropolyacids, ion associates or metal chelates. Sorption in the form of metal acido complexes is observed for most elements able to form negatively charged halide, cyanide, and thiocyanate complexes (Table 1). Sorption of chloride and thiocyanate metal complexes is the most wide-

Table 1. Sorption of elements by unloaded PUF from solutions in mineral acids.

Sorbable forms of elements	Element	Ref.
MF ₆ [−] MCl _n ^{q−n}	Nb, Sb, Ta	27–30
	Au	2, 31–34
	Fe	2, 33, 35–40
	Ga	2, 20, 33, 35, 36, 41
	Pt	42–45
	Rh	46, 47
	Sb	2, 48
	Sn	21, 33
	Te	49
	Tl	50, 51
	Ag, Au	2, 52
	Te	49
MBr ₄ [−]	Bi	39, 53
MI ₄ [−]	Au	54
M(CN) ₄ [−]	Au, Fe, Ga, Hf, In,	33
M(NCS) _n ^{q−n}	Mo, Nb, Pa, Sb, Sc,	
	Sn, Ta, W, Zr	
	Cd	55
	Co	56–67
	Cu	39, 66
	Fe	55–57, 60, 63, 64,
		66, 68–70
	Ga	33, 71
	Hf, Zr	33, 72
	Hg	14, 73, 74
	In	14, 33, 73
	Ir, Rh	75, 76
	Mo, W, Te	39, 66, 71, 77
	Os, Ru, Pd	78, 79
	Pd	60, 80, 81
	Pt	82
	Ti	83
	Zn	55, 57, 73, 84, 85
UO ₂ (NO ₃) ₂	U	2, 36, 86, 87
H _n MMO ₁₂ O ₄₀	As	88, 89
	Ge	90
	P	91–95
	Si	90, 91, 95

spread. Data on the sorption of fluoride,^{27–30} bromide,^{2, 49, 52} iodide^{39, 53} and cyanide⁵⁴ complexes are scarce.

The sorption of metal acido complexes is carried out both from solutions of hydrohalic acids and from mixtures of alkali metal salts with mineral acids, for example, LiCl–HCl, KNCS–HCl and KNCS–H₂SO₄. The use of these mixtures is especially typical of sorption of thiocyanate complexes. The time required for sorption equilibrium to establish depends on the nature of the sorbed acido complex and varies from several hours (for metal chloride complexes) to 10–30 min (for thiocyanate complexes).

It should be noted that the conditions for sorption of metal acido complexes on PUF are the same as conditions for extraction of these complexes with oxygen-containing solvents, in particular, diethyl ether. Polyurethane foams adsorb metal acido complexes as one- and two-charged anions of the composition MF₆[−], MX₄[−] [X = Cl, Br, I, CN, NCS and M(NCS)₂^{2−}] with high partition coefficients ($n \times 10^2$ – $n \times 10^4$ ml g^{−1}). The sorption capacity is also high, varying from ~ 0.2 to ~ 2 mmol per gramme of the sorbent, which makes up to 10% of the sorbent weight. As a rule, PUF based on polyethers sorb metal acido complexes better than polyester foams. The metal acido complexes can be quantitatively desorbed from PUF on treatment with acetone or dilute solutions of hydrohalic acids.

[‡] Acido complexes are complexes containing only acid anions as the ligands.

Sorption on PUF of acido complexes of platinum group metals has some specific features. Thus Rh(III) and Ir(IV) are poorly collected from thiocyanate solutions at room temperature; however, after short-term heating to 90 °C, sorption of these metals becomes quantitative.⁷⁶

The selectivity of PUF with respect to chloride and, especially, thiocyanate metal complexes is relatively low and depends on sorption conditions, namely, solution acidity, supporting salts and other substances present in the solution. The sorption of metals from fluoride solutions proved to be more selective. Polyurethane foams quantitatively collect Ta(V) and Sb(V) from 0.1–5 M HF as MF_6^- complexes and do not adsorb Co, Zn, Fe(III), Hf, Zr, Sn(IV), Nb, Pa, As(V), Mo, or W.^{27, 28}

Apart from metal acido complexes, PUF quantitatively sorb some elements, for example, As, Ge, P and Si, as heteropolyacids (see Table 1). In this case, too, the conditions of sorption of heteropolyacids on PUF coincide with conditions of their extraction with oxygen-containing solvents.

Like crown ethers and acyclic polyethers, PUF collect alkali and alkaline earth metals^{59, 96–98} as well as Ag, Pb and Tl(I)^{59, 98} in the form of ionic associates with large hydrophobic anion partners such as picrate or anilidonaphthalenesulfonate. The sequence of sorption of metal picrates is in agreement with the series of extractability of these metals with crown ethers, for example, 18-crown-6 or dicyclohexyl-18-crown-6. Polyether foams are better sorbents for these metals than polyester-based PUF.

The possibility of sorption of metal chelates on unloaded polyether type PUF has been demonstrated. Thus Hg, Pt(II) and Zn are sorbed as complexes with dithizone,^{2, 99} Y is sorbed as a complex with 8-hydroxyquinoline,^{100, 101} and Cd, Fe(II) and Eu, as complexes with 1,10-phenanthroline.^{102–106}

2. Sorption of organic compounds

The interest in the use of PUF as sorbents for preconcentration of organic compounds is in many respects due to a study¹⁰⁷ demonstrating that ether-based PUF collect quantitatively polychlorinated biphenyls (PCB) from large water samples. In the subsequent years, several dozens of publications have been devoted to sorption on PUF of polycyclic aromatic hydrocarbons (PAH), PCB, phenols and some other organic compounds from various water^{108–112, 125–127, 137–145, 147, 150–174} and air^{113–124, 128–136, 146, 148, 149} samples (Table 2).

It was found in relation to aromatic compounds that the partition coefficients of substances between PUF and the aqueous phase are proportional to their partition coefficients for the extraction into diethyl ether.¹⁰⁸ Similar results were obtained in a comparison of sorption of 59 organic dyes (triphenylmethane, xanthene, sulfophthalein) by polyurethane foams from water or aqueous ethanol with the extraction of the same compounds into diethyl ether or ethyl acetate.¹⁶⁰ Sorption of dyes depends on the nature, the structure, and polarity of the dye. The pattern of the dependence of sorption of ionising organic compounds (phenols and carboxylic acids) on the solution pH attests that these compounds pass to PUF as neutral species.^{108, 137, 138, 141, 142}

The efficiency of sorption of anionic^{105, 171} and cationic surfactants¹⁷² and 4-nitrophenylazo derivatives of phenols^{161, 163, 164} increases if they are collected as ionic associates with large hydrophobic counter-ions. In this case, sorption is substantially dependent on the hydrophobicity of the cationic and anionic components of the associate, the size and charge of the ions they contain, the concentration and the nature of the counter-ion, the composition of the aqueous medium, and the chemical structure of the sorbent.^{25, 105, 167–169}

The capacity of PUF with respect to volatile organic compounds sorbed from air has been studied to elucidate the dependence of the volume before breakthrough on the key parameters of the process: flow rate of the mobile phase, temperature, sample volume and some other.^{114, 115, 119–121, 129, 130} The relationship between the size of the PUF block, the volume of the air under analysis and the volume before breakthrough has been elucidated in relation to PCB. It was found that PUF blocks with thicknesses of 4 and 7 cm collect 90% of PCB from 500- and 900-m³ air specimens, respectively.¹³⁰ It was noted¹³² that a 15 cm-thick PUF block completely absorbs hexachlorobenzene, 3,3'-dichlorobiphenyl and 2,4',5-trichlorobiphenyl impurities from air specimens with volumes of 250, 330, and 2880 m³, respectively. Pankov¹¹⁹ demonstrated that the relationship between the specific retention volume of a compound on PUF ($v_{g, 293}$) and the vapour pressure ($p_{L, 293}^0$) of the pure target compound is described by correlation equations:

$$\log v_{g, 293} = -1.195 \log p_{L, 293}^0 - 1.884 (r^2 = 0.989, \text{PAH})$$

and

$$\log v_{g, 293} = -1.059 \log p_{L, 293}^0 - 1.764 (r^2 = 0.950, \text{PCB}),$$

where r is the correlation coefficient.

Table 2. Sorption of organic compounds by unloaded PUF.

Type of compound	Sorbable compounds	Ref.
Aromatic hydrocarbons	monocyclic aromatic compounds	2, 108
	polycyclic aromatic compounds	109–125
	polychlorinated biphenyls	107, 124, 126–136
Hydroxy-containing aromatic compounds	phenols	2, 108, 122, 137–142
	carboxylic acids	108
	alcohols	143, 144
Esters	esters of phthalic acid	145, 146
	esters of acetic acid	147
Insecticides	organochlorine	127–129, 133, 148–150
	organophosphorus	133, 151–157
	acaricides	158, 159
Dyes	azo dyes	160–166
	xanthene	160, 167
	acridines	160, 168
	sulfophthalein	160, 169
	other	160, 166
Other compounds	anionic surfactants	105, 170–172
	cationic surfactants	172, 173
	alkylammonium salts	174
	bilirubin	175

A number of studies have been devoted to the transport of phenols¹⁴¹ and organic dyes¹⁶⁶ through thin polyurethane membranes. Using a polyurethane membrane, ethanol has been isolated from aqueous solutions.¹⁴⁴

3. The mechanisms of sorption on unloaded polyurethane foams

A critical analysis of the views on the mechanisms of sorption of metal complexes on PUF has been reported in a monograph⁵ and in a review.¹⁰ The mechanisms discussed as the most probable ones include extraction, anion exchange, cation chelation, ligand exchange and ligand addition mechanisms.

The views on the extraction mechanism, proposed by Bowen in his first study² and confirmed subsequently by other researchers are underlain by the fact that the conditions of extraction of metal acido complexes into diethyl ether are similar to the conditions of sorption of these complexes on PUF. The relatively high sorption capacity of PUF calculated on the basis of sorption isotherms of Au(III),² Fe(III),^{2, 38} Hg,⁷³ Sb(V)⁴⁸ and Te⁴⁹ halide complexes and some ions (0.5–1.5 mmol g⁻¹) with relatively low specific surface area (0.03–0.08 m² g⁻¹) is regarded as evidence supporting this mechanism. Experimental data concerning the transport of Ga,^{20, 36} Fe(III)^{36, 37, 40} and Au(III)³⁴ halide complexes and uranyl nitrate^{36, 86} through polyurethane membranes indicate that the membranes collect compounds not only due to adsorption but also due to absorption processes. A layer-by-layer microscopic study of polyurethane foam membranes after sorption of coloured compounds, for example, iodine showed that they are uniformly distributed throughout the sorbent bulk rather than concentrated on the surface.² In several studies devoted to sorption of Ga,^{20, 35} Fe(III),^{35, 38} Sb(III, V)⁴⁸ Sn(II, IV)²¹ chloride complexes and Co and Fe(III)⁵⁶ thiocyanate complexes, PUF are characterised as solid polymeric analogues of oxygen-containing solvents.

Extraction of metal acido complexes by polyurethane foams increases in the presence of alkali metal salts, *i.e.*, a salting-out effect is observed, which is usually typical of liquid extraction. For example, when polyether-based PUF are used, the partition coefficient of Sn(IV) from 3 M HCl does not exceed 140 cm³ g⁻¹, whereas for a solution containing 10 M LiCl and 0.12 M HCl, this value is 5600 cm³ g⁻¹ (see Ref. 21). A similar increase in the partition coefficient was also observed for PUF based on polyesters; however, the values are much lower in this case, namely, 120 and 730 cm³ g⁻¹, respectively.

Actually, the extraction mechanism proposed in early studies^{20, 35–37, 48} reflected the known ability of polymers to dissolve metal salts and organic compounds, which was later (1982) called solid-phase extraction,¹⁷⁶ but did not disclose the factors that made this dissolution possible.

Even the first investigations of the sorption properties of PUF showed that these sorbents possess low anion-exchange capacity. It has been suggested^{2, 20} that these properties appear due to protonation of the electron-donating nitrogen and oxygen atoms incorporated in PUF macromolecules. Since the basicity constants of the groups present in the foamed polyurethane units are rather low, it has been considered that PUF can exhibit anion exchange properties only in highly acidic solutions.

In 1982, a cation chelation mechanism was proposed,⁵⁹ which provided a different interpretation of the anion exchange properties in PUF. In a study of sorption of thiocyanate metal complexes and some organic anions (in particular, picrate) in the presence of various salts, the researchers concluded⁵⁹ that polyester-based PUF exhibit complexing properties with respect to alkali and alkaline earth metal cations, Ag, Tl(I), Pb, NH₄, RNH₃⁺, and H₃O⁺. When binding cations, neutral macromolecules of foamed polyurethane are converted into macrocations with variable charge density. To maintain neutrality, an anion should be bound (or exchanged) together with the cation. Sorption of metal acido complexes and organic anions by polyether-type polyurethane foams increases in the sequence

Li < Na < Cs < Rb < K < NH₄ < Ag, Tl(I) << Ba < Hg < Pb. Since the same sequence was observed for the sorption of these substances by many crown ethers¹⁷⁷ and acyclic ethers,^{178, 179} it was suggested⁵⁹ that the selective binding of cations is ensured by the polyether segments of PUF, which are able to form a helix around the sorbed cation. To confirm the selectivity of cation binding, the sorption properties of PUF of various types were compared with the extraction capacity of macrocyclic ethers containing polymeric units similar to those found in foamed sorbents.⁵⁹ It was shown that the cation-binding capacity of PUF based on poly(ethylene oxide) is higher than that of PUF based on poly(propylene oxide). The results of a study of sorbates by IR spectroscopy attest in favour of the cation chelation mechanism of sorption of organic compounds on PUF. This study showed the presence of strong interactions between the ether units of PUF and sorbed thiocyanate metal complexes.⁵⁹ The presence of ester groups, which are conformationally more rigid, in the polymer chain of PUF has an adverse effect on the cation binding. This is confirmed experimentally by the facts that the sorption properties of polyester-based PUF are poorer than those of polyether-based PUF and that the pattern of influence of alkali metal halides on sorption changes. The sorption of anions by polyurethane foams based on esters varies according to Hofmeister lyotropic series: Li < Na < K < Rb < Cs.

The cation chelation mechanism has found quite a few advocates. This mechanism is believed to be responsible for the sorption on PUF of Cd,⁵⁵ Co,^{59, 61} Fe(III),⁵⁵ Mo, W, Tc,⁷⁷ Os,⁷⁸ Pd,⁸¹ Pt,⁸² Ru,⁷⁹ Zn,⁵⁵ Zr and Hf⁷² thiocyanate complexes from slightly acidic aqueous solutions and hexachloro platinum and iridium complexes from acetone and ethyl acetate.⁴²

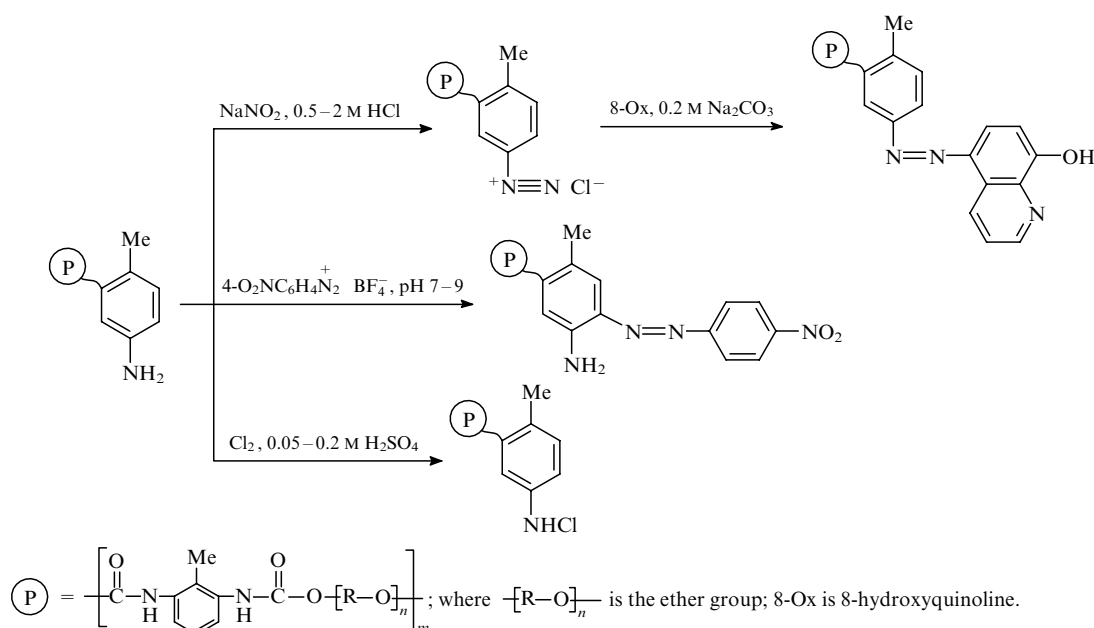
In the ligand exchange or addition mechanism, the polymer segments containing electron-donating nitrogen or oxygen atoms act as ligands able to coordinate metal ions. This 'ligand addition' has been considered to interpret the sorption of yttrium hydroxy-quinolate complexes¹⁰¹ and iron thiocyanate complexes³⁹ on PUF. It was proved using IR spectroscopy that the role of the ligand is played by the urethane group (–CO–NH–).

Sorption of organic compounds on PUF is explained in most cases in terms of the extraction and cation chelation mechanisms. According to the extraction mechanism, PUF are regarded as solid polymeric extractants which dissolve organic molecules in the polymer films that form the framework of these sorbents.¹⁰⁸ A piece of evidence supporting the extraction mechanism is provided by the fact that the efficiency of extraction of organic compounds by polyurethane foams can be increased by introducing inorganic salts in the aqueous solution–PUF system.¹⁰⁸ In the presence of alkali metal salts, sorption efficiency increases in the series: K < Na < Li. Double-charged cations influence the extraction efficiency to a markedly greater extent than single-charged ones, *i.e.*, a salting-out effect typical of extraction is involved. The extraction mechanism has also been used to interpret sorption by polyurethane foams of PAH,¹²⁵ phenols,^{108, 138, 141, 142} cationic dyes^{160, 167, 168} and organophosphorus and organochlorine acaricides.¹⁵⁸

Negatively charged forms of organic compounds such as anionic surfactants,¹⁷² sulfophthalein dyes^{160, 169} and azo dyes^{160, 161} are extracted by PUF by the cation chelation mechanism. This is indicated by the data on the influence of alkali metal and ammonium salts on sorption. Sorption of these compounds increases in the following order: Li < Na < Cs < Rb < K ~ NH₄.

In some publications, the important role of hydrophobic interactions and interactions giving hydrogen bonds in the sorption of organic compounds is noted. A reliable correlation has been established between the main parameter of PAH sorption, the partition coefficient (log *D*), and the hydrophobicity parameter of their molecules [the Hansch parameter defined as the partition coefficient in the 1-octanol–water system (log *P*_{ow})].¹²⁵ Two-parameter correlation equations relating the partition coefficients of phenols to their hydrophobicity parameters and

Scheme 1



medium pK_a values have been proposed.¹⁴² The logarithms of the partition coefficients of cationic surfactant homologues were found to follow a linear dependence on the number of carbon atoms in the alkyl groups of these compounds.^{25, 172}

Thus, various mechanisms of sorption of metal complexes and organic compounds by polyurethane foams have been proposed; each mechanism has its own adherents and has been confirmed by experimental data. A common drawback of the views in these mechanisms is that sorption is idealised. In most cases, consideration actually refers to special cases in which only one process takes place in the system, other processes being entirely suppressed. Meanwhile, real systems normally provide favourable conditions for the simultaneous occurrence of several processes.

4. Chemisorption processes involving polyurethane foams

Experimental data attesting to a previously unknown ability of the terminal toluene groups of PUF to be involved in oxidation, diazotisation and azo coupling reactions have been reported.^{180–182} When PUF samples are brought in contact with aqueous solutions of free active chlorine, sodium nitrite and 4-nitrophenyldiazonium tetrafluoroborate, chemisorption processes take place to give intensively coloured products. The composition of the products was determined using diffuse reflection spectroscopy, elemental chemical analysis and other techniques. The optimal conditions of heterogeneous chemical reactions with participation of PUF and the conjectural composition of the products are shown in Scheme 1.

The introduction of the diazo group into PUF provides activation of these materials toward covalent attachment of functional groups to their surface.¹⁸² Diazotised PUF enter into azo coupling reactions with azo components such as 8-hydroxyquinoline (Scheme 1), 1- and 2-naphthols, phenol, aniline and other compounds to give intensely coloured products. Heterogeneous chemical reactions involving PUF proceed under relatively mild conditions (aqueous solutions, room temperature, atmospheric pressure), the coloured products being rapidly formed at relatively low concentrations of compounds present in the aqueous phase. Therefore, PUF were recommended as new polymeric reagents for determination of free active chlorine and nitrite ions.^{180, 181}

IV. Sorption of elements on polyurethane foams loaded with organic reagents

Polyurethane foams can collect and retain substantial amounts of inorganic and organic compounds. This provides the possibility of

modifying PUF to improve their sorption properties, while preserving the required hydrodynamic characteristics of the material. This is done using oxygen- and nitrogen-containing extractants or chelating organic reagents. The general information about sorption of elements on PUF loaded with various oxygen- and nitrogen-containing extractants and chelating reagents is presented in Table 3. The major application of loaded PUF is preconcentration with subsequent determination of metal ions and organic compounds in waters.

Two ways of immobilising reagents, differing in the method of fixing of compounds in the PUF matrix, have been described, namely, physical and chemical immobilisation. Physical immobilisation is used most often because chemical fixing of reagents, which is carried out during the polymer synthesis, is a more laborious procedure. Organic compounds can be introduced into the foaming material owing to the hydrophobic nature of the polymer matrix and its dissolving capacity with respect to various compounds. Immobilisation of liquid extractants is an exceptionally simple procedure; this is attained by keeping PUF pellets or small cubes in an appropriate liquid extractant or in its mixture with some organic solvent. Excess liquid is then removed and the PUF samples are dried between sheets of filter paper. Foams obtained in this way contain 50 mass % to 80 mass % of an organic compound. Immobilisation is performed for liquid extractants, for example, tributyl phosphate,^{3, 183, 184, 187} trioctylamine,^{196, 197} bis(2-ethylhexyl) hydrogen phosphate,¹⁹² and for solutions of these compounds: tributyl phosphate in benzene,¹⁸⁵ trioctylphosphine oxide in diethyl ether, bis(2-ethylhexyl) hydrogen phosphate in nitrobenzene^{190, 191, 193} or in dichlorobenzene.^{194, 195}

Immobilisation of solid chelating reagents on PUF is carried out using two procedures. According to one procedure, the reagent is dissolved in a non-volatile organic solvent (plasticiser) and physically immobilised on PUF as described above. The other method consists of keeping the polymer in a solution of the reagent in a highly volatile solvent followed by removal of the solvent. In both procedures, it is required that the reactant solubility be rather high. This requirement is readily fulfilled in the second procedure because there is a wide choice of volatile solvents; however, the range of solvents suitable for the first procedure is substantially narrower. The solvents play a dual role in this case: they should efficiently dissolve the reagents and should also act as plasticisers for the polymeric sorbent. Tributyl phosphate^{57, 192, 213, 215} and α -dinonyl phthalate^{57, 209, 225} are used most often as plasticisers.

Table 3. Sorption of elements by polyurethane foams loaded with organic reagents.

Organic reagent	Element	Ref.	Organic reagent	Element	Ref.
Tributyl phosphate	Au	14, 183, 184	dithizone	Ag	211
	Bi	4, 57		Bi	212, 213
	Cr	185		Cd, Cu	214
	Nb	186		Hg	215–217
	Pd	4		Pb	218, 219
	U	162, 187		Zn	212, 218
Trioctylphosphine oxide	U	188, 189	diethyldithiocarbamates	As, Bi, Hg, Pb, Sb, Se, Sn	220–222
Bis(2-ethylhexyl) hydrogen phosphate	Ce	190, 191		Cd, Co, Cr, Cu, Fe, Mn, Ni	222–224
	Th	192		Hg	225, 226
	U	193–195		Sb	227
Trioctylamine	Co	196		REE	228, 229
	U	197, 198	diphenylcarbazide	Cr	230–232
Dibenzoylmethane	U	199, 200	benzoylhydrazone	Cu, Pd	233
Thenoyltrifluoroacetone	Co, Fe	201–203	phenylhydrazine	Mo	234
Dimethylglyoxime	Ni	204–206	dibenzo-18-crown-6	Pb	235
	Pd	207		AM ^a	236
1-(2-Pyridylazo)-2-naphthol	Au	14			
	Cd	57, 208			
	Co	57, 208–210			
	Fe, Mn	57, 209			
	Hg	14, 57, 73, 208			
	In	14, 73			
	Zn	57, 73, 208			

^a AM are alkali metals.

Immobilisation of various chelating reagents on PUF has been described, for example, dimethylglyoxime,^{204–207} 1-(2-pyridylazo)-2-naphthol,^{14, 57, 208–210} dithizone,^{211–219} ammonium pyrolydinedithiocarbamate,^{220, 221, 223} hexamethylenammonium hexamethylenedithiocarbamate,²²⁴ and sodium,²²² diethylammonium²²⁵ and potassium²²⁸ diethyldithiocarbamates. It was shown using numerous examples that the conditions of formation of compounds with PUF-immobilised reagents do not differ from the conditions of reactions taking place in aqueous solutions.

Parameters such as the strength of retention and the uniformity of distribution of the organic reagent in a polymer matrix are little studied. It was only found that on contact with large amounts of an aqueous phase (up to 1 litre), not more than 15% of the reagent is desorbed, whereas on treatment with acetone, ethanol and other organic solvents both the reagent and the resulting complex are removed from PUF almost completely.²¹⁷ It was shown in a study of operational characteristics of PUF loaded with 1-(2-pyridylazo)-2-naphthol,²¹⁰ that an increase in the reagent content leads to a poorer retention of the reagent on contact with water. The optimal amount of the reagent is 1 mass %.

As in the case of unloaded PUF, isolation and preconcentration of compounds on loaded PUF are carried out in either a static or dynamic regime. In the latter case, the flow rate of the analysed solution through the column can vary over a broad range, from 0.1 to 250 ml min⁻¹. The scope of the dynamic preconcentration technique can be extended by using plasticised PUF,^{210, 225} as this allows quantitative collection of the analyte for flow rates exceeding 100 ml min⁻¹. Nevertheless, the solution flow rates used most often are 0.1–10 ml min⁻¹.

Physical immobilisation of organic reagents is usually carried out for polyether-type PUF. No results of comparative studies of the properties of different PUF have been found in the literature; only in one study,²⁰⁹ was it noted that the use of polyether-type PUF allows a 4-fold increase in the solution flow rate with respect to that for the polyester foam in the collection of Co, Mg and Fe using the polymer loaded with 1-(2-pyridylazo)-2-naphthol.

V. Classification of sorption processes involving polyurethane foams

A classification of sorption systems involving PUF has been proposed,²⁵ based on the views of various types of sorbent–sorbate intermolecular interactions developed by Kiselev.²³⁷ According to this classification, three types of sorption systems with participation of PUF can be distinguished, depending on the type of intermolecular interactions between the sorbent and the sorbate (Table 4).

The first type includes unloaded PUF in the polymer chains of which the active centres are represented by hydrophobic hydrocarbon chains and aromatic groups and electron-donating nitrogen and oxygen atoms contained in urethane, amide, ester, ether or terminal toluidine groups.

The second type comprises PUF loaded with alkali metal ions and mineral acids. This modification becomes possible due to protonation of nitrogen atoms incorporated in polar groups (first of all, terminal toluidine groups), which takes place in acidic solutions, due to introduction of cations capable of complexation with polyether (polyester) units in the polymer macromolecule. Upon binding alkali metal or ammonium cations or some other ions, polyurethane foams are converted into macrocations with variable charge density, which depends on the nature of the cation involved, salt concentration, and the nature of the PUF unit. Since this binding is less typical of PUF based on esters, it is possible to increase the selectivity of sorption on passing from polyether foams to those based on polyesters. The properties of the initial polymers would differ from the properties of PUF loaded in this way; thus, the latter can be used to recover negatively charged species.

Finally, PUF, loaded with various organic reagents upon immobilisation of the reagent without covalent bonding with the sorbent belong to the third type.

In the majority of cases, the main role in binding the sorbates on unloaded polyurethane foams is played by hydrophobic interactions and hydrogen bonds. Hydrophobic interactions play

Table 4. Classification of sorption systems with PUF according to the main types of sorbent–sorbate intermolecular interactions.

Type of sorption system	Main types of intermolecular interactions	Groups of compounds sorbed
Unloaded PUF	hydrophobic	polycyclic aromatic hydrocarbons ionic associates containing large hydrophobic cations ionic associates containing large hydrophobic cations and anions ionic surfactants phenols heteropolyacids alkali metal and ammonium salts
PUF loaded with alkali metal ions and mineral acids	hydrophobic + H-bonding H-bonding + donor–acceptor ion–dipole ion–ion ion–ion + donor–acceptor ion–ion + hydrophobic	metal acido complexes heteropolyacids sulfophthalein dyes anionic surfactants 4-nitrophenylazo-derivatives of phenols
PUF loaded non-covalently with organic reagents	chemical bond between the metal and the functional group of the organic reagent	metal complexes with organic reagents

a crucial role in the collection of PAH, associates containing simultaneously large hydrophobic cations and anions and associates containing hydrophobic cations. Compounds of the two first-mentioned groups are sorbed quantitatively on unloaded PUF (95%–99.9%); this can be used to develop procedures for preconcentration followed by spectroscopic determination of these coloured (luminescing) compounds.

The efficiency of sorption of compounds the molecules of which contain polar groups together with hydrophobic fragments is determined by a number of factors, which was demonstrated convincingly in relation to phenols.¹⁴² Of the group of compounds under consideration, either molecules incorporating hydrophobic fragments with Hansch parameters ($\log P_{ow}$ in the octanol–water system) greater than 3 (e.g., 1-naphthol), or relatively strong acids (e.g., 2,4,6-trinitrophenol) can be of interest from the practical standpoint. The main types of intermolecular interactions involved in the binding of strong acids and alkali metal salts include hydrogen bonding and donor–acceptor and ion–dipole interactions. In the case of chemical interactions taking place due to high reactivity of the terminal toluidine groups, chemical individuality of the sorbed molecules is lost upon the formation of surface compounds and, thus, sorption becomes irreversible, unlike the cases described above.

Ion–ion interactions make a crucial contribution to the sorption on PUF loaded with alkali metal ions and mineral acids of compounds such as thiocyanate metal complexes, heteropolyacids, single- and double-charged anions of sulfophthalein dyes, anionic surfactants and 4-nitrophenylazo derivatives of phenols. Binding of negatively charged species to PUF, which has an electrostatic nature, can be enhanced by hydrophobic interactions of anions containing hydrophobic groups. Usually, the compounds listed above are quantitatively sorbed on PUF; most of them, are intensively coloured, which accounts for their high practical significance.

In sorption systems of the third type, PUF function as hydrophobic polymeric matrices that fix organic compounds, the key interactions being due to the formation of chemical bonds between metal ions and functional groups of the reagent.

VI. Analytical application of polyurethane foams

Polyurethane foams are of substantial interest for analytical chemistry. These sorbents are characterised by high efficiency combined with sorption capacity with respect to many classes of sorbates, chemical and mechanical strength and stability against organic solvents. The advantages of PUF include the presence of a membrane structure, which ensures good hydro- and air-fluid dynamics of the sorbents and allows preconcentration of trace

elements and organic compounds from large samples of water and air. These sorbents are relatively inexpensive and readily available.

Sorption on PUF is used for separation, preconcentration and determination of trace elements and organic compounds from water and air. Determination of elements and organic compounds after preconcentration or separation can be carried out by a variety of methods. Most often, preconcentration by sorption is combined with photometry, diffuse reflection spectroscopy, atomic-absorption spectroscopy and chromatographic techniques. Determination can be done either directly in the sorbent or in a solution after desorption of the target components using an appropriate eluent. In some cases, determination is carried out after decomposition of the sorbent on treatment with mineral acids, for example, HNO_3 ¹⁸⁴ or its mixture with HCl .^{44, 54, 192}

1. Separation and preconcentration

The success of preconcentration and separation by sorption on PUF depends on a rational choice of the sorption system, the composition of the aqueous phase and on the procedure used for separation and preconcentration. The practice of preconcentration by sorption on PUF has some specific features differing from those used with other sorbents. Preconcentration and separation of elements and organic compounds on PUF can be performed in either a static or dynamic regime.

Static sorption can be performed in two ways. The traditional procedure is based on shaking (mixing) of the solution to be analysed with a known amount of the sorbent; air bubbles should be necessarily removed from the sorbent. Usually, PUF are used as cubes, cylinders, cylindrical discs or pellets cut out or knocked out of a polymer sheet. According to the second procedure, PUF blocks or discs situated in the solution under analysis are squeezed at some intervals either manually, for example, by the bottom of a glass measuring cylinder, or using a special automatic device.[§]

In the dynamic version of sorption, the solution under analysis is passed through a chromatographic column packed with PUF cubes or cylinders. Various methods for packing the columns have been developed; a vacuum procedure is used most often. In yet another specific method of preconcentration on PUF, called the pulsating column technique, the solution to be analysed is pumped through a sorbent layer located in a glass or plastic medical syringe. Since the sorbent is flexible, the cylindrical polyurethane foam plug can be easily compressed (or released) when the syringe

§ The automatic device consists of an eccentric shaft operated by an engine, which makes one or several glass or plastic pistons move up and down and thus forces the solution through the PUF sample placed under the piston.

piston moves. The pulsating column technique is very convenient regarding process automation in the sorption–desorption regime. More detailed information about different procedures of sorption on PUF from aqueous solutions can be found in the monograph⁵ and in reviews.^{9,10} Various types of samplers used for the collection of organic compounds from air by sorption are described in the same publications.

Numerous studies have been devoted to PUF for the separation and preconcentration of metals, mainly, as acido complexes. Some examples are presented below.

The separation of the Ta–Nb (from 1 M HF), Mo–Re, Mo–Tc (from 0.1 M HF + 1 M NH₄F) pairs on 4.5 × 0.9 cm columns packed by polyether-based PUF (0.27 g of the sorbent) has been described.²⁸ It was shown that Ta, Re and Tc are desorbed quantitatively from the column on treatment with 1 M HNO₃.²⁸ Separation of Ga and Fe in the presence of large amounts of aluminium (1:1000) is attained by sorption from 6–7 M solutions of HCl by polyether-based polyurethane foams.³⁵ Procedures for the separation of binary and ternary mixtures (W–La, W–Al, La–Ga, La–W, Ga–Al, Al–W–Ga and Mo–La–Al)⁷¹ under dynamic conditions using columns packed with 1 g of PUF at a flow rate of 1–5 ml min^{−1} have been developed. The separation is based on different sorbability of elements from thiocyanate solutions, which increases in the series Al < Ga < La < Mo < W. The Mo and La ions are desorbed from the column with acetone, while Al, Ga and W, by 1 M HCl, 2 M NH₃ and an HCl–acetone mixture, respectively.

The difference between the rates of sorption of elements on PUF underlies the procedure of separation of Te and Se.⁴⁹ Tellurium is sorbed quantitatively (> 99%) over a period of 2 min from a solution containing 1 M HCl and 5 M NaBr, while quantitative sorption of selenium requires that the contact time be increased to 2 h.

Procedures for separation of Os from Ru,⁷⁸ Pd from Pt,⁸² Rh from Ir⁷⁶ and Ru from Rh⁷⁹ based on the difference between the rates of formation of thiocyanate metal complexes have been developed. It was found that palladium can be collected at room temperature from a solution (0.002–0.006 M KNCS and 2 M KCl) in the presence of a large amount of platinum (1:20).⁸² To separate Ru from Os or Rh, a 0.3–0.4 M solution of KNCS containing 2 M NaCl is heated for 5 min at 90 °C and the Ru(NCS)₆^{3−} complex is sorbed by polyether-based polyurethane foams. The degree of recovery of Ru is 95%, while Os and Rh are sorbed under these conditions to not more than 5%.^{78,79} For separation of Rh and Ir (0.2 M KNCS + 0.2 M LiCl), the solution is heated for 30 min at 90 °C; as this takes place, rhodium is transferred quantitatively in the Rh(NCS)₆^{3−} complex. The complex is sorbed by PUF to 94 ± 1% and iridium, to not more than 5%. The procedure allows separation of rhodium in the presence of a large amount of iridium (1:5).⁷⁶

The preconcentration of cobalt and iron as thiocyanate complexes from large (up to 1 litre) samples on a PUF-packed column at a flow rate of 30 ml min^{−1} has been described.⁵⁶ The recovery of metals present in a concentration of 1 µg litre^{−1} was 96%. An efficient method for preconcentration of Co, Fe and Zn on 5 × 2 cm columns packed with 1.5 g of PUF (*v* = 5 ml min^{−1}) has been proposed.⁵⁷ It was shown⁷³ that Zn, Hg and In are sorbed quantitatively on a PUF column from a 0.2 M solution of KNCS at pH 2–3 and at flow rates of 25–50, 10–25 and 20–50 ml min^{−1}, respectively. Zinc is desorbed using 1 M HNO₃, and mercury and indium, by 1 M KNCS in 80% acetone. Molybdenum is recovered from sea water using sorption of its thiocyanate complexes on PUF with subsequent desorption with acetone.⁷⁷

A number of studies have been devoted to the use of PUF for the preconcentration of PCB,^{107, 126–128, 153} PAH,^{109, 110, 125} phenols,^{139, 140, 165} organophosphorus and chlorinated acaricides^{158, 159} and organophosphorus insecticides from water. It was noted that PUF offer a number of advantages over other polymeric sorbents and carbons for preconcentration of PAH,

PCB, and chlorine- and phosphorus-containing insecticides present in water.^{118, 127, 132, 135, 136} Polyurethane foam sorbents provide highly efficient recovery and allow a very high sampling rate (up to 800 litres min^{−1}).

2. Photometry

Two variants of using PUF in photometric analysis can be distinguished. The simplest, although not the most popular method is based on the sorption of elements on PUF as coloured compounds, desorption by acetone and spectrophotometric determination in the eluate. A classical example of using this method is determination of Co, Fe, Mo and Cu,⁶⁶ Ti,⁸³ Co,²³⁸ Fe²³⁹ as intensely coloured thiocyanate complexes after desorption from PUF on treatment with acetone. This technique was used to determine iron in glass and ceramic materials.¹⁰³ The method includes the preparation of Fe(II) phenanthroline, its sorption on PUF as an ionic associate with perchlorate ions, desorption by acetone and spectrophotometric determination at 510 nm. The range of iron concentrations determined in this way is 0.05–3 µg ml^{−1}. The method for cadmium determination in industrial zinc oxide specimens is based on the sorption of the [Cd(Phen)₂]²⁺ associate with dithizone as the counter-ion.¹⁰² A method for platinum determination in glass with a limit of detection of 0.1 µg ml^{−1} has been developed.⁹⁹ This includes sorption of the complex with dithizone on PUF, desorption by HCl-acidified acetone and spectrophotometric determination at 530 nm.

In some cases, a different, more suitable reagent is added to the eluate to increase the sensitivity and selectivity of the spectrophotometric determination. A method for determination of cobalt in nickel salts and in steels is based on the collection of cobalt on PUF from thiocyanate solutions, desorption with 80% ethanol and the subsequent determination in the eluate using 2-(2-benzothiazolylazo)-2-cresol.²⁴⁰ The method allows determination of cobalt in the presence of large amounts of Ni, Mo and Fe. A photometric method was described for arsenic determination in glass; the method includes preparation of the oxidised form of molybdoarsenic acid, its sorption on PUF, desorption with 0.1 M HNO₃ and determination in the eluate as the reduced form after the addition of SnCl₂.⁸⁹ A reported⁸⁴ method for determination of zinc in cadmium salts is based on sorption of zinc thiocyanate complexes on PUF, desorption on treatment with water and subsequent determination using 4-(2-pyridylazo)resorcinol. The same principle underlies determination of cobalt in natural waters.²¹⁰ The procedure includes preconcentration of cobalt from a 10-litre sample by sorption under dynamic conditions on a column with PUF loaded with 1-(2-pyridylazo)resorcinol.

The second variant is associated with the techniques of thin layer spectrophotometry, which rationally combines the preconcentration of elements on PUF with direct determination of the absorption of light by the solid phase.^{53, 62, 94, 185, 214, 216, 230} The essence of the method is in the sorption of coloured compounds by a PUF specimen shaped like a thin parallelepiped with dimensions corresponding to those of the cell (2 × 1 × 0.1 cm), transfer of the sorbent into a cell filled with an organic solvent and measurement of the optical density. The solvent serves as an immersion liquid reducing light scattering. Methods have been reported for determination of bismuth as an iodide complex,⁵³ cobalt as the thiocyanate,⁶² phosphate ions as the reduced form of the molybdophosphoric heteropolyacid,⁹⁴ zinc and bismuth,²¹² divalent mercury chloride and phenylmercury chloride²¹⁶ as dithizonates; and chromium as blue peroxochromic acid and a complex with diphenylcarbazine.^{185, 230} However, these methods are characterised by relatively narrow ranges of linearity of calibrating plots and relatively low reproducibility of the results.

Good prospects for the use of PUF in a flow-injection system were first demonstrated in relation to photometric determination of zinc in specimens of biological origin.⁸⁵ In this system, zinc is collected in the 'on-line' mode as the thiocyanate complex on a

microcolumn with PUF (0.3×3 cm, 100 mg of the sorbent), eluted with water and determined with 4-(2-pyridylazo)resorcinol. A flow-injection system has been used²⁴¹ for the photometric determination of aluminium with methyl thymol blue after separation of the interfering ions as thiocyanate complexes by sorption on a microcolumn with PUF (0.3×7 cm, 200 mg of the sorbent). The calibration plot is linear in the $0.25\text{--}2.0$ $\mu\text{g ml}^{-1}$ range, the productivity of the method is 17 samples per hour. Determination of 1 $\mu\text{g ml}^{-1}$ of aluminium can be carried out in the presence of large amounts of iron (1 : 170), zinc (1 : 100), copper and cobalt (1 : 50). This method has been used to determine aluminium in silicates and ores. The same procedure is employed to separate Fe, Cu, Zn and Co in a flow-injection method of determination of nickel in brasses, bronzes and silicates.²⁴² A method for determination of carbaryl with a limit of detection of 12 $\mu\text{g ml}^{-1}$ after collection on a PUF microcolumn and desorption by dichloromethane has been proposed; on-line spectrophotometric detection was carried out at 280 nm.²⁴³

3. Diffuse reflection spectroscopy

The combination of preconcentration on PUF and subsequent determination of the sorbed substances by diffuse reflection spectroscopy is a promising expedient for analytical chemistry. The possibility of this combination was first discussed by Dmitrienko and coworkers.^{63,64} It was shown²⁵ that PUF offer a number of advantages over other sorbents regarding their use in sorption–photometric and sorption–luminescence procedures and in test methods. First of all, this facilitates the final stage of analysis because the sorbate can be easily separated from other components present in the sorption system, which looks like a coloured tight pellet; owing to the uniform distribution of the analyte over the sorbent matrix, PUF pellets can be used without any additional operations.

In diffuse reflection spectroscopy, the Kubelka–Munk function (F) is related to the analytical signal, diffuse reflection (R), and the sorbate concentration in the following way:

$$F = \frac{(1 - R)^2}{2R} = 2.3 \varepsilon c s^{-1},$$

where $\varepsilon = n \times 10^4$ is the molar extinction coefficient of the sorbate ($n = 1\text{--}10$), c is the sorbate concentration, s is the light scattering coefficient. Methodical aspects of the quantitative measurements of the diffuse reflection of sorbates on PUF are considered in a paper.²⁴⁴ The main factors influencing the accuracy and reproducibility of diffuse reflection measurements, namely, sample layer thickness, sample humidity, the brand of the PUF used and the sorbate concentration, have been studied. For all the compounds studied, the Kubelka–Munk function was found to be linearly related to the sorbate concentration not only in the PUF matrix but also in aqueous solution within the limits of the linear sections of sorption isotherms. The limits of detection of intensely coloured ($\varepsilon \approx n \times 10^4$) compounds in the PUF matrix reach $n \times 10^{-2}$ μg in a $0.04\text{--}0.07$ g PUF pellet or $n \times 10^{-4}$ $\mu\text{g ml}^{-1}$ for a sample volume of $25\text{--}100$ ml.

Various methods are used to obtain a coloured compound in the sorbent phase. One method is based on the sorption on PUF of the coloured compounds formed in the solution under analysis upon the reaction between a specially added analytical reagent and the target component. Numerous publications have been devoted to determination of metal ions and organic compounds by this method. For example, in a sorption–photometric determination of cobalt^{63–65} and iron,^{63,64,69} they are transferred into coloured thiocyanate complexes and sorbed on PUF. The limits of detection are $n \times 10^{-3}$ $\mu\text{g ml}^{-1}$. To increase the selectivity of analysis, sorption is carried out in the presence of various masking compounds. A similar method was used to determine silicon as the oxidised and reduced forms of molybdosilicic acid with limits of detection of 3×10^{-3} and 1×10^{-2} $\mu\text{g ml}^{-1}$, respectively. A sorption–photometric procedure for determination of ionic sur-

factants using PUF is based on sorption of the associates formed by surfactants and coloured hydrophobic counter-ions. Sulphothalein dyes are used as the counter-ions in the determination of cationic surfactants,¹⁷³ while tris(1,10-phenanthroline)iron(II) was used for anionic surfactants.^{105,171} This procedure makes it possible to determine ionic surfactants present at a level of $n \times 10^{-2}$ $\mu\text{g ml}^{-1}$. A sorption and photometric method for determination of phenols and 1-naphthol is underlain by sorption of their coloured azo derivatives.^{161,163–165} Azo derivatives of phenols were synthesised by azo coupling with 4-nitrophenyldiazonium tetrafluoroborate. To enhance the recovery, sorption was carried out in the presence of cetyltrimethylammonium bromide. This procedure provides determination of phenols with limits of detection of $n \times 10^{-3}$ $\mu\text{g ml}^{-1}$.

The second method is related to the use of loaded PUF. In this case, the coloured compound is formed directly in the sorbent phase due to complexation or redox reactions between the target component present in an aqueous solution and an analytical reagent immobilised on PUF. Polyurethane foam loaded with dimethylglyoxime was proposed for sorption–photometric determination of nickel,^{64,206} and diphenylcarbazide-loaded PUF was proposed for chromium(VI) determination.^{64,231,232} A sorption–photometric determination of ascorbic acid is based on reduction of heteropolyacids immobilised on PUF.²⁴⁵ The procedure allows determination of 0.3 to 2.4 $\mu\text{g ml}^{-1}$ of ascorbic acid. The time of analysis is 75 min. When the reduction of heteropolyacid is carried out on exposure to microwave radiation, the duration of the analysis decreases to 6.5 min.²⁴⁶

The third method for preparation of coloured analytical forms in the PUF phase is based on chemisorption processes involving the terminal groups of these polymers. In this case, a higher selectivity is to be expected. This technique was used, for example, to determine nitrite ions¹⁸⁰ and free active chlorine¹⁸¹ in water.

4. Luminescence

A number of studies have been devoted to the use of PUF in luminescence analysis. The key factors influencing the intensity of fluorescence of sorbed molecules such as the thickness of the sample layer, sample humidity, the structure of the polymeric framework of PUF and the sorbate content have been studied in relation to the $[\text{Ru}(\text{Phen})_3]\text{Cl}_2$ complex, pyrene, rhodamine 3B, rhodamine 6G and butylrhodamine sorbed on PUF.^{244,247} It was found that the polymer framework of PUF has virtually no influence on the fluorescence emission and fluorescence excitation spectra of the sorbates; the spectra of sorbates on different PUF normally do not differ from one another and in most cases, they are similar to the spectra of these substances in aqueous solutions. The limits of detection of compounds with intense fluorescence in the PUF matrix are $n \times 10^{-3}$ μg (the weight of PUF $\approx 0.04\text{--}0.07$ g) or $n \times 10^{-5}$ $\mu\text{g ml}^{-1}$ for a sample volume of $25\text{--}100$ ml. The range of linearity of calibrating plots coincides, as a rule, with the initial linear sections of sorption isotherms and holds up to a change in the sorbate concentration by one to two orders of magnitude.

In most cases, compounds that luminesce on the sorbent surface (for example, metal complexes with organic ligands) are obtained by sorption from the solution in which they have been synthesised. A sorption–luminescence method for yttrium determination includes the formation of a complex with 8-hydroxyquinoline, sorption of the complex on PUF and measurement of the luminescence intensity at $510\text{--}513$ nm ($\lambda_{\text{excit}} = 398$ nm). The method was applied for determination of yttrium in lanthanum¹⁰⁰ and scandium¹⁰¹ oxides. In a highly sensitive sorption–luminescence method of selenium determination in soil, the target element is sorbed as 4,5-benzodiazoselenol, which is prepared by the reaction with 2,3-diaminonaphthalene.²⁴⁸ In a method for determination of Eu in scandium oxide, the mixed-ligand complex of this element with thenoyltrifluoroacetone and 1,10-phenanthroline is sorbed by polyurethane foam and then Eu is determined by luminescence directly in the sorbent, the limit of detection being

$1 \times 10^{-6} \%$.¹⁰⁶ Thallium is sorbed on PUF as the chloride complex, then the sorbate is treated with rivanol, a diamino derivative of acridine, and the fluorescence intensity is measured at 497 nm ($\lambda_{\text{excit}} = 367 \text{ nm}$).⁵¹ Only gallium is sorbed together with thallium. The analysis of these elements is not interfered with by the presence of large amounts (1 : 1000) of Cu, Co, Ni, Cd, Zn, Hg, In and La and alkali and alkaline earth metals; the limit of detection is $0.5 \mu\text{g litre}^{-1}$.

A method for determination of Cr(III) based on the quenching of fluorescence of rhodamine 6G sorbed on PUF has been described.²⁴⁹ The limit of detection equals 8 ng ml^{-1} for a sample volume of 25 ml.

A scheme of analysis has been proposed to perform fast screening of water samples for the content of PAH. According to this procedure, PAH are collected on PUF and their total amount is determined by the sorption-luminescence method.¹²⁵ Individual PAH are determined in the eluate after desorption of the sorbed impurities by acetonitrile using high-performance liquid chromatography (HPLC) with a fluorescence detector.²⁵

5. Atomic-absorption and atomic-emission spectroscopy

The preconcentration of elements by sorption on PUF is often combined with determination in eluates by atomic-absorption spectroscopy (AAS) and atomic-emission spectroscopy with inductively coupled plasma (ICP AES). The flame AAS method was applied to determine platinum⁴⁴ and thallium⁵⁰ after preconcentration of the elements as halide complexes on PUF followed by desorption on treatment with acetone.

Combination of group preconcentration of elements by sorption on PUF loaded with ammonium pyrrolidinedithiocarbamate (PUF-APDTC),^{220, 221, 223} a mixture of hexamethylenammonium hexamethylenedithiocarbamate with methyltriethylammonium chloride (MTOA)²²⁴ or on PUF loaded with sodium diethyldithiocarbamate²²² followed by determination of elements by non-flame AAS or ICP AES proved successful. A procedure for determination of As, Bi, Sb, Hg, Sn and Se in natural waters²²⁰ includes collection by sorption on columns with PUF-APDTC, elution of the element pyrrolidinedithiocarbamates with methanol, generation of hydrides directly in a methanol solution by the reaction with NaBH_4 and subsequent determination by ICP AES. The limits of detection of elements are, ng ml^{-1} : 0.2 (As), 30 (Bi), 0.03 (Se, Sb and Sn).

In determination of Cd, Co, Cu, Fe, Hg, Ni and Pb in high-purity oxalic acid,²²⁴ trace elements are concentrated under dynamic conditions on columns with PUF-APDTC or PUF-APDTC-MTOA; the degree of recovery of elements is higher than 97%. The components are desorbed by methyl isobutyl ketone (for AAS determination) or 4 M HNO_3 (for ICP AES determination). The limits of detection are 0.1 (Cd), 0.3 (Pb), 1 (Ni), 2 (Co and Cu) ng g^{-1} and 0.1 (Hg) $\mu\text{g g}^{-1}$ for non-flame AAS and 0.05 (Cd), 0.1 (Cu), 0.2 (Ni) and 1 (Pb) $\mu\text{g g}^{-1}$ for ICP AES.

The column version of the solid-phase extraction using PUF loaded with APDTC was used²²¹ to collect As, Bi, Hg, Sb, Se and Sn impurities in waters of various types. The degree of recovery of elements on passing of 150 ml of a sample ($\text{pH} \sim 4.5$) at a flow rate of 2 ml min^{-1} through a column was 97%–100%. After elution with methanol, the concentrate was analysed by ICP AES; the limits of detection were, ng ml^{-1} : 3 (As, Se), 8 (Bi), 0.12 (Hg), 2 (Sb) and 6 (Sn). It should be noted for comparison that the use of non-flame AAS after desorption of the elements with methyl isobutyl ketone decreased the limits of detection of elements down to 0.06 (As and Sb), 0.1 (Bi and Sn), 0.08 (Se) and 0.3 (Hg) ng ml^{-1} .

A method for lead determination in sea food has been proposed;²⁵⁰ lead is collected on a microcolumn packed with PUF loaded with 2-(2-benzothiazolylazo)-2-cresol, desorbed with 0.1 M HCl and determined by flame AAS. The limit of detection of lead by this method is $1 \mu\text{g l}^{-1}$.

A flow-injection system has been used²⁵¹ for atomic-absorption determination of zinc in waters and biological materials after preconcentration by sorption on a microcolumn packed with PUF.

6. X-Ray fluorescence spectroscopy

X-Ray fluorescence spectroscopy has been used to determine Ga,⁴¹ Co,^{58, 60} Fe, Pd, Pt and Zn.⁶⁰ As,⁸⁸ Ge,⁹⁰ PO_4^{3-} (see Refs 92, 93) methyl- and phenylmercury chloride, inorganic mercury²²⁶ and U.²⁵² Indirect determination of phosphorus on the basis of molybdenum or antimony after preconcentration on PUF as phosphomolybdate⁹² or molybdoantimonylphosphoric acid⁹³ has fairly low limits of detection (0.1 and $0.02 \mu\text{g ml}^{-1}$, respectively). The latter procedure is more selective: large amounts of silicon do not interfere with the determination of phosphorus. The relative standard deviation does not exceed 0.05. In an X-ray fluorescence determination of arsenic⁸⁸ and germanium,⁹⁰ they are transformed into arsenomolybdate and molybdogermanate, which are sorbed on PUF. The range of concentrations determined in this way is fairly broad: 0.5 – 3.5 and 0.25 – $35 \mu\text{g ml}^{-1}$, respectively. Arsenic can be determined in the presence of large amounts of PO_4^{3-} and SiO_4^{2-} (1 : 10) and an equal amount of germanium. The limits of detection are 40 and 70 ng ml^{-1} and the relative standard deviations do not exceed 0.07 and 0.09 for arsenic and germanium, respectively.

Determination of Co, Zn, Pd, Pt, Fe is carried out using sorption of their thiocyanates from acid solutions in the presence of NH_4Cl .⁶⁰ The ranges of linearity of the calibrating plots are rather narrow: 1–5 (Co, Zn, Fe) and 1–10 $\mu\text{g ml}^{-1}$ (Pd, Pt), the corresponding relative standard deviation being not more than 0.05. In sorption–X-ray fluorescence determination of chloride, methyl- and phenylmercury chloride, PUF loaded with sodium diethyldithiocarbamate is used.²²⁶

7. Neutron activation method

Direct determination of sorbed elements by neutron activation analysis (NAA) was shown to be, in principle, possible in a number of studies.^{14, 31, 227} The NAA method with a neutron flux density of $3 \times 10^{13} \text{ neutron cm}^{-2} \text{ s}^{-1}$ (irradiation for 10 min) allows determination of Au, In, Hg and Zn in the polyurethane foam matrix after collection of these elements from thiocyanate media.¹⁴ It was noted that irradiation of PUF for more than an hour results in polymer destruction; irradiation in H_2SO_4 leads to complete dissolution. Determination of gold in natural waters after sorption from 6 M HCl on ether-based polyurethane foams has been described.³¹ Neutron-activation determination of antimony is preceded by its isolation using PUF loaded with potassium diethyldithiocarbamate.²²⁷

8. Enzymic methods

In enzymic methods of analysis, PUF are used as polymeric supports for immobilised enzymes. A method for the immobilisation of cholinesterase comprising capture of an enzyme into a starch gel followed by impregnation of the gel into the PUF matrix has been proposed.²⁵³ An analytical system in which an enzymic minireactor is combined with an electrochemical sensor within one unit has been developed²⁵⁴ to determine toxic substances of the anticholinesterase action (for example, insecticides) in air and in liquid media. As the air or solution sample under analysis is pumped through the minireactor, the inhibitor is collected on the immobilised enzyme and inhibits it. The combination of preconcentration and analytical reaction in one unit with the sensor increases the method sensitivity and shortens the response time. The limit of detection of organophosphorus insecticides by such a system is 0.1 – 4.5 ng ml^{-1} , that for carbamates is 0.5 – 20 ng ml^{-1} .

A method for immobilisation of horse-radish peroxidase^{255, 256} and alkaline phosphatase²⁵⁷ in a chitosan film followed by impregnation into PUF has been developed. This procedure was used to develop highly sensitive test methods for

determination of mercury²⁵⁵ and organomercury compounds.²⁵⁶ The oxidation of *o*-dianisidine in the presence of thiourea by hydrogen peroxide is used as the indicator reaction. This procedure provides mercury(II) determination at a level of 1 ng ml^{-1} ; the lower limits of determination of methyl-, ethyl- and phenylmercury are 0.008, 0.01 and $25 \text{ } \mu\text{mol litre}^{-1}$.

A test procedure for determination of $0.05\text{--}10\,000 \text{ ng ml}^{-1}$ of lead has been described.²⁵⁷ In the development of this procedure, the inhibitory action of lead on the activity of PUF-immobilised alkaline phosphatase in the hydrolysis of *p*-nitrophenyl phosphate was utilised. It was noted that the key advantages of PUF over polystyrene and chromatographic paper used previously for enzyme immobilisation include a long (1–1.5 years) period of maintenance of enzyme activity; the researchers also noted good metrological characteristics of the developed procedures.

9. Chromatographic methods

The most important applications of PUF in chromatographic methods of analysis include preconcentration and isolation from waters and air of PAH,^{110–113, 117, 122, 124} PCB^{107, 121, 124, 131, 133, 153} and chlorine- and phosphorus-containing insecticides.^{127, 128, 133, 134, 152} After collection on PUF, organic compounds are determined using gas chromatography (GC) and HPLC in combination with various types of detector: flame ionisation (FID), electron capture (ECD), mass-spectrometric (GC/MS technique), N/P-selective and UV and fluorescence detectors. The existing chromatographic methods for the determination of trace amounts of organic compounds consist of several stages: collection of the trace elements on PUF, desorption, evaporation of the solvent and analysis of the concentrate.

Various solvents have been proposed for desorption of compounds from PUF: acetone,^{11, 107, 110, 117, 152} hexane,^{107, 133, 134, 153} methanol,¹¹⁷ an acetone–hexane mixture,¹³³ diethyl ether and petroleum ether.¹²¹ Solvent desorption is carried out in the Soxhlet apparatus for 18–24 h.^{107, 113, 115, 116, 118, 130, 132–134, 149} In some cases, samples are treated with ultrasound to intensify the process.¹²² Supercritical fluid extraction (SFE), which makes it possible to shorten the desorption time to 10–20 min,^{124, 156} and a method based on extraction of impurities with a small amount of an organic solvent after compression of PUF to 10% of its initial volume in a special column can provide alternatives to the prolonged and cumbersome procedure of Soxhlet desorption.¹²³ It has been shown¹²³ that 4 ml of dichloroethane or 6 ml of a 10% solution of acetone in hexane is sufficient for quantitative elution of eighteen PAH from a PUF sample with an initial volume of 115 cm^3 .

The preconcentration of organic compounds from waters is carried out in a dynamic regime; the flow rate reaches 270 ml min^{-1} . Traces of PAH are collected from water samples having large volumes (4–60 litres) using columns filled with one or several cylindrical inserts of PUF ($45 \times 45 \text{ mm}$).^{109, 110} A water sample heated to $62 \pm 2 \text{ }^\circ\text{C}$ is passed through a column at a flow rate of $250 \pm 10 \text{ ml min}^{-1}$. It was noted that pre-heating decreases the loss of PAH caused by co-precipitation on the suspended particles present in water samples.¹⁰⁹ For most of PAH including 3,4-benzopyrene, the degree of recovery amounts to 90%–98% for the model samples prepared from distilled water and 65%–85% for real potable or river water samples.^{109, 110} It was demonstrated in relation to 3,4-benzopyrene that PAH samples sorbed on PUF are stable for 7 days when the storage temperature is $4 \text{ }^\circ\text{C}$.¹⁰⁹ The PAH are desorbed by successive treatment with acetone and cyclohexane and determined by GC with a FID or by HPLC with a luminescence detector.^{110, 111}

The efficiency of PUF as sorbents for the isolation of PCB ($2\text{--}20 \text{ ng litre}^{-1}$) from natural water with a view to subsequent GC determination has been evaluated.^{107, 126–128, 135} When large sample volumes (up to 1790 litres) are passed through columns packed with PUF cylinders ($3.8 \times 2.2 \text{ cm}$) at a flow rate of

250 ml min^{-1} and then elution with acetone or hexane is carried out in a Soxhlet apparatus, 80%–100% of PCB is recovered. The influence of the flow rate on the degree of recovery of organic compounds under dynamic conditions has been studied. It was noted that an increase in the rate from 10 to 100 ml min^{-1} has no influence on the completeness of PCB recovery; however, an increase in the flow rate to 250 ml min^{-1} decreases the degree of recovery to 30%–60%.¹²⁸

Polyurethane foams are used to collect thirteen organochlorine insecticides (DDT, Lindane, Aldrin, *etc.*) and polychlorinated biphenyls by passing water through a ($20 \times 2 \text{ cm}$) column packed with PUF at a flow rate of 100 ml min^{-1} .^{127, 128} The collected compounds were washed out from the column by successive treatment with acetone and hexane and determined by chromatography.

Several types of samplers which allow a flow rate of $800 \text{ litres min}^{-1}$ to be reached have been developed for analysis of air.^{117, 118, 121, 128, 133–135} The samplers are stainless-steel, glass or plastic tubes filled with cylindrical inserts made of PUF, in some cases, in combination with other sorbents or with glass-fibre filters. Prior to the use, sorbents are subjected to prolonged (up to 24 h) purification by means of various organic solvents and water in the Soxhlet apparatus.^{113, 117, 133, 134} A large potential of portable samplers based on combination of PUF with other sorbents such as Tenax CG^{121, 135} and XAD-2^{118, 121, 128} for preconcentration of PAH, PCB and chlorine-, phosphorus- and nitrogen-containing insecticides in urban air samples has been demonstrated. For a sampling velocity of $0.1\text{--}0.3 \text{ m}^3 \text{ min}^{-1}$, the recovery of compounds is not less than 75%.¹²¹ After desorption with a diethyl ether–petroleum ether mixture (15 : 85)¹¹¹ or 5% diethyl ether in hexane¹³³ in a Soxhlet apparatus and evaporation of the solvent, the concentrate was analysed by various chromatographic methods: HPLC with UV detector and GC with ECD, PID and N/P-selective detectors. One sampler of this type was used to determine organochlorine compounds in the air above the Arctic.¹³⁴ Air samples with a volume from $300\text{--}600 \text{ m}^3$ to $2000\text{--}4000 \text{ m}^3$ were pumped through a sampler for a period from 8 h to 2–7 days at a flow rate of $750\text{--}800 \text{ litre min}^{-1}$. Solid particles were retained on the glass-fibre filter, while the vapours of organochlorine compounds were sorbed in two cylindrical PUF inserts. The impurity components were desorbed by 100–300 ml of hexane for 8 h in a Soxhlet apparatus, then the solvent was partially removed and the concentrations of the impurities were determined using GC with an ECD, GC/MS and HPLC with an UV detector. The Arctic air was found to contain various PCB isomers, DDT and other organochlorine compounds whose concentrations are several pg m^{-3} .

A method developed¹¹³ for determination of PAH in air at the ng m^{-3} level includes the following stages: preconcentration by sorption on PUF for 24–48 h at a flow rate of $0.5 \text{ m}^3 \text{ min}^{-1}$, successive elution with pentane and a mixture of dichloromethane (30%) with pentane, solvent evaporation from the eluate and analysis of the concentrate by GC/MS or by HPLC with a fluorescence detector.

A procedure for isolation, preconcentration and identification of volatile mutagens present in air has been described.¹¹⁷ The procedure includes sorption on PUF, elution with methanol or acetone, removal of the solvents, bioassays and analysis of the concentrate by GC/MS or by HPLC with a fluorescence detector.

Eighteen PAH were determined using GC/MS in exhaust gases after preconcentration for 20 min on a PUF-packed column and desorption with a small volume of dichloromethane or 10% of acetone in hexane.¹²³

Combination of the desorption of components collected on PUF using supercritical fluid extraction with subsequent determination of these components by the GC/MS technique was reported to be efficient.¹²⁴ This combination underlies a scheme for determination and identification of PAH, PCB and n-alkanes present in exhaust gases and the cigarette smoke. The scheme implies preconcentration of organic impurities on PUF followed

by desorption by the CO₂ fluid directly to the separating chromatographic column and allows gas-chromatographic analysis to be carried out over a period of less than an hour.

10. Test methods

The high efficiency of preconcentration by sorption on PUF of many compounds, the intensive colour of the sorbent observed in some cases, the ready availability and low cost of the sorbent are attractive features stipulating the use of PUF in test methods of analysis — simple and cheap methods for detection and determination of substances.²⁵⁸ A colour change of the sorbent after the reaction indicates the presence of the target component, and the content of the component is found by comparing the intensity of the sorbent colour with the appropriate scale or by measuring the length of the coloured zone or the time it takes for the characteristic colour to appear. The reliability of visual detection can be improved in some cases using portable miniphotometers which record light reflection from solid samples.

The possibility of using PUF in test methods of analysis was first mentioned by Braun and Farag.²¹⁸ Determination was preceded by element preconcentration on chromofoams (the term was introduced by Braun²¹⁸), *i.e.*, PUF loaded with photometric reagents. When these foams, as small cubes, are brought in contact with the solution under analysis, the white polymer acquires a colour typical of the given photometric reaction. These reactions are highly sensitive, for example, for sorption in the static regime, tenths (Co,²¹⁸ Cu,^{214, 218, 233} Cd,²¹⁴ Pd,²³³ Pb,^{218, 219} Cr,²³⁰ Mo²³⁴) and in some cases, even hundredths (Ag,²¹¹ Ni,²⁰⁵ Cu,²¹⁴ Zn,²¹⁸ PO₄⁹⁴) of a microgram of an impurity can be determined in a sample volume not exceeding 1–2 ml. The sensitivity of determination increases by at least an order of magnitude when Co,²¹⁸ Cu,²¹⁸ Cd,²¹⁴ Cr²³⁰ and Mo²³⁴ are sorbed in the dynamic regime. Detection of metals at a level of several nanograms in ml is attained by passing relatively large volumes of a solution (~1 litre) through a chromofoam filled column. The use of these materials ensures higher sensitivity of analysis than the use of impregnated paper or than drop reactions.^{205, 214, 218, 219, 230} Chromofoams are also suitable for a semi-quantitative determination, which implies either comparison with standard colour scales after sorption in the static regime or measurement of the length of the coloured zone in the column after letting-through the solution under analysis. Usually, the colour intensity of chromofoams is linearly related to the metal concentration in the aqueous solution.

One more way of using these sorbents in test methods of analysis, not associated with the preparation of loaded PUF, is also possible. Pellets of unloaded PUF complete with ampoules containing solutions of reagents have been used as test kits.^{105, 163, 165, 172, 180, 181} The reproducibility of the results of visual detection based on a colour scale (*s_r*) varies in the range of 0.1–0.5. Test kits based on PUF for determination of Co, Ni, Fe(III), nitrite ions, free active chlorine, total content of phenols, and anionic and cationic surfactants have passed metrological certification, have been registered as a type of test system²⁵⁹ and are currently produced in industry. The test systems based on PUF are simple to produce, reliable in operation and suitable for determination of toxic substances in waters of various types including potable and mineral waters, extracts from soils or juices. If necessary, the test form can be retained and analysed in a laboratory using diffuse reflection spectroscopy or, after desorption of compounds, HPLC.¹⁶⁵

VII. Conclusion

The presented data demonstrate that polyurethane foams are of considerable interest for the analytical chemistry of inorganic and organic compounds. Characteristic features of these sorbents include high efficiency in combination with versatility, chemical and mechanical strength, stability against organic solvents, relatively low cost and ready availability. The unique sorption

properties of synthetic polymeric materials are largely due to their cellular membrane-like structure, which allows the molecules being sorbed to penetrate inside the sorbent, and to the combination of various hydrophilic and hydrophobic active sites and reactive terminal groups.

The applications of PUF in analytical chemistry are diverse. These sorbents are used for preconcentration of elements and organic substances from water and air and in spectroscopic, sorption–spectroscopic and chromatographic methods of analysis. The good prospects of using PUF in flow-injection analysis are demonstrated. Other applications of these materials are also noted, including the use as polymer matrices for enzyme immobilisation in enzymic methods of analysis.

Polyurethane foams are of interest not only regarding practical use but also in purely scientific aspects. In our opinion, the scope of application of PUF in analytical chemistry has not been adequately appreciated because most studies are aimed at the solution of applied problems of substance preconcentration and only few publications deal with investigation of physicochemical processes that proceed during sorption. Too little attention is devoted to elucidation of the relationship between sorption parameters and the properties of the sorbed molecules and evaluation of the contributions of intermolecular sorbent–sorbate interactions. Virtually no works are related to the study of physicochemical properties of the polyurethane foams themselves.

The study of heterogeneous chemical reactions involving the PUF surface are of considerable interest. This line of research, which is successfully developing in other fields of chemistry, can provide important results that would allow one to approach the problem of target-directed change of the properties of PUF by surface modification.

One may hope that PUF would be used more and more extensively in hybrid methods of analysis based on the combination of preconcentration by sorption with the subsequent determination in the sorbent matrix using diffuse reflection spectroscopy, luminescence or X-ray fluorescence spectroscopy and in test methods of analysis.

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Non-carbon nanotubes: synthesis and simulation

A L Ivanovskii

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Abstract. The discovery of a new allotropic form of carbon, extended nanometre-sized quasi-unidimensional tubular structures (carbon nanotubes), as well as broad prospects for the use of nanomaterials based on them initiated numerous studies in the search for, and design of, nanotubular structures based in other compounds. Some properties and the main methods for the synthesis of non-carbon nanotubes are considered. Studies on the simulation of the electronic structures of these unique objects are analysed. Results of experimental and theoretical studies along these lines are discussed. The bibliography includes 328 references.

I. Introduction

Intense studies on the nanotubular form of matter [tubulenes or nanotubes (NT)] have started following the discovery in 1991 of hollow cylindrical carbon-based structures, the lengths of which were several orders greater than their diameters, in cathodic condensates formed upon electrical arc discharge between graphite electrodes.¹ The new quasi-unidimensional carbon cluster was called 'fullerene tubulene' and its electronic spectrum (ES) was calculated.² It was found that the electronic spectrum of the carbon tube studied was characteristic of metals.

From the very beginning, considerable attention by experimenters and theoreticians was given to nanotubes as representatives of a new quasi-unidimensional allotropic modification of carbon in the series of previously known modifications, *viz.*, 3D (diamond) → 2D (graphite) → 1D (carbyne) → 0D (fullerene). With time, nanotubes, which were exotic objects of unique experiments and theoretical calculations, became the subject of numerous physicochemical studies; their unusual properties became the basis for many daring technological solutions. At present, NT find broad practical application; now they are commercial products and are subject to marketing studies.

Data on the structures and properties of carbon nanotubes, on the methods of their synthesis and on their uses can be found in many publications; they have been generalised in a number of monographs (see, *e.g.*, Refs 3–7) and in many reviews (see, *e.g.*, Refs 8–32).

In a number of reviews recently published in Russian scientific journals,^{15, 16, 21, 24–27} the methods of synthesis and study of carbon NT were discussed.^{15, 16} The main principles of the theoretical simulation of the geometrical and electronic structures of NT were described in a monograph⁷ and in papers.^{21, 26} The methods for the synthesis of such NT were described in detail by Rakov.²⁴ He also reported the most recent data on the chemistry and application of carbon NT considered as promising materials for modern technologies. Tarasov *et al.*²⁵ discussed the possibility of use of NT as 'tanks' for the storage of hydrogen. Basic information about carbon NT can be found elsewhere.^{33, 34}

Shortly after the paper by Iijima¹ was published, scientists were challenged by a number of questions that are of major importance to the development of the physics and chemistry of NT and for the prospects of their practical application.

1. What is the nature of NT and what is the mechanism according to which they are formed? Are there any physical or chemical restrictions limiting the scope of compounds which can be obtained in a nanotubular form?

2. What physicochemical properties should a compound possess to be a potential initial substance for the synthesis of NT?

3. What are the specific features of methods that can be used to obtain non-carbon NT? What is their value in materials science and technology?

From the very start, the concept of non-carbon NT was developed due to combined efforts of experimenters (syntheses of NT and studies of their functional characteristics) and theoreticians (simulations of new nanotube forms, prediction of their structures and properties).

In 1992, the first non-carbon NT based on lamellar molybdenum and tungsten disulfides were synthesised.³⁵ In 1994, the possibility of existence of tubulenes based on hexagonal boron nitride (BN-nanotubulenes) was predicted.^{36–38} Their dielectric properties were presumed to remain stable upon changes in their geometrical characteristics. This prediction was very important for the development of nanoelectronics; it initiated numerous studies on the synthesis of such NT.

A large number of non-carbon NT have been synthesised to date or their existence has been predicted. In addition to the NT mentioned above, others based on germanium silicide and tran-

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sition metal dichalcogenides, sulfides and chlorides have been synthesised. The molecular and electronic structures of various hypothetical NT containing boron, phosphorus, silicon, germanium and transition metal diborides were simulated; the mechanisms of their growth were discussed and the properties of certain nanotubular structures were studied.

Boron–nitrogen and dichalcogen-containing NT were the subject of special analysis.^{12, 29} Some data on the synthesis and properties of non-carbon NT can be found in monographs^{5, 7, 8} and reviews^{11, 14, 19, 21, 24} devoted to carbon tubulenes.

The present review discusses the general state of studies on the synthesis and simulation of the molecular and electronic structures of non-carbon NT which were developed most intensely in the last years.

Along with the ‘purely non-carbon’ NT listed above, we also consider the class of ‘transitional’ nanotubular structures containing both carbon and other *p*-elements (boron, nitrogen and silicon). These NT possessing diverse properties can either be obtained together with carbon NT within the same synthetic procedure or synthesised using methods specifically developed for this purpose. Of these, chemical substitution is the most promising method in which carbon NT are used as the starting material.

The overwhelming majority of non-carbon NT have been obtained (or their synthesis is anticipated) on the basis of compounds that, like carbon, have lamellar (quasi-two-dimensional) crystal structures. Therefore, classifications and descriptions of atomic structures of non-carbon NT are performed, and their geometrical models are built,^{7, 12, 21, 29} on the basis of the concepts and methods developed for carbon NT.^{3–10, 15–32} Let us summarise briefly those to be employed below.

Ideal carbon NT have the form of cylinders whose walls are formed by hexagons, with carbon atoms in the vertices. The process of formation of a nanotubulene can be visualised as the rolling of a ‘band’ of carbon atoms cut out of a graphite monolayer (graphene network). A graphite layer can be ‘cut’ in different ways: along lines which are perpendicular to the C–C bonds or pass through these bonds, or else at a definite angle, namely the so-called chiral angle θ (Fig. 1*a*). As the resulting ‘bands’ roll and their edges are linked together, two main NT types appear, *viz.*, non-chiral and chiral. The so-called zigzag and dented non-chiral NT are distinguishable. The structures of the main NT types are shown in Fig. 1*b*.

Using the base vectors $\mathbf{a}_1$ and $\mathbf{a}_2$ of the graphene network, the following vector can be defined:

$$\mathbf{c}_h = n\mathbf{a}_1 + m\mathbf{a}_2.$$

The main geometrical parameters of a tubulene, *i.e.*, the diameter (D) and the chiral angle (θ), are related unambiguously to the base vectors of the graphene network through the following relationships involving the indices n and m :

$$D = \frac{|\mathbf{c}_h|}{\pi} = a\sqrt{\frac{3(n^2 + m^2 + mn)}{\pi}},$$

$$\theta = \arctan\left(-\frac{\sqrt{3}m}{2n + m}\right),$$

where a indicates the interatomic distances in the planar network.

In terms of these indices, the corresponding NT are denoted as (n, m) -NT. All (n, m) -NT with $0 < \theta < 30^\circ$ are regarded as chiral (spiral). Non-chiral NT have $\theta = 0$ and 30° . At $\theta = 0$, a family of zigzag-shaped $(n, 0)$ -NT is formed; these were named according to the type of tube ‘cross-section’ (see Fig. 1). The chiral angle for the dented (n, n) -NT equals 30° .

The NT ends may be open or closed by ‘caps’ formed by fullerene hemispheres. Other (*e.g.*, conical) ‘cap’ types are also possible. Single-layer and multilayer NT are known. The latter can consist of a system of concentric tubulenes or have a scroll-type structure. Nanotubes can be single or form diverse aggregates

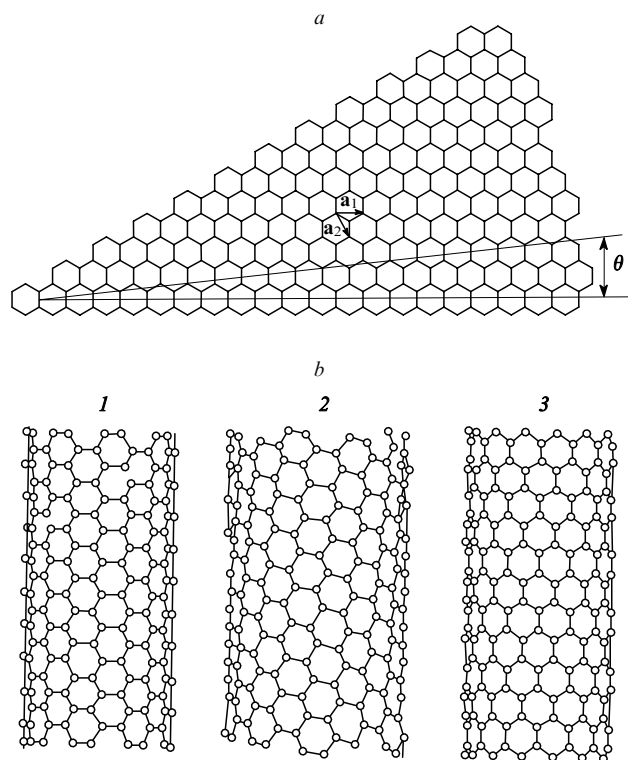


Figure 1. Model for the NT formation upon graphene layer rolling into a cylinder (*a*) and nanotube types (*b*).

NT: (1) non-chiral dented (n, n) ; (2) chiral (n, m) ; (3) nonchiral zigzag-like $(n, 0)$.

(braids, splices, *etc.*) that may involve other nanospecies (fullerenes). Many possible aggregates formed by carbon NT are described in a review by Rakov.²⁴ The majority of NT contain various defects (topological defects, rehybridisation defects, ‘broken’ bonds). Directed introduction of defects into NT makes it possible to adjust flexibly their functional properties. More detailed information about NT types, their geometry, and their properties mentioned above can be found in a number of papers.^{3–32}

The material of this review is organised according to the following scheme. First, modern methods for the synthesis of non-carbon NT are considered. Further, we describe methods for the preparation of nanotubulenes from *p*-element compounds (BN, BC_x , CN_x , $\text{B}_x\text{C}_y\text{N}_z$), which are most structurally similar to carbon NT, and other classes of chemical compounds (transition metal dichalcogenides and oxides). Finally, we characterise methods (template synthesis and film ‘folding’) which are rather versatile and can be suitable for the synthesis of NT based on various melts and inorganic compounds.

After that, we discuss the results of theoretical simulation of the molecular and electronic structures of non-carbon NT by the methods of quantum chemistry and molecular dynamics. Data on the structural features and possible methods for the synthesis of hypothetical NT based on boron, silicon, phosphorus, CN_x , GaN, transition metal dichalcogenides and diborides and ‘hybrid’ nanotubular structures are considered. Special attention is paid to predictions of NT stability and properties. Data on the electronic properties of a number of NT formed in the B–C–N system are briefly discussed.^{7, 21}

Data about the physicochemical properties of non-carbon NT are far from being exhaustive yet, and their analysis is beyond the scope of this review. Some of the most interesting parameters of certain groups of non-carbon NT are briefly mentioned in the corresponding sections.

II. Methods for the synthesis of non-carbon nanotubes

1. Synthesis of nanotubes in the B–C–N system

The structures of nanotubes formed in the B–C–N system are similar to those of carbon tubulenes. The review of the methods for the synthesis of such non-carbon NT is given using the sequence in which the methods for the synthesis of carbon NT were considered by Rakov.²⁴ This will allow us to compare the potential of ‘traditional’ (for carbon NT) synthetic methods to that of new methods suggested for the synthesis of non-carbon NT.

a. Electric arc synthesis

Electric arc synthesis is the simplest method widely used for the synthesis of carbon NT (see Refs 9, 11, 15, 16, 24, 32). Numerous attempts to use this method for the synthesis of nanotubulenes in the B–C–N system have been reported. Of course, the standard method^{11, 15, 24} should be modified so as to ensure the introduction of not only carbon but also boron and nitrogen into the reaction zone. As a rule, this is done using an appropriate composition of air (*e.g.*, the synthesis is performed in a flow of nitrogen) and/or of the electrode.

Since boron nitrides are insulators,^{7, 36–38} in pure form they are unsuitable for the preparation of electrodes. BN-Nanotubulenes were first obtained in an electric arc discharge (in a helium atmosphere) between a copper cathode and an anode made of boron nitride enclosed in a tungsten shell.³⁹ The cathodic deposit was found to contain a wide variety of boron–nitrogen nanostructures with diverse morphology, including BN-nanotubulenes. The tubes consisted of a number of layers (the inner and outer diameters varied from 1 to 3 and from 6 to 8 nm, respectively, and the distance between the walls was ~ 0.33 nm); their lengths exceeded 200 nm. The ends of NT were ‘capped’ with tungsten-containing nanoparticles (which presumably consisted of tungsten borides or nitrides). The growth mechanism of BN-nanotubulenes was assumed³⁹ to involve catalysis by metal atoms.

A number of boron-containing phases, *e.g.*, ZrB₂ and HfB₂, have been studied as electrodes for the electric arc synthesis of NT in a flow of nitrogen.^{40–43} In the latter case, the plasma contained metal atoms, which could serve as growth catalysts for BN-nanotubulenes.

Cumings⁴⁴ reported a high-performance method for the synthesis of NT based on BN; the electrodes consisted of elementary boron (99 at.%) and admixtures of cobalt or nickel (up to 1 at.%), which served as catalysts. The pressure of nitrogen in the chamber was kept at 380 Torr; the current was 60 A. The residue on the cathode arranged on the bottom of the chamber was grey; a thin layer of the product was also found on the chamber walls. Analysis of the structure of the product obtained showed that it contained only double-layer NT (with diameters of the outer and inner BN-cylinders equal to 2.9 and 2.2 nm, respectively, and with a distance of ~ 0.37 nm between their walls). These tubes formed bunches (bundles). No metal admixtures were found in the NT; the stoichiometric composition of the tubes matched the ratio B:N = 1:1. It should be noted that double-layer NT were also obtained from BN using HfB₂ cathodes.⁴⁰ The growth mechanism and kinetics of such double-layer NT have not been ascertained.

Using scanning electron microscopy (SEM), it was found that NT bundles are often joined to form ‘knots’ that have their own structures. These junctions consist of boron nanocrystals coated by multilayer shells, *i.e.*, the specific cocoons. Nano-cocoon layers are formed by graphite-like boron nitride. Cumings⁴⁴ suggested a method for removal of boron nanocrystallites from nanococoons; as a result, the latter become empty and resemble the well-known carbon ‘onion-bulb’ structures, the so-called onions.^{3–6} It was suggested that hollow BN-nanococoons should be considered as a new nanomaterial for chemical and electrochemical industries. It

is possible to vary the properties of such material deliberately by filling the cocoons with definite atoms or molecules.

Vaporisation of porous BC₄N was accompanied by simultaneous formation of carbon, BN- and mixed BNC-nanotubulenes;⁴⁵ however, homogeneous boron carbonitride NT could not be obtained, probably, because of differences between the vapour pressures of gaseous boron nitrides and carbon.

b. Laser synthesis

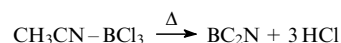
In addition to such methods to obtain carbon NT as vaporisation of the target (graphite) under electron and ion beams, sunlight, Joule heat (resistance vaporisation), yet another method became popular,²⁴ *viz.*, ablation of targets under laser irradiation. Attempts to use laser irradiation for the synthesis of nanotubulenes containing B, C and N have been reported.^{46, 47} Hexagonal BN served as the target and high pressure of nitrogen was maintained in the chamber. The products contained BN-nanotubulenes and particles of cubical boron nitrides. A CO₂ laser was used to synthesise single-layer BN-nanotubulenes on a multigram scale.⁴⁸ It was found that the zigzag-shaped tubes form bunches; furthermore, small amounts of double-layer BN-nanotubulenes and fullerene-like clusters of boron nitride were detected.

Nanotubes (and nanoparticles) containing B, C and N atoms were also obtained by other methods of target irradiation. For example, electron microscopy allowed Golberg *et al.*⁴⁹ to observe *in situ* the formation of single- and multi-shell fullerene-type nanoparticles of boron carbide upon exposure of lamellar BC₃ to an electron beam; it cannot be ruled out that a densely packed structure, *viz.*, diamond doped with boron, was formed inside these particles. Proton–ion bombardment of boron pyronitride resulted in a microcomposite material which incorporated blocks of BN-nanotubulenes and possessed enhanced plasticity.⁵⁰

c. Pyrolytic synthesis

Catalytic pyrolysis of hydrocarbons in the presence of metal catalysts is becoming one of the most widespread and promising methods for the synthesis of carbon NT.²⁴

Pyrolysis of a CH₃CN–BCl₃ system in the presence of a cobalt powder at ~ 1270 K was first used⁵¹ to obtain nanotubulenes and nanofibres with diverse morphologies and compositions. More detailed studies⁵² of the reaction



showed that its products contained NT whose composition was close to BC₂N. However, the composition homogeneity was violated considerably in the NT walls and spontaneous separation occurred (presumably, during the NT growth) to give C/BN ‘islets’. The most stable NT contained BN layers separated by graphite-like carbon layers.⁵²

Sen *et al.*⁵³ found systems suitable for the synthesis of BCN- and CN-nanotubes using the pyrolytic method. These were obtained using the 1:1 (CH₃)₃N–BH₃ adduct and pyridine, respectively. The reactions were carried out at ~ 1270 K with cobalt as a catalyst. The products contained nanotubes with diverse chemical compositions and morphologies.

Pyrolysis of a mixture of acetylene with diborane (in an atmosphere of helium and hydrogen)⁵⁴ gave boron-containing carbon NT whose compositions varied from C₃₅B to C₅₀B. The boron content in such tubes was close to the nitrogen content in CN-nanotubulenes.⁵³ Nitrogen-containing carbon NT were also found in products of catalytic pyrolysis of triazine.⁵⁵ Ma *et al.*^{56, 57} used B₄N₃O₂H as the precursor for the synthesis of BN-nanotubulenes.

d. Substitution reactions

Han *et al.*^{58–60} described a new chemical method for the synthesis of NT based on replacement of carbon atoms by nitrogen and/or boron atoms in carbon NT. Carbon tubes obtained by one of the known technologies were used as the starting materials. This

method was employed to obtain a wide variety of boron–carbon (B_xC_{1-x}), boron–carbon–nitrogen ($B_xC_{1-x-y}N_y$) and boron–nitrogen (BN) multi- and single-layer NT, as well as their bundles.^{58–66}

For example, Han *et al.*⁶⁰ synthesised ($B_xC_{1-x-y}N_y$)-nanotubes using a mixture of B_2O_3 with a product of arc synthesis which contained up to 70% carbon NT, together with fullerene-like nanoclusters and amorphous carbon with an admixture of particles of the metal catalysts (Fe/Ni). The reactions were carried out in a flow of nitrogen in the temperature range 1523–1803 K. The products were analysed using transmission electron microscopy and electron energy loss spectroscopy (EELS) (Fig. 2).

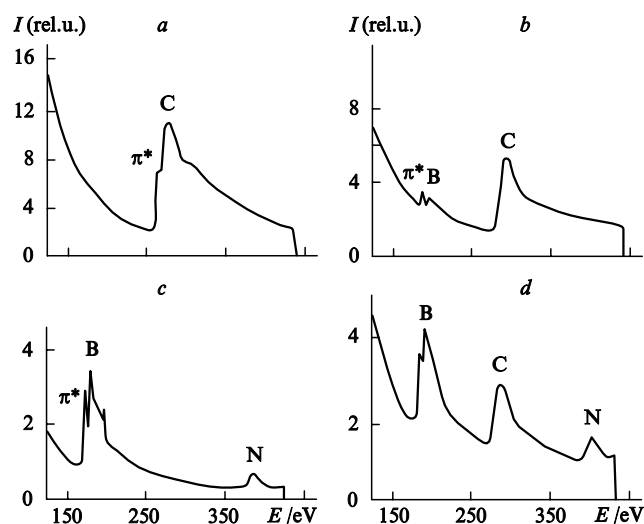
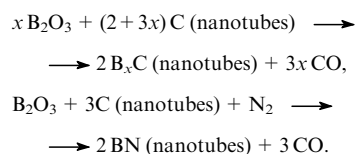


Figure 2. Electron energy loss spectra for the original carbon NT (a), NT with the composition B_xC_{1-x} ($x \approx 0.1$) (b), 'stoichiometric' BN-nanotubulenes (c), nanotubes $B_xC_{1-x-y}N_y$ ($x = y \approx 0.1$) (d) obtained by chemical substitution.⁶⁰

The characteristic peaks in the spectra correspond to the presence of the respective elements, *viz.*, B, C and N.

Heating at 1523 K for 30 min resulted exclusively in boron–carbon NT (with the ratio B:C ≈ 0.1) joined as bundles. A mixture of single-layer (B_xC_{1-x}), ($B_xC_{1-x-y}N_y$)- and BN-nanotubulenes was obtained at higher temperatures (~ 1623 K). On subsequent increase in temperature (to 1803 K), the original carbon NT was destroyed completely; the resulting major fraction was a mixture of hexagonal, rhombohedral and turbostratic boron nitride with insignificant admixtures of nano-sized BN-structures: nanocones, polyhedral nanoclusters and nanofibres. No formation of BN-nanotubulenes was detected. The morphology of the BCN-nanotubulenes obtained resembled that of the original carbon NT in many respects. ($B_xC_{1-x-y}N_y$)-Nanotubulenes were also obtained⁶⁷ as reaction products of carbon nanotubulenes and CN_x -nanotubulenes with B_2O_3 and ammonia. The reactions leading to BC- and BN-nanotubulenes can be described^{58,59} by the following equations:



The maximum boron content in (B_xC_{1-x})-nanotubulenes did not exceed ~ 10 at.%. The bundles in ($B_xC_{1-x-y}N_y$)-nanotubulenes differed in the C : (B + N) ratios (Fig. 3). In certain cases, the 'stoichiometry' of N : B ≈ 1.0 was reached. This is due to the selective character of substitution:⁶⁰ the probability that 'pure' BN-nanotubulenes (or, at least, boron–nitrogen clusters in the

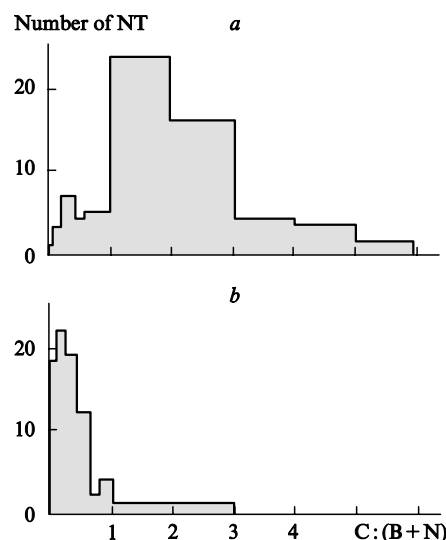


Figure 3. Composition histogram of multilayer BCN-nanotubulenes synthesised by chemical substitution from carbon NT (at 1773 K in a flow of nitrogen),⁶³ (a) without oxides, (b) in the presence of MoO_3 .

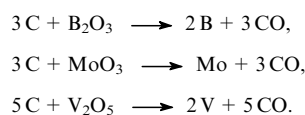
walls of the original carbon NT) are formed is much higher than the probability of NT formation if the replacement of carbon atoms by boron and nitrogen is purely statistical.

An interesting result was obtained by Han *et al.*⁶⁰ Inside single-layer BN-nanotubulenes, endohedral polyhedral BN-nanoclusters, described as four-shell octahedral BN-fullerenes with the composition $B_{12}N_{12}@B_{76}N_{76}@B_{208}N_{208}@B_{412}N_{412}$ (resembling carbon onion structures), were detected.⁶⁸ Similar hybrid nanotubular structures consisting of fullerenes located inside carbon NT ($C_n@C$) and carbon NT incorporating endofullerene chains ($M@C_n@C$) were also reported.^{69,70}

Attractive features of the method suggested by Han *et al.*^{58–61} are its ease and efficiency. The potential of the method is only limited by the amount of the original material available, *viz.*, carbon NT. Yet another important factor is the fixed size of the NT obtained in the system B–C–N, which is determined by the parameters of the matrices, *i.e.*, the carbon NT. The obvious drawback of the method is that it is difficult to synthesise NT with homogeneous chemical compositions.

This method was further developed^{63,65,66} and used for the synthesis of bundles of multilayer BN-nanotubulenes. A mixture of carbon NT and boric anhydride was complemented with MoO_3 (see Ref. 63) or a mixture of MoO_3 with PbO (see Ref. 65) or MoO_3 with V_2O_5 ;⁶⁶ the process was conducted in a flow of nitrogen at 1503–1773 K. Analysis of the reaction product involving molybdenum trioxide by transmission electron microscopy (TEM) showed that it contained bundles of multilayer BN-nanotubulenes, the major fraction of which (up to $\sim 82\%$) had non-chiral zigzag geometry.⁶⁶ The ends of such NT were open in contrast to the NT obtained^{58–60} in the absence of metal oxides.

The following scenario of the growth of BN-nanotubulenes was suggested,⁶⁶ taking into consideration that transition metal oxides are efficient oxidants for carbon. In the first stage, the terminal structures ('caps'), which close the carbon NT, are removed.



As a result, the gas phase can access the intra- and interlayer space of multilayer carbon NT. Further, carbon is simultaneously replaced outside and inside the carbon NT (Fig. 4). These

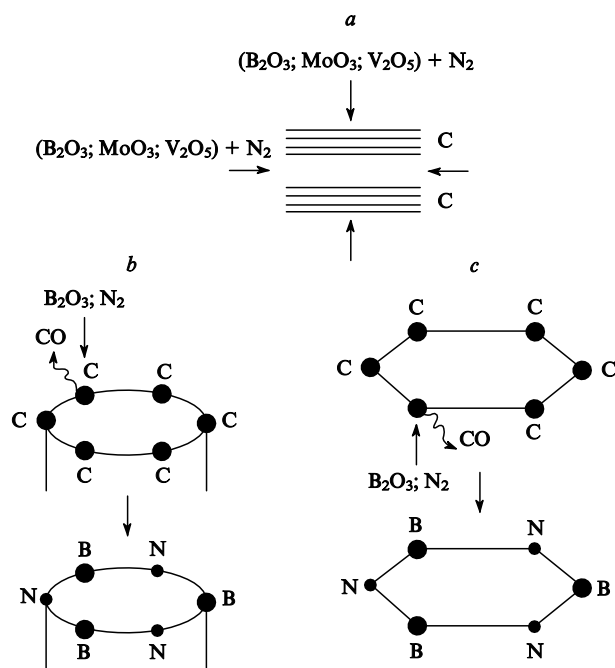


Figure 4. Scheme of the reaction of oxides and N_2 with multilayer carbon NT (a) in the reaction with its 'open' end (b) and its side surface (c) during chemical substitution in the synthesis of BN-nanotubulenes.⁶⁶

processes mostly involve the diffusion mechanism;⁷¹ as a result, growth of BN-nanotubulenes occurs.

High-resolution TEM was used to study the structure of BN-nanotubulene bundles obtained in the presence of PbO as the activator.⁷² All NT had zigzag geometry, their diameters ranged from 20 to 30 nm and their axes were arranged strictly parallel. It was suggested to consider this product as a new nanomaterial. It is characterised by invariable dielectric parameters and low chemical reactivity (in comparison with carbon NT).

High-resolution TEM analysis of the structures of multilayer BN-nanotubulenes showed that 'packs' of adjacent layers with hexagonal and rhombohedral types coexist, the wall structure changes from dented to zigzag-shaped and noticeable polygonisation of NT cross-sections takes place.⁷³

The substitution method was also used to obtain 'nanocables', i.e., BN-nanotubulenes filled with an alloy of Ni (40%) and Fe (60%).⁷⁴ In the first stage, carbon NT with nanoparticles of the alloy at the ends were obtained. These NT were then placed in a mixture of gaseous B_2O_3 and N_2 and kept for 30 min at the melting point of the alloy (1723 K). Two processes occurred simultaneously, viz., filling of the cavities with the iron–nickel alloy (due to the capillary effect), and change in the composition of the tube ('shell') due to chemical substitution.

It should be noted that the first SiC-nanotubulenes were obtained using the substitution reaction.⁷⁵ Large-diameter carbon NT and gaseous SiO were used as the starting materials.

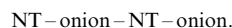
e. Miscellaneous methods

A number of methods for the synthesis of BCN-nanotubulenes based on thermal reactions have been suggested.

Carbothermal reduction of amorphous boron oxide with simultaneous nitridation (at 1373–1723 K)⁷⁶ gave a product containing cylindrical BN-nanotubulenes with various configurations (including bent or kinked ones, T-shaped, 'bamboo-shaped') and nanostructures in the form of concentric truncated cones. The overall reaction can be described by the following equation:



Cylindrical (closed) multilayer NT formed bundles; their junctions contained multi-shell onion-type BN-particles which served as growth centres. The tube diameters ranged from 10 to 500 nm; the length-to-diameter ratios ranged from 3 to 30. Nanotubes grew both in the gas and in the solid phase. The growth of bamboo-shaped NT involved alternation of cylindrical and onion-type fragments:



It was assumed that certain structures incorporated B_3N_4 heptagons, which ensured contacts at the junctions of cylindrical fragments. The obvious drawback of this synthetic method is that the forms of the nanotubulenes obtained are too diverse and that no method to control the formation of NT with required parameters is available.

Nanotubes and nanocones based on BN were also obtained by thermal treatment of rhombohedral β -boron at 1470 K in the presence of graphite-like boron nitride and lithium vapour.⁷⁷ Growth of zigzag-shaped NT was observed at the edges of graphite-like BN particles. BN-Nanofibres were found to appear upon annealing (~ 2000 – 2370 K) of BN powder in the presence of iron.⁷⁸

2. Dichalcogenide nanotubulenes

Transition metals dichalcogenides MX_2 ($X = S, Se, Te$) were the first inorganic compounds to attract the attention of researchers as compounds that are potentially suitable for the synthesis of tubular nanostructures. These compounds have a distinct quasi-two-dimensional structure. For example, molybdenum and tungsten disulfides have lamellar structures (of the MoS_2 type, space group $P6_3/mmc$) consisting of packs of $S-(Mo,W)-S$ layers; the metal atoms are in a trigonal-prismatic environment⁷⁹ and the layers are packed due to van der Waals forces.

Numerous NT based on tungsten, molybdenum and niobium dichalcogenides have been synthesised to date, mostly by chemical methods.

The formation of fullerene-like species and fragments of cylindrical nanostructures consisting of WS_2 and MoS_2 was first observed upon thermal treatment of tungsten or molybdenum films on quartz substrates in a flow of H_2S/H_2 .^{35,80} Remskar *et al.*^{81,82} used chemical transport reactions to obtain MoS_2 and WS_2 cylindrical nanocrystals and tubular structures (MoS_2 microtubes several millimetres long with wall thickness smaller than 0.1 μm). Galvan *et al.*^{83–85} proposed a low-temperature ($< 100^\circ C$) activation method to obtain WS_2 -nanotubulenes involving treatment of condensed tungsten disulfide with concentrated nitric acid. A new material consisting of WS_2 -based NT was obtained using WO_x nanoparticles.⁸⁵

In the synthesis of fullerene-like molybdenum disulfide particles, a gas phase reaction of MoO_{3-x} with H_2S at 1073–1223 K gave MoS_2 -nanotubulenes as side products.^{86,87} The tubes consisted of 5–10 MoS_2 layers on average, were several micrometres long and were mixed with MoS_2 (2H-polytype).

The methods for the preparation of dichalcogenide nanotubes (and nanofibres) and for the synthesis of fullerene-like polyhedral particles of these compounds are being developed in parallel.⁸⁸ Both NT and polyhedral hollow or filled nanoparticles of d -metal dichalcogenides are often obtained in a single experiment.

Molybdenum disulfide particles with 3–5 nm diameters were synthesised⁸⁹ by laser ablation of MoS_2 targets. Laser-induced vaporisation of tungsten and molybdenum disulfides in argon at 720–1320 K gave⁹⁰ various hollow and metal-filled multilayer nanoparticles. For example, the major fraction obtained upon vaporisation of WS_2 at 1320 K consisted of nanoparticles with 10–15 nm diameters containing 4–8 concentric layers of WS_2 . The bulk of filled nanoparticles was found to contain a stabilised β -W phase, which is unstable under ordinary conditions, as the filler metal. In addition, the products contained tubular nanostructures.

Certain properties of dichalcogenide NT were summarised in a review by Zhu *et al.*⁸⁸ Hollow WS₂-onions are promising as solid lubricants;^{89,91} their tribological properties can be optimised by filling the cavities with tungsten carbide. The synthesis of such 'composite' particles is based on the pyrolysis of WC nanoparticles in hydrogen sulfide.⁹²

The properties of MS₂-nanotubulenes have not been studied in sufficient detail. It was found that disulfide nanotubes are semiconductors; they possess low chemical reactivities.⁹³ Normally, multilayer NT contain numerous defects in the outer layers, whereas the inner walls generally have nearly ideal structures, which is reflected in the conducting properties of NT.^{94–96} The coalescence and the growth mechanism of WS₂-nanotubulenes to give 'braids' have been studied;⁹⁷ a method for changing the conducting properties of these NT under the effect of the substrate was suggested.⁹⁸ The application of WS₂-nanotubulenes in scanning microscopy was discussed;⁹⁹ several versions of the growth mechanism of these NT were suggested¹⁰⁰ and the adsorption of methane on their surfaces was studied.¹⁰¹

In addition to the syntheses of nanotubulenes based on transition metal disulfides, attempts were undertaken to obtain nanostructures of other dichalcogenides as well. For example, bombardment of niobium diselenide with electrons resulted in NbSe₂-nanotubulenes, a few nanometres long, closed on one end.^{101,102} By varying the accelerating voltage and the current density, NbSe₂-onions were obtained as well. A similar technique was used successfully to synthesise MoTe₂- (Refs 103–106) and WSe₂-nanotubulenes.¹⁰² Nath and Rao¹⁰⁷ considered a method to obtain NT by reduction of tungsten and niobium triselenides or by decomposition of ammonium selenometallates in an atmosphere of hydrogen. Recently, methods for the preparation of CuInS₂-nanotubulenes¹⁰⁸ and Bi₃Se₄-nanorods¹⁰⁹ were proposed.

3. Oxide nanotubes

Transition metal oxides are widely used to construct diverse nanostructured functional materials in the form of films, nanorods, and mesoporous materials.^{110–122} Some of these nano-objects are obtained with the use of carbon NT. For example, filling the internal cavities of carbon NT with V₂O₅, MoO₃, PbO, or Bi₂O₃ particles followed by chemical removal of the carbon shell gave oxide nanofibres and nanotubular ceramics.^{123–125}

Nanotubulenes of transition metal (vanadium and titanium) oxides have not been synthesised until recently.^{126–133} The sol–gel method was found to be efficient for this synthesis^{126–129} (for more detail about colloid methods to obtain nanostructures, see Refs 134 and 135).

Krumeich *et al.*¹²⁶ used the sol–gel method to obtain multilayer vanadium oxide NT (VO_x-nanotubulenes). Ethanolic solutions of vanadium(V) triisopropoxide and an amine C_nH_{2n+1}NH₂ (4 ≤ n ≤ 22) or α,ω-diamine H₂N[CH₂]_nNH₂ (14 ≤ n ≤ 20) in the molar ratio 2:1 were stirred for 1 h in an inert atmosphere and hydrolysed. Ageing of the system for 12–96 h resulted in an orange composite, which gave a black product upon hydrothermal treatment for 2–7 days (at 450 K) in an autoclave. The composition, structure and certain properties of the product obtained were examined by X-ray diffraction, XPS and TEM and by magnetic susceptibility measurements.

It was found that the major components of the composites were nanostructures with tubular morphologies, whose outer and inner diameters were 5–50 and 15–150 nm, respectively, and whose lengths were up to 15 μm. Special experiments to study the cross-sections of the resulting VO_x-nanotubulenes showed them to be multilayered.^{127,128} Both spiral (scroll-shaped) NT and those in the form of a set of concentric cylinders with organic molecules intercalated between the cylinders were detected. Spiral NT are formed most commonly. Mixed structures were also observed. Figure 5 shows the cross-section types of multilayer NT. The figure shows the defects of NT packs. Certain NT contain regions with parallel arrangement of VO_x-layers, both inside the tubes and

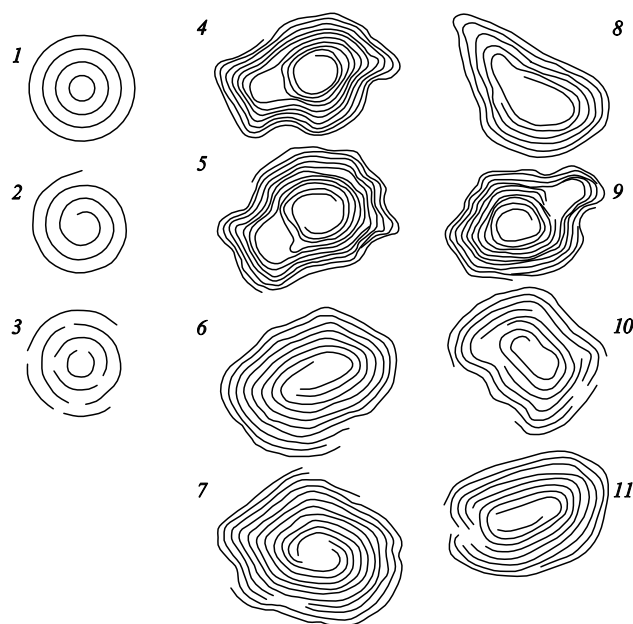


Figure 5. Models (1–3) and different cross-section structures (4–11) of multilayer NT;¹²⁷

(1) concentric cylinders ('Russian matreshka'), (2) scroll, (3) 'papier-mache'; (4–11) typical cross-sections of vanadium-oxide NT.

in the vicinity of junctions between the adjacent tubes. The number of NT layers varies from 2 to 30; they are built of tetrahedra (VO₄) and of square pyramids (VO₅).¹²⁶ These polyhedra also serve as structural elements of the crystalline phases α-V_{1.08}P_{0.92}O₅, (NH₄)₂V₃O₈, K₂V₃O₈ and BaV₇O₁₆·nH₂O. The distance between the adjacent NT layers (1.6–3.8 nm, Table 1) changes proportionally to the length of the alkylamine molecule serving as the intercalant. The overall molecular formula of NT can be written as VO_xO_{y/2}[C_nH_{2n+4}N]_y. Attempts to obtain 'pure' VO_x-nanotubulenes by removal of organic molecules upon thermal treatment are probably hopeless, as the tubes undergo complete degradation at temperatures > 520 K. It is more likely that amines can be replaced by cations of alkali or alkaline-earth metals (*e.g.*, Na⁺, K⁺, Mg²⁺, Ca²⁺, Sr²⁺). This method may become efficient for modifying the properties of VO_x-nanotubulenes. Replacement of monoamines by diamines in NT results in a noticeable decrease in the interlayer distances (from 1.6–3.8 to 0.9–1.0 Å). Specimens of the composite manifest semiconducting properties.

Table 1. Chemical composition, distances between the VO_x-layers, magnetic moments of vanadium atoms (MM) and relative concentrations of V⁴⁺ ions in VO_xO_{y/2}[C_nH_{2n+4}N]_y-nanotubulenes.¹²⁶

Composition	Interlayer distance /nm		MM /μ _B	[V ⁴⁺] (%)
	XRD ^a	ED ^a		
VO _{2.40} [C ₄ H ₁₂ N] _{0.25}	1.66	1.58	1.16	45
VO _{2.30} [C ₆ H ₁₆ N] _{0.27}	1.96	1.62	1.41	66
VO _{2.47} [C ₁₀ H ₂₄ N] _{0.27}	2.50	2.17	0.99	33
VO _{2.40} [C ₁₁ H ₂₆ N] _{0.27}	2.59	2.16	1.20	48
VO _{2.40} [C ₁₂ H ₂₈ N] _{0.26}	2.77	2.21	1.17	45
VO _{2.42} [C ₁₄ H ₃₂ N] _{0.27}	3.02	2.43	1.13	42
VO _{2.45} [C ₁₆ H ₃₆ N] _{0.26}	3.20	2.63	1.03	35
VO _{2.37} [C ₁₈ H ₄₀ N] _{0.26}	3.48	2.86	1.25	52
VO _{2.43} [C ₂₂ H ₄₇ N] _{0.30}	3.80	3.16	1.18	46

^a Data obtained by X-ray (XRD) and electron (ED) diffraction.

Two new methods for the preparation of VO_x -nanotubulenes from vanadium oxotrichloride and pentoxide as the starting compounds have recently been proposed.¹³⁰ Both processes are carried out in two stages. In the first stage, a solution of VOCl_3 (or V_2O_5) with the amine $\text{C}_n\text{H}_{2n+1}\text{NH}_2$ ($11 \leq n \leq 20$) is hydrolysed to give a gel; in the second stage, hydrothermal treatment is conducted to yield NT. If V_2O_5 is used, amines are directly intercalated between the pentoxide layers. The resulting NT can be described by the general formula $\text{VO}_{2.42 \pm 0.03} \cdot (\text{C}_n\text{H}_{2n+4}\text{N})_{0.27 \pm 0.01}$ ($11 \leq n \leq 20$). If VOCl_3 is used, the general formula of the NT is $\text{VO}_{2.45 \pm 0.05}(\text{C}_n\text{H}_{2n+4}\text{N})_{0.27 \pm 0.01}$ ($11 \leq n \leq 16$). The NT morphology is similar to that described above. The low cost of the product obtained is worth a special note.¹³⁰

Pillai *et al.*¹³¹ succeeded in synthesising a unique type of multilayer vanadium oxide NT with periodically alternating distances between the VO_x -layers by changing pH of the medium. Ammonia was added to the reaction mixture obtained upon hydrolysis of an ethanolic solution of vanadium(V) triisopropoxide to pH 10. The final product was obtained in accordance with the procedure described above (see Ref. 126). It was found that the outer diameters of the resulting NT (> 250 nm) were much larger than those of the NT obtained without ammonia (at pH 4–8); however, the lengths of the former (2–5 μm) were much smaller than those of the latter. The walls of the NT obtained in the presence of NH_3 are composed of regularly alternating VO_x layers; between these, amine molecules and NH_4^+ are intercalated alternately (the VO_x – VO_x interlayer distances are 2.0 and 0.9 nm, respectively). The NT structures contain various defects, for example, violation of periodic alternations of the interlayer distances; in certain cases, breakdown of layers (both inner and outer ones) occurred. The fact that NT contain defects was interpreted¹³¹ as an indication of their high stability. The overall chemical formula of the new NT could be expressed as $[(\text{NH}_4)_y\text{VO}_x][(\text{C}_n\text{NH}_3)_z\text{VO}_x]$; the defects are present in the $[(\text{C}_n\text{NH}_3)_z\text{VO}_x]$ layers. It is possible to control the structure of vanadium-oxide NT by changing the pH of the gel. It is assumed¹³¹ that ‘pure’ $[(\text{NH}_4)_y\text{VO}_x]$ -nanotubulenes with small interlayer distances can be synthesised at pH ~ 12 . On the other hand, it is known¹²⁷ that it is ammonium vanadate $[(\text{NH}_4)_2\text{V}_3\text{O}_8]$ that is formed under these conditions.

In addition to particles with well-shaped tubular morphologies, products with ribbon-like structures and intermediate forms could be revealed by SEM in these composites.

Syntheses of TiO_2 -nanotubulenes from solution¹³² and with the use of mesoporous Al_2O_3 (see Ref. 133) were reported.

4. NiCl_2 -Nanotubulenes

Hacohen *et al.*¹³⁶ were the first to synthesise halogen-containing nanotubular structures, namely, NiCl_2 -nanotubulenes. Nickel dichloride has lamellar structure (of the CdCl_2 type, space group $R3m$); its specific feature is that it has ferro- and antiferromagnetic types of spin ordering inside the layers and between them, respectively. Multilayer NT were obtained; their cross-sections were up to ~ 7 nm, while the lengths were several micrometres. The tubular structures remained stable for a few days. It is assumed¹³⁶ that the most interesting applications of such structures may be related to their unusual magnetic characteristics.

5. Miscellaneous methods for the synthesis of non-carbon nanotubes

a. Template synthesis

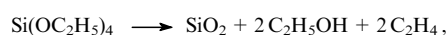
The template method of synthesis is used to obtain nanotubular composites, *i.e.*, multilayer NT containing layers with different chemical compositions. Stable NT (normally, carbon nanotubes) are used as the support, which is then coated with layers of various metals or compounds.^{124, 137–141}

The interest in nanotubular composites is due both to the possibility of preparation of tubular forms of those materials which are as yet unknown as isolated NT, and to specific proper-

ties of the composites themselves (*e.g.*, they behave as ‘interfaces’ between the adjacent cylinders of different chemical nature).

It should be noted that the method for the application of coatings on carbon NT is similar to that for the chemical modification of their surfaces, in which the composition of the outer layers of multilayer carbon NT is carried out by doping (substitution).^{142–146}

Seeger *et al.*¹⁴² proposed a method for the application of SiO_x -coatings on multilayer carbon NT at room temperature (in addition to the high-temperature method¹³⁸). The low-temperature (colloid) method is based on the formation of positively charged centres on the surface of multilayer carbon NT followed by deposition of negatively charged colloidal SiO_x particles onto this surface. The high-temperature method¹³⁸ is based on the thermal decomposition ($T > 503$ K) of tetraethoxysilane

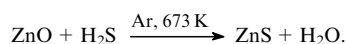


adsorbed on multilayer carbon NT.

The low-temperature SiO_x coatings had the form of continuous amorphous layers 3–10 nm thick with included nanocrystallites; the high-temperature process resulted in a non-uniform SiO_x layer, ~ 10 nm thick (complete covering of the support surface could not be reached). In both cases, no chemical interaction occurred between the contacting SiO_x layers and the multilayer carbon NT; the oxide film coated the NT directly without formation of any intermediate (*e.g.*, carbide) layers.

The method used to obtain ZnS-nanotubulenes¹⁴⁷ may be regarded as a combination of the template and substitution approaches. Highly structured semiconducting zinc oxide films which incorporated single-crystal ZnO columns obtained by non-equilibrium electrodeposition on a conducting substrate (glassy SnO_2) were used as the support.^{148–150} The columns (several micrometres high, with diameters of 100–300 nm) were oriented orthogonally to the substrate.

The process of formation of ZnS-nanotubulenes is based on the ion-exchange reaction



After exposure for 15 min, the thickness of the ZnS layer on the ZnO columns was ~ 15 nm; complete transformation of ZnO-columns into ZnS-nanotubulenes did not occur. The untransformed column matrix (ZnO) was removed by treatment with dilute H_2SO_4 . The resulting hollow ZnS tubes (open or closed) with wall thickness of ~ 10 nm maintained the surface morphology of the original crystallites; their cross-sections had polygonal shapes.

It is expected that other types of substitution may result in a wide range of NT with diverse chemical compositions, *e.g.*, tubular forms of semiconducting CuO, CuS, CdS, CdTe, ZnTe, *etc.*

b. Film ‘rolling’

As noted above, it is compounds which form phases with quasi-2D structures under equilibrium conditions that are usually considered as potential candidates for the synthesis of NT.

A fundamentally new approach to the problem of obtaining the nanotubular form of matter has been developed.^{151, 152} It was proposed to form NT from thin films. The principle of this method (which is subdivided¹⁵¹ into the ‘general’ and ‘special’ methods) is demonstrated in Fig. 6.

‘General’ method. A thin film is applied on a double-layer support the top layer of which can be removed by selective etching. Following the etching, an edge of the film is detached from the support, bent and placed atop the film. The tubular structure is formed in the bent region (see Fig. 6). For instance, this method was used to obtain silicon–germanium NT up to 12 μm long and with a diameter of ~ 230 nm. The thickness of one layer was 16 nm and was determined by the conditions of the film deposi-

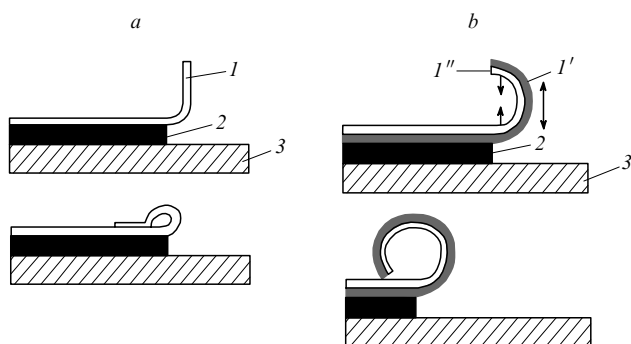


Figure 6. General (a) and special (b) film 'rolling' methods for obtaining NT;¹⁵¹

(1) single-layer (double-layer) film that forms nanotubes; (2) a top support layer removed upon selective etching; (3) a bottom support layer. Arrows show the force directions when a double-layer film is rolled.

tion. Yet another procedure of the synthesis of SiGe films¹⁵¹ gave NT with up to 50 nm diameter and a wall thickness of ~6 nm.

'Special' method. Double-layer films made of different materials are used; the interatomic distances in the material of the outer film layer (l') should be larger than those in the inner film layer (l'') (see Fig. 6). After etching and detaching a film edge from the substrate, each material tends to restore its original structure; owing to the resulting mechanical stress, the free film edge bends upwards, makes a full turn and forms a tube. In the case of prolonged etching, the film edge can make several turns to give specific rolls that resemble the familiar 'scroll'-type carbon tubes. This method made it possible to obtain tubes up to 20 μm long and with a diameter of 530 nm from double-layer InAs/GaAs,¹⁵² InGaAs/GaAs¹⁵³ and SiGe/Si films¹⁵⁴ and from epitaxial SiGe films.¹⁵⁵

It is important that the thickness of NT 'walls' obtained by this method, *i.e.*, the number of layers in the multilayer NT, depends exclusively on the film technology used and can vary over a wide range, down to a monoatomic layer. The approach suggested^{151, 152} does not impose fundamental restrictions on the chemical compositions of individual NT layers, which allows tubular hetero-structures to be formed from multilayer films. Yet another important advantage is that it is possible to set exactly the location of the NT on the support: it is defined by the position of the film edge and by the etching time. Thus, the main factors in the manufacturing of NT within this approach are the choice of the film deposition method (which defines the size and chemical composition of the resulting NT), the time of chemical etching and the elastic properties of the material of the NT-forming film. It is expected¹⁵¹ that this approach will provide single-crystal NT of many semiconductors.

III. Simulation of the structures and prediction of the properties of nanotubulenes based on boron, silicon, germanium and phosphorus

The search for new methods for the synthesis of non-carbon NT is performed in parallel with active studies on theoretical simulation of their configuration and electronic structure. Generally, the majority of studies employ zone or cluster models, as well as modern methods of density functional theory (DFT). Furthermore, structural features and kinetics of NT formation are studied by molecular dynamics methods. Details on specific approaches and computational schemes can be found in the original studies discussed below.

In addition to the conventional energy and electronic characteristics of NT, such as energy bands, electronic state densities (SD), interatomic interaction parameters and charge states, the

so-called strain energy is often calculated (E_{str}). This parameter is defined as the difference between the energy of the flat atomic layer and the corresponding NT. It is considered as an estimate of the energy required to transform a compound in crystalline (lamellar) modification to the tubular form. By comparing the E_{str} for the known (carbon) NT and hypothetical non-carbon NT, it is possible to make conclusions on the probability of accessing the latter.

Compounds that have stable or metastable lamellar phases become the most common subjects of a theoretical search for non-carbon NT. In general, the methods used to build geometrical models of such NT resemble those for the carbon NT.^{7, 21, 26, 30} Their classification is also carried out by analogy with carbon NT (using n , m indices).

1. Boron-based nanotubulenes

A number of studies^{156–165} deal with prediction of the tubular structures of boron, which are electron-deficient in comparison with carbon NT. A number of techniques were used to simulate the boron NT formation process.

The formation of B-nanotubulenes was simulated by the 'cluster assembling' method. In the first calculation stage, the Hartree–Fock and DFT methods were used to determine the sizes and configurations of small (several atoms) isolated boron clusters; after that, their association was considered. For example, starting from a B_7 hexagonal pyramid, a large number of topologically different B_n clusters were constructed: quasiplanar (quasi-2D), convex and three-dimensional. Planar structures were found to be most stable (see also Refs 166 and 167). Convex structures are less stable. The stability of these structures increases^{156, 159} if they incorporate a combination of two base clusters, *viz.*, hexagonal and pentagonal pyramids.

Boustani *et al.*¹⁶⁴ and Gindulyte *et al.*¹⁶⁵ simulated boron-based NT. They evaluated the stability of the isomers of the tubular form of the B_{32} cluster, the structures of which are shown in Fig. 7. It was found that the stability of these isomers decreases with a decrease in the diameter. In contrast, as the diameter increases (the curvature of the cylinder walls decreases), their energies approach that of the most stable planar form of boron.

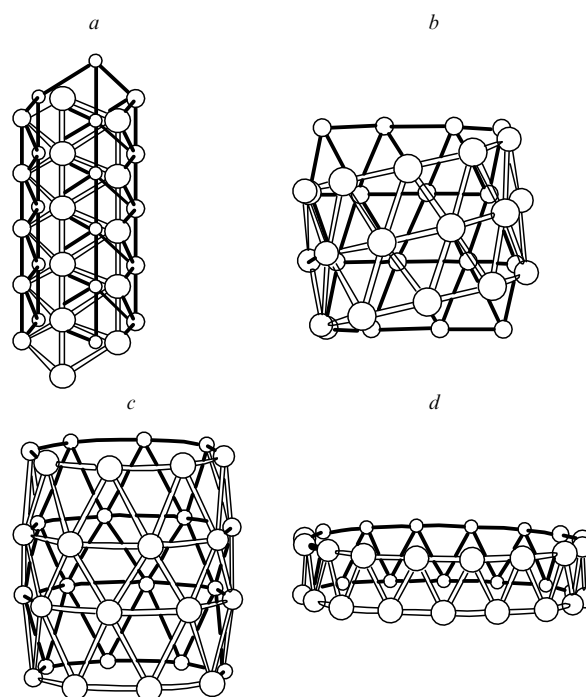


Figure 7. Model structures with C_{2h} (a), C_2 (b), D_4 (c, d) symmetry types for cylindrical B_{32} clusters with different diameters.¹⁶⁴

A competition between the following factors affecting the stability of the isomers was noted:¹⁶⁴ first, the high deformation energy of the planar layer, which increases abruptly with an increase in the curvature and prevents the formation of tubes with small diameters; second, the energy gain due to the coupling of broken (side) bonds in planar layers when they are rolling into a cylinder. Thus, it is quite possible to synthesise boron NT, but their diameters should be relatively large. Examples of such extended boron NT built like carbon NT were considered by Gindulyte *et al.*¹⁶⁵

The formation of NT in the bulk of α -boron quasi-crystals may be expected.¹⁵⁸ Calculations of local structural deformations for a 'compressed' boron quasi-crystal with rhombohedral lattice showed that closed hollow structures considered as precursors of the growth of extended NT are possible in this system.¹⁶⁸ The formation of boron NT may be critically affected by admixtures of various elements, *e.g.*, carbon or nitrogen.

2. Nanotubulenes based on silicon and germanium

The possibility of preparing NT consisting of silicon, which is a carbon analogue, still remains debatable. This is explained by great differences in the energy states of the atoms of these elements. It is known¹⁶⁹ that the most stable electronic configuration for the carbon atom is sp^2 , whereas for silicon it is sp^3 . Therefore, graphite is the most energetically favourable crystalline form for carbon, whereas a diamond-like structure is the most favourable for silicon. In the nano-state, carbon exists as atomic chains, hollow fullerene-like clusters and NT, whereas silicon does not form any polyhedral nanoparticles.¹⁷⁰

The first calculations of the energy and electronic states of hypothetical silicon-based NT formed by rolling of ribbon-shaped graphite-like structures of a layer composed of silicon atoms [nonchiral (6,6)- and (10,0)-NT and chiral (8,2)-NT] were carried out by the DFT method.¹⁷¹ The dependence of the electronic properties of such NT on their types is similar (see the corresponding reviews^{7,21,26,30}) to that of similar carbon NT. This is evident from the state densities for silicon NT shown in Fig. 8: the zigzag (10,0)-NT is a semiconductor with narrow energy gap, whereas the dented (6,6)-NT has metallic conductivity. Of interest are comparative energy evaluations of various carbon and silicon structures. The total energies (E_{tot}) of a silicon atom within a graphite-like network and in an NT are 0.79 and 0.83 eV lower than in crystalline silicon. The energy of cohesion (E_{coh}) of silicon atom in NT is only 82% of E_{coh} in a diamond-like crystal, whereas the E_{coh} of carbon atom in NT and in crystal (graphite) differ by no more than 1%. According to estimates,¹⁷¹ the energies required for rolling of networks consisting of carbon and silicon atoms into tubular structures are very similar (0.04–0.05 eV per atom). Presumably, the main problem in the synthesis of silicon NT is that it is difficult to obtain silicon in a lamellar (graphite-like) form.

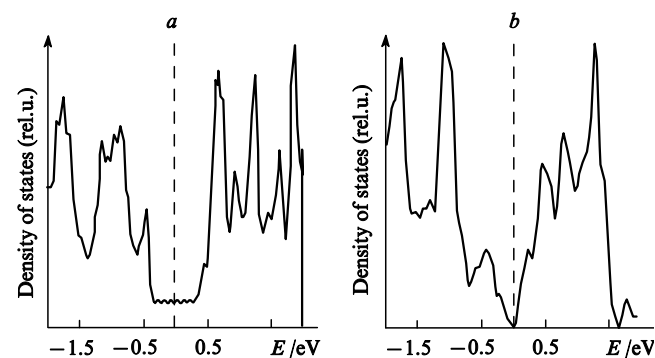


Figure 8. Full densities of states for silicon (6,6)- (a) and (10,0)- (b) nanotubulenes.¹⁷¹

Vertical lines show the Fermi energy.

Calculations on mixed carbon–silicon NT showed¹⁷² that the Si $\rightarrow$ C replacement energy within carbon NT is ~ 3.1 eV per atom. If a silicon admixture is present, it generates resonance states ~ 0.7 eV above the Fermi level in the electronic spectrum of a metallic carbon (6,6)-NT. A silicon atom within a semiconducting carbon (10,0)-NT gives rise to a local electronic level arranged ~ 0.6 eV above the valence band.

Seifert *et al.*^{173,174} calculated the electronic states and analysed the stability of silicon-containing NT based on silanes and siloxanes with complex composition. In such NT, the silicon atoms forming the tube frame are surrounded by hydrogen atoms or by hydrogen atoms and OH groups.

Like silicon, crystalline germanium has a diamond-like structure with sp^3 bond type; its quasi-2D modifications (of the CaSi_2 type¹⁷⁵ or CaGe_2 type¹⁷⁶) are also known. Recently, polymers containing networks of germanium atoms (GeH hexagonal layers) were synthesised.¹⁷⁷ According to calculations,¹⁷⁸ these compounds should be semiconductors (the width of the forbidden band is $E_g \approx 1.4$ eV). The DFT method was used¹⁷⁹ to simulate the electronic properties of hypothetical ($n,0$)- and (n,n)-NT ($n = 6-10, 20$) based on GeH. The cross-sections of (8,0)- and (8,8)-GeH-nanotubulenes, which are the most stable of those described above, are shown in Fig. 9. It was shown^{7,21,26,30} that the dependence of the energy deformation of NT on its diameter (D) has the form:

$$E_{\text{str}} \approx \frac{1}{D^2}. \quad (1)$$

All of these tubes are semiconductors; the forbidden band width varies considerably depending on the NT diameter [from 1.33 to 1.16 eV for (20,20)- and (7,0)-NT, respectively]. Possible methods for the synthesis of these NT include¹⁷⁹ topochemical reactions and synthesis from molecular GeH_4 .

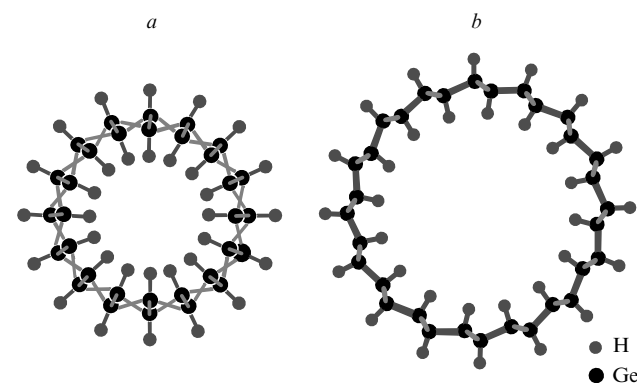


Figure 9. Structures of cross-sections (8,0)- (a) and (8,8)- (b) for GeH-nanotubulenes.¹⁷⁹

3. Phosphorus nanotubulenes

Orthorhombic black phosphorus is the most stable allotropic form of elementary phosphorus. The crystals of black phosphorus consist of graphite-like networks, the distance between which (0.36 nm) is much longer than the length of the P–P bonds in the network (0.223 nm). Unlike the planar graphene layers, the networks of phosphorus atoms are 'bulged'; this is explained by the repulsion of unshared electron pairs in the neighbouring atoms.

Seifert and Hernandez¹⁸⁰ compared the electronic and energy characteristics of an isolated network of black phosphorus with those of a number of hypothetical single-layer NT. In the initial stage, the structures of P-nanotubulenes (of zigzag and dented types) were constructed from ribbons of planar graphite-like layer of phosphorus atoms rolled to make a cylinder. After that, their geometry was optimised with respect to the axial displacements of atoms. Generally, relaxed structures of P-nanotubulenes are

similar to the structures of carbon NT and only differ in the type of six-membered rings. In the case of P-nanotubulenes, these rings have the form of cyclohexane rings consisting of phosphorus atoms.

The strain energy (E_{str}) of phosphorus NT is considerably higher than the E_{str} of carbon NT with similar diameters. This difference increases as the tube diameter decreases, which is explained¹⁸⁰ by changes in the electronic configurations of the carbon and phosphorus atoms in the networks. As a graphene network consisting of sp^2 carbon atoms folds, the increase in the wall curvature increases the contribution of the sp^3 orbitals.¹⁸¹ For a phosphorus network consisting of sp^3 phosphorus atoms, minimisation of the repulsion energy of unshared electron pairs of adjacent atoms occurs due to the maximum increase in the distances between adjacent phosphorus atoms upon their displacement from the network plane (the network ‘bulging’ mentioned above). As such a ‘bulged’ network is folded, the distances between the unshared electron pairs of certain phosphorus atoms decrease, resulting in rapid increase in E_{str} . However, the E_{str} of phosphorus NT at $D > 1.23$ nm is no higher than 0.1 eV per atom, which is comparable with the deformation energies of the corresponding carbon NT.

These energy estimates suggest that there are no obstacles to the existence of P-nanotubulenes. However, it should be expected that NT with rather large diameters will be formed. The following methods may be used to obtain P-nanotubulenes: the template method, a modification of the method for the synthesis of thin phosphorus films upon luminescent decomposition of PH_3 ¹⁸² and sublimation of phosphorus in the presence of catalysts.

It was noted¹⁸⁰ that phosphorus NT should have semiconducting characteristics invariable with respect to diameter changes (E_g changed in the range from 0.9 to 1.99 eV). Considering that the properties of phosphorus and arsenic are similar, the possibility that As-nanotubulenes may exist cannot be ruled out.

IV. Theoretical models of nanotubes based on *p*- and *d*-element compounds

1. Models of nanotubes consisting of B, C and N atoms

It was found in early studies^{4–8} of carbon NT that their properties could be affected by doping.

The cyclic cluster model and the semiempirical quantum-chemical MNDO method were used to study the charge distribution in carbon (6,6)-NT doped (one atom per unit cell) with one of the atoms: B, N or Si, in neutral, anionic and cationic state.¹⁸³ It was found that the distortions introduced by the dopants propagated along the NT to longer distances than across the NT. Distortions from charged dopants have a longer range than those from neutral atoms.

The local structural deformations of carbon NT appearing upon doping with single boron or nitrogen atoms were estimated.¹⁸⁴ In the case of nitrogen, the effects of structure relaxation are weak. Doping with boron resulted in displacement of the nearest carbon atoms by ~ 0.011 nm along the B–C bonds.

Scanning tunnelling spectroscopy and calculations within the DFT were used to study the effect of boron atoms on the properties and growth of carbon NT.^{185,186} Doping of multilayer carbon NT with boron confers on them metallic properties; the boron atoms are segregated to form separate islets in NT walls.¹⁸⁵ A boron admixture prevents the formation of ‘caps’ and favours the preferable growth of $(n,0)$ type NT.¹⁸⁷ This mechanism does not apply to dented NT; this fact can be used for growing selectively NT of certain geometries. Electrophysical studies¹⁸⁸ showed that doping of carbon NT with boron increases the paramagnetic susceptibility of the latter. Furthermore, their thermal factors of electrical conductivity are positive.

a. Boron nitride

Boron nitride was the first compound suggested for the synthesis of non-carbon NT. Quantum-chemical methods^{36–38} revealed a

number of interesting features of BN-nanotubulenes. Unlike carbon NT, the conducting properties of which are determined by their diameters and chiralities,^{4–8} BN-nanotubulenes are wide-gap semiconductors ($E_g \approx 5.5–6.0$ eV), which is important for the development of materials with predetermined properties. More detailed information about the electronic and energy characteristics of ‘ideal’ single- and multilayer BN-nanotubulenes can be found in a monograph⁷ and in a number of reviews.^{21,29,30}

In recent years, BN-nanotubulene structures were mostly simulated using the molecular dynamics method.^{76,189} The properties of the following tube types were compared:⁷⁶ chiral, zigzag-shaped, dented (built of graphite-like networks of B_3N_3 hexagons) and those built of four- (B_2N_2) and eight-membered (B_4N_4) rings. The latter type of BN-nanotubulenes were found to be the less stable.

The elastic properties of BN-nanotubulenes were estimated:¹⁹⁰ their Young modulus (Y) was 14 times higher than that for crystalline graphite-like BN, and comparable to the extremely high Y predicted^{191,192} for carbon NT (1–6 TPa). This agrees with the subsequent measurements¹⁹³ of the Young modulus for multilayer and single-layer carbon NT (0.4–4.0 TPa). The experimental studies¹⁹⁴ on the elastic properties of multilayer BN-nanotubulenes give values which are in good agreement with calculations¹⁹⁰ ($Y \approx 1.22 \pm 0.24$ TPa). Of the currently known elongated nanostructures with dielectric properties, BN-nanotubulenes are characterised by extreme values of the Young modulus comparable to those of glassy fibres.^{195,196}

The growth mechanisms of BN-nanotubulenes depend on their structures and differ considerably for $(n,0)$ - and (n,n) -nanotubes.^{197,198} The determining role in the growth process belongs to the specifics of the formation of terminal structures by virtue of B–N binding, these bonds being much more favourable than the B–B and N–N bonds. Zigzag NT stop to grow once ‘caps’ have formed. Dented NT grow by addition of extra atoms near the NT ends. The role of BN-rings of different types (in particular, five-membered rings) in the formation of BN-nanotubulene ‘caps’ and polyhedral boron nitride clusters, which are heteroatomic fullerene analogues, was discussed.^{199–207}

b. Boron carbides

Unlike BN-nanotubulenes, the type of electronic properties of BC_3 -nanotubulenes changes from metallic to semiconductor-type with the increase in their diameters.²⁰⁷ It is possible to increase the conductivity (hole concentration) of such NT by partial replacement of carbon atoms by ‘superstoichiometric’ boron atoms. Halogen atoms can serve as electron donors, as is observed for a number of intercalated graphites. The value of E_{str} for BC_3 -nanotubulenes is lower than that for carbon NT, which is in agreement with experimental data on their syntheses (see above).

c. Carbon nitrides

The existence of condensed carbon nitride (CN_x) and the extreme (comparable to that of diamond) hardness of $\beta\text{-C}_3\text{N}_4$ (the $\beta\text{-Si}_3\text{N}_4$ structure type) were predicted.^{208,209} Subsequently, CN_x was synthesised successfully (in amorphous, film and nanocrystalline states^{210–217}) and both various polymorphous modifications of crystalline CN_x and its tubular nanostructures were simulated theoretically.

Fundamental electronic properties of CN_x with the structures of the $\alpha\text{-Si}_3\text{N}_4$,^{218–220} Zn_2SiO_4 and $\alpha\text{-CdIn}_2\text{Se}_4$ ^{219,220} types and of a series of its quasi-2D modifications^{219–222} were considered. A lamellar structure containing graphite-like networks formed by a combination of triazine rings with nitrogen bridges was suggested for C_3N_4 .²²¹ Each carbon atom in the network is bound to three nitrogen atoms; each of the latter has only two closest neighbours. Planar C_3N_4 -networks can be packed according to $ABAB\dots$ type (the Bernal structure) or $ABCABC\dots$ type (the rhombohedral graphite structure).²²² The mean C–N bond length is ~ 0.136 nm (which is close to the sum of the Sleyter radii for the carbon and nitrogen atoms), the C–N–C bond

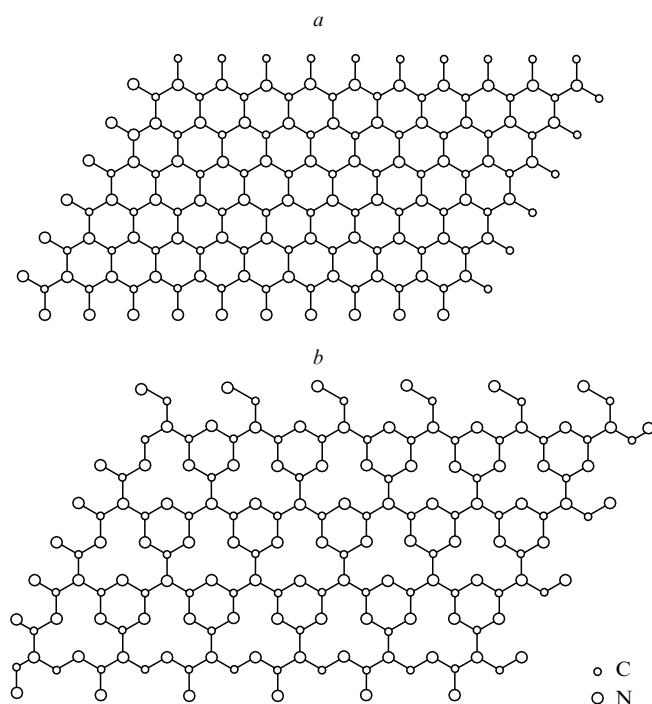


Figure 10. Planar networks used to simulate NT with compositions CN (a) and C₃N₄ (b).²²⁵

angle is 116° (see Ref. 221). It was found²²³ that vacancies appearing in the N-sublattice of cubic C₃N₄ favour its transformation into a pseudoplanar form. A number of other densely packed and lamellar modifications of carbon nitride have also been suggested (see the review²²⁴).

The structures of non-chiral single-layer (*n,n*)- and (*n,0*)-CN-nanotubulenes with different stoichiometry are described by networks similar to those of the C₃N₄ layers mentioned above and a hypothetical graphite-like layer with the composition CN (Fig. 10).^{225,226} All CN_{*x*}-nanotubulenes, irrespective of their structures and diameters, have metallic conductivity. Their deformation energy increases with a decrease in diameter, but it is smaller than that of carbon NT. In turn, E_{str} for CN-nanotubulenes is smaller than E_{str} for NT based on C₃N₄ (Fig. 11). It is assumed²²⁵ that the interlayer distances in multilayer CN_{*x*}-nanotubulenes will be ~0.04 nm smaller than those in multilayer carbon NT. The *sp*²-configuration of nitrogen atoms favours the stability of NT.

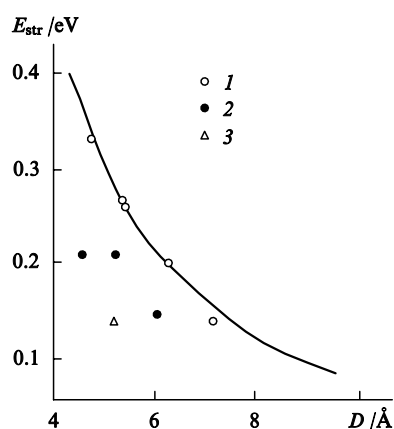


Figure 11. Deformation energy – diameter relationships for C- (1), C₃N₄- (2) and CN-nanotubulenes (3).²²⁵

The formation of fullerene-like molecules, NT and CN_{*x*} crystals was simulated by the molecular dynamics method.²²⁷ The simulation started from a planar fragment of a graphite network forming a cluster of 96 carbon atoms; in this system, the structural deformation upon replacement C → N in the N:C range 0.07–1.00 was studied. The CN_{*x*} layer remained planar up to the nitrogen content of ~20%; then it became ‘corrugated’ due to deviation of atoms (up to ~0.07 nm) away from the plane. It is believed²²⁸ that this results from occupying the antibonding π^* -orbitals (which is visible in photoelectron spectra) and formation of new, rather stable N–N bonds. The CN_{*x*} crystals may have various types of the layered packing of such deformed nitrogen–carbon networks. In should be noted that when a critical nitrogen content (~20%) is reached, a different type of structural evolution of this system is possible to result in NT or a fullerene-like molecule.²²⁷ It is important that stabilisation of the tubular and molecular states is attained at different system stoichiometry, *viz.*, CN and C₃N₄, respectively.

It is of note that only CN_{*x*}-nanotubulenes and nanofibres with relatively small *x* values ($x \leq 0.04$ –0.05) are known.^{229–236} Their electronic properties are interpreted on the basis of calculations for carbon NT containing nitrogen admixtures.^{236,237} In the general case, replacement of some carbon atoms in an NT by nitrogen atoms (electron dopants) increases the population of the energy bands and ‘metallisation’ of the NT. Admixtures of nitrogen create donor levels near the edge of the conduction band in carbon NT.^{236,237} Introduction of nitrogen atoms results in the formation of local pyridine-like fragments within NT walls; this explains the subtle features of electronic state distribution near the Fermi level, which may be important when creating nano-sized devices with hetero-transitions based on these NT.²³⁶

d. Boron carbonitrides

Theoretical construction of nanotubular structures was carried out based on a lamellar form of boron carbonitride BC₂N the electronic spectrum of which has been studied previously.^{238–240} It was assumed that the intralayer charge anisotropy, which causes the formation of ‘channels’ with increased and decreased electron density in BC₂N networks,^{238–243} would be preserved when these networks are rolled into cylinders (according to the chiral type) and would result in spiral motifs. As a result, circular currents would appear in BC₂N-nanotubulenes, and such NT may be considered as nano-solenoids (Fig. 12).

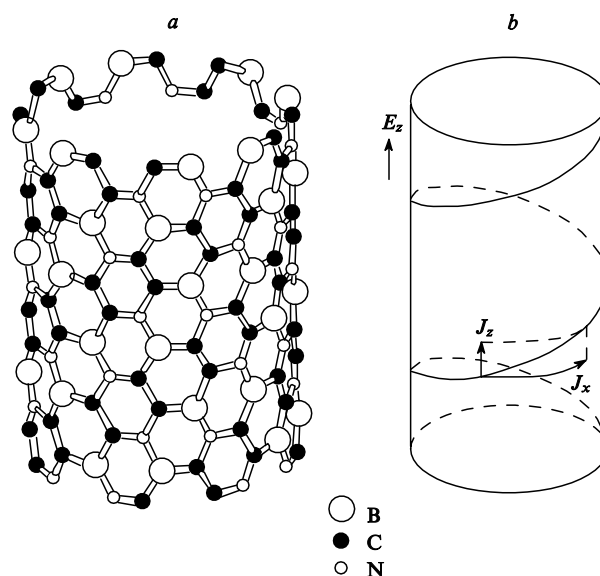


Figure 12. A variant of the atomic structure of a BCN-tube (a) and the scheme of circular currents therein (b).²⁴¹ E_z is the direction of the external field.

Nanotubes with small diameters maintain the conductivity type characteristic of the original BC_2N monolayers. The metallic type of conductivity of (n,m) -NT can change to the semiconductor type at certain diameters and chirality. The most stable are those (n,n) -NT which contain the maximum number of strong C–C and B–N bonds. Miyamoto *et al.*²⁴³ analysed the conditions required for the appearance of circular currents in such NT.

Attempts were made to describe the role of defects in the properties of BC_2N -nanotubulenes.^{241, 243} Partial replacement of carbon atoms by boron (or nitrogen) resulted in donor (or acceptor) admixture states for $\text{B}_{1+x}\text{C}_{2-x}\text{N}$ (or $\text{BC}_{2-x}\text{N}_{1+x}$) in the electronic spectra. Miyamoto *et al.*²⁴³ considered the role of electron (or hole) carriers in the formation of chiral currents in BC_2N -nanotubulenes.²⁴³

Analysis of the general trends in the formation of the atomic structure of BC_2N -nanotubulenes performed on the basis of results of theoretical studies showed that such nanotubulenes are characterised by the formation of BN- and C-islets.^{244, 245} The BC_x -nanotubulenes should undergo similar spontaneous segregation into regions consisting of carbon atoms and BC_3 fragments. These phenomena can give rise to quantum dots and hetero-transitions.

2. Nanotubes based on gallium nitride and selenide

The possibility of obtaining tubular structures for other compounds of Group III–V elements, which do not form lamellar structures under equilibrium conditions, was analysed for GaN (Ref. 246) and GaSe.²⁴⁷

In the first stage, the structures of a hypothetical crystalline graphite-like GaN were simulated by the DFT method and the equilibrium distances Ga–N in the layer were determined (0.178 nm).²⁴⁶ The difference between the bond energies of sphalerite-like (s) and graphite-like (g) phases of gallium nitride was found to be small, namely, 0.36 eV per atom. This value is smaller than the energy difference between s-GaN and its metastable cubic (sodium chloride-like) modification (0.5 eV per atom), which is considered²⁴⁶ to be evidence of the possibility of obtaining a lamellar allotrope of GaN.

The next simulation stage involved calculations of the electronic structure and E_{str} of gallium–nitrogen (n,n) - and $(n,0)$ -NT as a function of their diameters. Sawada and Hamada²⁴⁸ estimated the minimum possible NT sizes corresponding to zigzag-like (5,0)- and dented (2,2)-NT. It was found that E_{str} changes inversely to the square of the NT diameter; the geometry type of the walls of such tubes (unlike carbon ones²⁴⁹) only slightly affects E_{str} . On the contrary, this factor becomes important for the dielectric properties of GaN-nanotubulenes: although both tube types are wide-gap semiconductors [e.g., the values of E_g for (5,5)- and (9,0)-GaN-nanotubulenes are 2.15 and 2.16 eV, respectively], dented (n,n) -NT, like the hypothetical g-GaN, have indirect type of inter-band transitions. Zigzag-like $(n,0)$ -NT have direct type of the transitions. The E_g of $(n,0)$ -tubes decreases most significantly with a decrease in diameter. The GaN-nanotubulenes (like BN-nanotubulenes⁷) were found to manifest a relaxation effect: the atoms of the cationic (Ga) and anionic (N) sublattices are displaced by ~ 0.005 nm from the surface of an ideal cylinder: the gallium atoms are displaced towards the tube axis, whereas the nitrogen atoms are displaced in the opposite direction. Similar properties are also typical of GaSe-nanotubulenes.²⁴⁷

It is assumed that GaN-nanotubulenes can be obtained by template synthesis using carbon NT as the substrate.²⁴⁶ This will probably result in multilayer tubes with various chemical compositions (C/GaN nanotubular composites) with a metal–semiconductor interface. To date, tubular composites which are carbon NT partially filled with GaN, as well as separate GaN rods with 7–10 nm diameters and up to 40 μm long, have been synthesised.²⁵⁰ These specimens were obtained in an electric arc in an atmosphere of nitrogen with a graphite cathode and an anode containing a mixture of gallium nitride, graphite and nickel powder.

‘Pure’ GaN-nanotubulenes [with E_g values ~ 0.45 eV higher than those of the cubic phase of GaN (see Refs 246, 251, 252)] can be used in nanosized optoelectronic devices that are necessary, e.g., in colour displays.

3. Sulfide nanotubes

Nanotubes based on lamellar molybdenum and tungsten disulfides were constructed^{253, 254} from fragments of triple-layer packages S–(Mo,W)–S rolled into cylinders along certain chosen directions of the two-dimensional lattice. The tubes were classified (by analogy with the carbon NT) as non-chiral zigzag-like (n,n) - and dented $(n,0)$ -NT. The theoretical electron diffraction patterns built for these structures²⁵³ well describe the experimental data.²⁵⁵ Seifert *et al.*^{253, 254} used the DFT method in the strong bond approximation to study the dependence of the electronic properties and stability of a series of disulfide NT on their diameters. For example, the diameters of $(n,0)$ - and (n,n) - WS_2 -nanotubulenes ($n = 6, \dots, 22$) ranged²⁵⁴ from ~ 1.1 [for (6,6)- and (10,0)-NT] to ~ 3.1 nm [for (18,18-NT)]. For MoS_2 -nanotubulenes, the diameters ranged from 0.8 to 2.6 nm.²⁵³ The maximum diameters of model NT used in these studies were close to the minimum diameters of the disulfide NT synthesised.

The energy and electronic characteristics of all disulfide NT have certain common features,^{253, 254} which are also characteristic of crystalline phases.^{255, 256} Three bands are observed in the valence band of WS_2 -nanotubulenes, viz., A, B and C (Fig. 13), which result from contributions of quasi-framework $\text{S}3s$ - (band A), hybridised $\text{S}3p$ – $\text{W}5d$ - (band B) and $\text{W}5d$ -states (band C). The $\text{W}5d$ -states dominate in the vicinity of the lower edge of the conduction band. All (W,Mo) S_2 -nanotubulenes are narrow-gap semiconductors. However, $(n,0)$ -NT are semiconductors with direct transition in point Γ , whereas the family of (n,n) -NT is characterised by indirect transition type (Fig. 14). The forbidden band width increases with a decrease in the tube diameter, but it

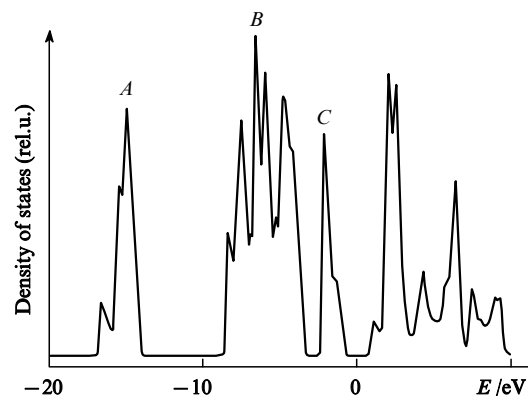


Figure 13. Full density of states for (18,18)- WS_2 -nanotubulene. $E_F = 0$.²⁵⁴

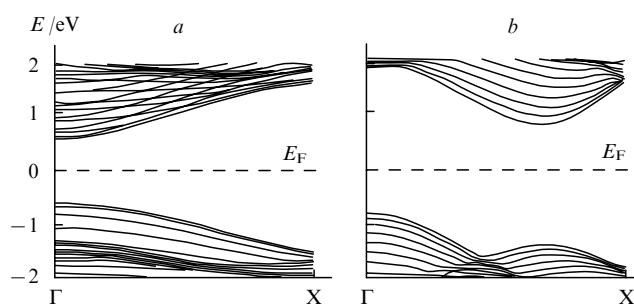


Figure 14. Energy zones for (22,0)- (a) and (18,18)- (b) WS_2 -nanotubulenes.²⁵⁴

Horizontal lines show the Fermi energies.

remains smaller than the E_g for three planar S–(W,Mo)–S layers. This result agrees with optical experiments²⁵⁶ which showed that E_g in the electronic spectrum of WS₂-nanotubulenes was smaller than that for crystalline tungsten disulfide.

Charge transfer in disulfide NT occurs in the direction W(Mo) → S.^{253,254} For MoS₂-nanotubulenes, the effective charges are ~0.9 e (0.44 e per sulfur atom), which is much smaller than the formal ionic charges in the crystal (Mo⁴⁺, S²⁻). The deformation energies for disulfide NT are higher than those of carbon NT with the same diameters. In turn, the E_{str} of zigzag-like (Mo,W)S₂-nanotubulenes is somewhat higher than the E_{str} for dented ones.

Seifert *et al.*²⁵³ studied the effect of topological defects (in the form of four- and eight-membered rings) on the structure of the ‘caps’ on closed NT and polyhedral nanoparticles (Mo,W)S₂ (see also Ref. 257). Milosevic *et al.*²⁵⁸ considered the general geometrical aspects of the structure of dichalcogenide NT, determined the symmetry groups of single-layer NT based on 2H- and 3R-polytypes of MoS₂ and WS₂ and discussed some of their properties that depend on the system symmetry (in particular, such as splitting of the energy bands, rules of selection and structures of the phonon spectra).

It is assumed²⁵³ that the semiconductor conductivity type of (Mo,W)S₂-nanotubulenes can be changed to the metallic type if the constituent molybdenum or tungsten atoms are partially replaced by niobium atoms. Recently,²⁵⁹ annealing of Nb₂O₅-coated W₁₈O₄₉ nanorods at 1100 °C in H₂S atmosphere gave the first ‘mixed’ NT with the composition W_{1-x}Nb_xS₂ ($x \leq 0.2$). Their properties have not been studied so far.

The DFT method was used to evaluate the stabilities and simulate the electronic properties of hypothetical (*n,n*)- and (*n,0*)-NbS₂-nanotubulenes²⁶⁰ ($n = 6, \dots, 22$, the NT diameters ranged from ~1.0 [for (6,6)- or (10,0)-NT] to ~2.4 nm [for (14,14)-NT]). It was found that the strain energy E_{str} of NbS₂-nanotubulenes obeys Eqn (1), and that it is higher than that of carbon NT with the same diameters. This fact was explained by a higher energy consumption for rolling of a fragment of an S–Nb–S triple-layer sheet into a tube, in comparison with similar consumption required for rolling of a graphene monolayer. The energy bands of the tubes considered above differ only slightly from each other and from the energy bands of planar niobium disulfide layers.²⁶¹ The states of these bands near the Fermi level (predominantly of Nb4*d*-type) have high density, which determines their metallic properties; this, in turn, gives a reason to expect²⁶⁰ that NbS₂- and NbSe₂-nanotubulenes may manifest superconductivity. It was noted²⁶⁰ that the onset of superconductivity may be due to an increase in the electron–phonon interaction and an increase in the critical temperature (T_c) in tubular niobium disulfide structures in comparison with the T_c for its crystal [~ 5.6 – 6 K (see Ref. 262)].

It was suggested that NbS₂-tubes could be obtained by thermal treatment of NbO_x nanorods in an H₂S atmosphere or by using template synthesis on carbon NT as the templates. The latter method gave²⁶³ long nanostructures, *viz.*, niobium disulfide tubes and rods.

4. Boride nanotubes

A broad class of lamellar materials comprises metal diborides (MB₂) and other MX₂-phases (X = Be, Si, Ga, Hg, Zn, Cd, Al, Cu, Ag, Au) with the AlB₂ type structure (space group $D_{6h}^{19} - P6/mmm$).^{264,265} These materials aroused particular interest due to the discovery, in 2001, of a superconducting transition in MgB₂ ($T_c \approx 40$ K).²⁶⁶ Since then, superconducting MgB₂ has been obtained as single crystals, dense and porous ceramics, films, long wires and bands, as well as in a nano-structured state; numerous studies of its properties have been carried out (see the reviews^{267,268}).

Chernozatonskii²⁶⁹ analysed whether MgB₂ can exist as an NT. Double-layer MgB₂-nanotubulenes were simulated by rolling

(by the chiral and non-chiral types) ribbon-like fragments cut from two adjacent layers of a MgB₂ crystal. It was assumed that stabilisation of the electron-deficient boron layer occurred due to partial electron transfer (Mg → B); the bond between the coaxial, oppositely charged Mg- and B-cylinders is partially ionic, and the distance between them is similar to the interlayer distance in an MgB₂ crystal. According to molecular dynamics estimates, diboride (*n,n*)-NT, which have a minimum deformation energy if the diameter of the ‘outer’ B-tube is ~19 Å [for (11,11)-MgB₂-nanotubulenes], are more stable. The author’s conclusions are based on estimates of the lattice instability of the MgB₂ and AlB₂ type structures²⁷⁰ formed by alternating (in the sequence ...MXMX...) planar hexagonal metal networks (M) and graphite-like non-metal layers (X).

Synthesis of magnesium-diboride NT is most likely to give tubes of a dented type. Considering the results of calculation of the electronic structures of crystalline MgB₂ (see Refs 267, 271–274), it is assumed²⁶⁹ that such tubes should have metallic conductivity. It is also assumed that they may have superconducting properties (see Refs 7 and 272 on the superconductivity in carbon NT).

A number of NT structures based on ZrB₂ have been reported. It is assumed²⁶⁹ that the ‘caps’ of closed MB₂-nanotubulenes can have the form of structures with defects in the M- and B-shells as five- and four-membered rings. Probably, diborides may also exist as multilayer structures, such as multilayer NT, or as onions. Such systems as (7,7)@(11,11)@(15,15)-NT and (MgB₂)₁₈₀@(MgB₂)₂₈₈, the so-called bifullerene, may serve as examples.

The DFT method was used to calculate several structures,²⁷⁵ the prototypes of AlB₂-nanotubulenes. It was found that all diboride NT should have metallic conductivity.

V. Models of hybrid nanotubular structures

1. Intercalated BN-nanotubulenes

Particular interest is attracted to the control of the properties of NT and synthesis of new nanocomposite materials with nontrivial functional properties based on these. Chemical modification of NT is one of the most effective methods to solve these problems. The properties of NT can be changed in various ways, for example,

(1) by introducing compounds — intercalants (atoms or molecules) — into the internal cavity of single-layer or multilayer NT, into the space between layers (neighbouring walls) of multilayer NT or into cavities between the adjacent NT in NT braids or in nanotubular crystals;

(2) by adding foreign atoms or molecules to the broken bonds of atoms belonging to the terminal groups of open NT, to atoms of the ‘caps’ of closed NT or to atoms of the outer surface of NT walls (adsorption on NT surface);

(3) by replacing partially the NT atoms by atoms of some other kind (NT ‘doping’).

These modification methods became most popular for carbon NT (see the reviews^{15–17,21–28}). For non-carbon NT, simulations of intercalated nanotubulenes and ‘symbiotic’ tubular structures are used most frequently. In the latter case, this idea was used for the possible formation of various 1D-heterostructures [the so-called symbiotic boron carbonitrides, *viz.*, (C + BN)-nanotubulenes] in addition to ‘ideal’ NT with a regular distribution of different kinds of atoms over the nodes in a B–C–N system.²⁷⁶ It is expected that the conducting properties of such NT would vary widely. Certain experimental data on their synthesis were mentioned above.

Chernozatonskii *et al.*²⁷⁷ considered hypothetical BCN-nanotubular structures consisting of alternating C- and BN-fragments as representatives of ‘symbiotic’ NT. Considering the similarity of the bond lengths C–C (0.142), C–N (0.150) and B–N (0.145 nm in graphite-like planes), such heterostructures can be formed,²⁷⁶ *e.g.*, as a result of the growth of carbon NT on

substrates containing BN nanocrystallites, or as a result of the formation of BN-nanotubulenes on diamond crystallites, or due to both processes occurring simultaneously. Yet another way to obtain these kinds of structures is chemical doping; as the carbon atoms are replaced by B and N, the latter form BN-‘islets’ within the original carbon NT.

Simulation of symbiotic tubular structures in the B–C–N system made it possible to predict a number of interesting properties for them.^{277, 278} It was suggested to consider C–BN-nanotubulenes containing rings of carbon atoms as a new class of quasi-one dimensional systems with quantum dots in which the local disturbance of the energy of electronic states exceed a certain characteristic value (usually $kT_{\text{room}} \approx 0.024$ eV). The crystal orbital method in one-orbital approximation was used to calculate the electronic spectrum of zigzag-like $(n,0)$ -BN-nanotubulenes ($n = 5, 6, 9, 27, 72$) in which a number of (B,N)-atomic rings in the bulk or at the ends of open tubes were replaced by rings of carbon atoms. The states of the terminal carbon rings form a number of discrete levels around the dielectric gap of BN-nanotubulenes; as the number of carbon atoms increases, these levels are transformed into mini-bands. For example, the spectrum of carbon states (in the dielectric gap) for $(27,0)$ -CBN-nanotubulenes consists of two groups of levels the widths of which are 0.7 and 1.7 eV. A similar effect (Fig. 15) was noted for the states of bridging carbon rings between the fragments of neighbouring NT. It is assumed that the existence of ‘quantum dots’ (or ‘quantum rings’,^{278, 279} *i.e.*, conducting carbon rings at the ends or between dielectric BN-nanotubulenes) can result in unusual properties of these structures, *e.g.*, lead to resonance effects in external magnetic fields. Lammert *et al.*²⁸⁰ discussed the results of doping of carbon NT with boron and nitrogen admixtures carried out in order to obtain structures containing chains of quantum dots. Such structures can be regarded as models of novel quantum nano-devices.

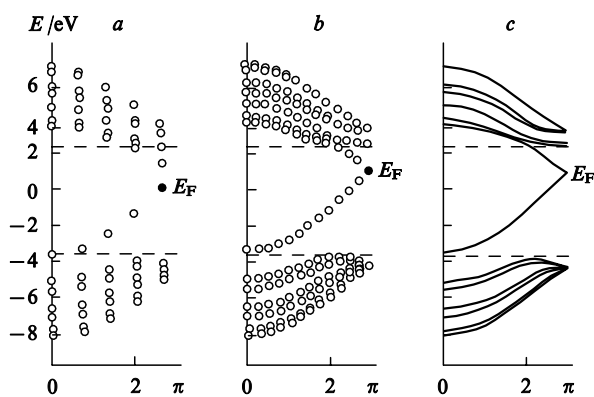


Figure 15. Energy zones for $(\text{BN})_3\text{C}_2(\text{BN})_3$ fragments of ‘symbiotic’ $(n,0)$ -nanotubes;²⁷⁷ $n = 9$ (a), 24 (b), 72 (c).

The electronic characteristics of the hetero-transitions in NT consisting of the C/BN, $\text{BC}_2\text{N}/\text{BN}$ segments (the superlattice model) were found²⁷⁹ to be stable against changes in the radii, chirality type and the number of layers in these NT.

Intercalated boron-nitride NT present yet another type of ‘tubular composites’. Rubio *et al.*²⁸¹ calculated the electronic spectra of $(4,4)$ -BN-nanotubulenes which incorporated potassium or aluminium ‘fibres’ arranged along the cylinder axis. The evaluated intercalation energies (the differences between the full energies of the composite and its constituents, namely, the NT and the metal ‘fibre’) were much smaller than the intercalation energies for similar systems with carbon NT. In the system $\text{K}@ (4,4)\text{-BN-nanotubulene}$, no new states appear in the electron energy spectrum. In the system $\text{Al}@ (4,4)\text{-BN-nanotubulene}$, additional

levels of Al s, *p*-type appear in the energy gap, and the electronic spectrum of this system becomes similar to a superposition of the spectrum of a monoatomic chain of aluminium atoms and the spectrum of $(4,4)$ -BN-nanotubulene. The density of electron carriers, which define the conductivity of intercalated BN-tubes, is concentrated inside the cylinder, hence such NT are preferable (as compared to carbon NT) when making nano-wires with predefined parameters. It is deemed possible to intercalate silver and gold atoms into BN-nanotubulenes.

Hernandes *et al.*²⁸² presented a new idea that a molecular diode can be created on the basis of carbon NT intercalated with boron and nitrogen. A nano-diode consists of a carbon $(10,0)$ -NT (with metallic conductivity). A ‘fibre’ along the axis of this tube has two parts, *viz.*, one formed by boron atoms (*p*-dopants) and the other formed by nitrogen atoms (*n*-dopants). According to calculations, *n*–*p*-doping results in a potential barrier (~ 1 eV) between the adjacent sections of the tube containing the boron and nitrogen parts of the ‘fibre’, respectively. Jishi *et al.*²⁸³ discussed the electronic states of (n,n) - BC_3 -nanotubulenes ($n = 2, 3, 4$) intercalated with a chain of bromine atoms.

2. ‘Symbiotic’ nanostructures: metal – carbon cages (met-carbs) in nanotubes

The effect of intercalation on the properties of NT for more complex systems was considered by Ivanovskii *et al.*^{284, 285} It was noted²⁸⁴ that the formation processes, stabilities and properties of $\text{M}@ \text{C}$ type nanosystems obtained upon intercalation of NT with atoms of various metals depends on the nature of the intercalant and the atoms that form the NT. For example, lead, zinc, nickel and copper atoms readily penetrate the carbon NT (these metals are either inert to carbon under equilibrium conditions or form unstable carbide phases²⁸⁶). On the contrary, introduction of atoms of Group IV – VI *d*-metals, which readily form carbides, is hindered: their strong interactions with the carbon atoms in the NT walls would result in the deformation and destruction of the latter. Obviously, similar reasons should prevent the synthesis of $\text{M}@ \text{NT}$ type nanostructures (where M are atoms of the Group IV – VI *d*-elements) based on BN-, BC- and BCN-nanotubulenes.

It is assumed^{284, 285} that new nanostructures incorporating Group IV – VI *d*-metals can be prepared if the latter are introduced into NT as their ‘own’ stable nanostructures. For example, these are represented by polyhedral clusters containing metal atoms along with carbon atoms, the so-called met-carbs, discovered not so long ago (in 1992).^{287, 288} Metallocarbohedranes with the composition M_8C_{12} are the most stable of them. Metal – carbon nanoparticles with other compositions and structures have also been obtained (see, *e.g.*, the reviews^{289–293}).

Ivanovskii *et al.*^{284, 285} calculated the energy and electronic characteristics of hybrid quasi-one-dimensional nanosystems ($\text{M}_8\text{C}_{12}@ \text{NT}$), *i.e.*, crystals formed by regular chains of met-carbs $\{[\text{M}_8\text{C}_{12}]_\infty$, where $\text{M} = \text{Sc}, \text{Ti}, \text{V}, \text{Zr}, \text{Nb}\}$ arranged along the axis of single-layer C-, BN-, BC_x -, $\text{B}_x\text{C}_{1-x-y}\text{N}_y$ -, Si- and GaN-nanotubulenes.

Analysis of the electronic structures of a number of systems belonging to quasi-unidimensional $\text{M}_8\text{C}_{12}@ (12,0)\text{-NT}$ type (Fig. 16) was carried out with consideration of the chemical composition of the NT, mutual arrangement of met-carbs and NT (displacement of the met-carbs along the axis and rotation around the tubulene axis were simulated) and the electron concentration (EC) in the system defined by the nature of the transition metal.²⁸⁴ 1D-Crystals incorporating the following met-carbs were considered: Sc_8C_{12} , Ti_8C_{12} , V_8C_{12} , Zr_8C_{12} and Nb_8C_{12} . It was found that the electronic spectrum of a quasi-1D $\text{Ti}_8\text{C}_{12}@ \text{BN}$ crystal consists of five occupied bands formed by the $\text{N}2s$ -, $\text{C}2s, 2p$ -, $(\text{C}2s, 2p + \text{N}2p)$ -, $(\text{N}2p - \text{B}2s, 2p + \text{Ti}3d)$ -, $\text{C}2p$ - and $\text{Ti}3d$ -states. The first four bands contain the states responsible for the chemical bonds in Ti_8C_{12} nanostructures and in BN-nanotubulenes. The states of transition metals around the Fermi level are responsible for the bonds of the neighbouring met-carbs in the chain and for the chain – NT interactions.

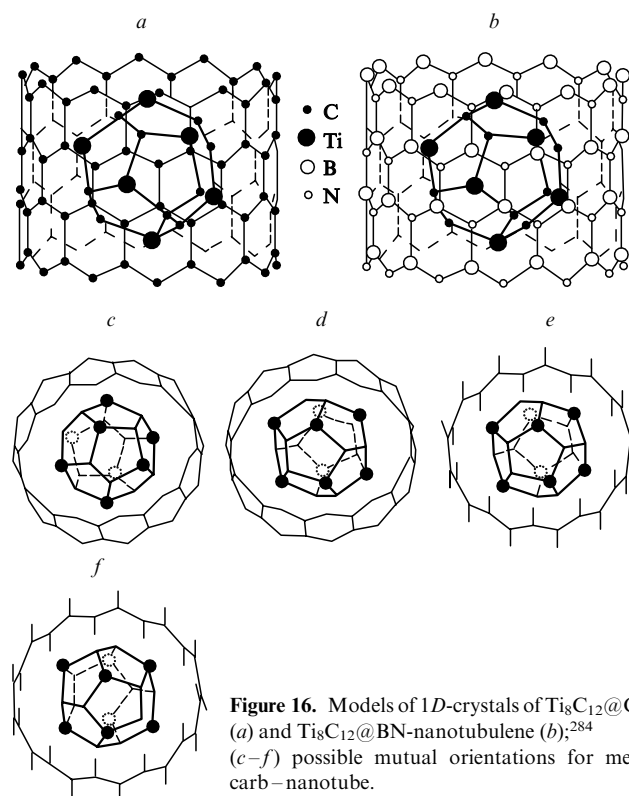


Figure 16. Models of 1D-crystals of $\text{Ti}_8\text{C}_{12}@\text{C}$ - (a) and $\text{Ti}_8\text{C}_{12}@\text{BN}$ -nanotubulene (b);²⁸⁴ (c–f) possible mutual orientations for met-carb-nanotube.

It should be noted that stabilisation of a $[\text{Ti}_8\text{C}_{12}]_\infty$ polymeric chain occurs in a 1D-crystal of $\text{Ti}_8\text{C}_{12}@\text{BN}$ -nanotubulene. However, the interatomic bonds in the NT and met-carbs change by no more than 1%–3%. In other words, the main types of the bonds which make these structures stable in the ‘isolated’ state are preserved in the crystal, which is evidence in favour of the stability of the simulated ‘symbiotic’ nanosystems. Ivanovskii *et al.*^{284,285} analysed the stability of this type of 1D-crystal depending on the position of the met-carbs and the NT and on the nature of the metal atom. Calculations for 1D-crystals incorporating Sc_8C_{12} and BN-nanotubulene in which the number of electrons per met-carb is less than 8 [as compared to the number of electrons per met-carb for $\text{Ti}_8\text{C}_{12}@(12,0)\text{-BN}$ -nanotubulene] showed that there are no bonds between the met-carbs. In contrast, the increase in EC on going to the $\text{V}_8\text{C}_{12}@(12,0)\text{-BN}$ -nanotubulene system favours a noticeable increase in the population of these bonds (by ~54%). Thus, it is possible to control both the bond strength and the stability of a system as a whole, as well as its dielectric properties, by changing the EC in the system (for example, by changing the chemical composition of the met-carbs by ‘doping’ them²⁹³).

It should be noted that a number of hybrid systems incorporating two types of stable nanostructures, *viz.*, fullerenes enclosed into an NT ($\text{C}_n@\text{C}$ type)⁶⁹ and NT incorporating endofullerene chains ($\text{M}@\text{C}_n@\text{C}$ type),⁷⁰ have recently been synthesised.

VI. Conclusion

Development of methods for the synthesis of non-carbon NT is now the leading direction in experimental studies on these unique subjects. Along with attempts to apply the methods known for the synthesis of carbon NT to the synthesis of other inorganic compounds in nanotubular form, elaboration of many ‘special’ synthetic methods is currently in progress.

In addition to physical methods, such as electric arc synthesis and laser ablation,^{3–6,15,16,24} which are particularly popular for producing carbon NT, chemical synthesis is becoming more and more important. In many cases, carbon NT serve as starting materials for the synthesis of non-carbon NT (chemical substitution, template synthesis).

It is difficult at the moment to compare the methods existing for the synthesis of non-carbon NT with respect to their productivity and effectiveness. It is possible that, even in the future, it will be hard to prefer some specific ‘versatile’ method, because the efficiency of each synthetic method depends on the chemical nature of the non-carbon NT.

The stage at which experimental studies are today is characterised by research into the synthesis of as wide a range of non-carbon NT as possible. The majority of studies describe the synthetic procedures and report the chemical compositions and morphology of the products. However, studies on physicochemical and functional properties are only occasional. These are only reported in selected studies and are far from being comprehensive.

Although it is possible to speak now of inorganic, physical, colloid, polymer and analytical chemistry of carbon NT,²⁷ it is too early to distinguish any particular areas of chemistry of non-carbon NT. The materials science of non-carbon NT is also in its infancy. Many suggestions to use them in practice are based on theoretical simulations and are far from technological solutions. The wide-scale production of non-carbon NT is also a problem yet to be solved.

Theoretical models have been developed for those non-carbon NT which have (or assumed to have) the closest similarity to carbon tubulenes. Ideal models of non-carbon NT in the shape of ideal cylinders rolled from a monoatomic sheet (or a polyatomic layer) remain the basis for describing these structures. Problems of describing various defects in non-carbon NT, processes of their growth and association into ‘braids’, films and crystals still need to be solved. There are no published data on the electronic and energy characteristics and properties of composite NT (*e.g.*, oxide NT that comprise oxide layers and an organic component). Problems of theoretical simulation also include NT reactivity and deviation of non-carbon NT from ideal morphology.

* * *

When this review was being prepared for publication, new interesting results appeared dealing with the synthesis and study of the properties of new non-carbon NT and materials based on them, as well as with their theoretical simulation. The most important studies are briefly considered below.

Tang *et al.*²⁹⁴ proposed a simple method for the synthesis of boron–nitrogen NT by thermal treatment of a mixture of elementary boron and iron oxide (in the ratio 15 : 1) in a flow of gaseous NH_3 . Chemical deposition from the gas phase onto a support containing Al_2O_3 particles with sizes of several micrometres gave multilayer (containing from two to five concentric layers) BN-nanotubulenes with unusually large inner diameters (8–10 nm).²⁹⁵ Guo *et al.*²⁹⁶ developed a two-stage process for chemical deposition from the gas phase, which allowed them to obtain Y-shaped splices of boron–carbon–nitride NT. Ma *et al.*²⁹⁷ obtained a ‘coaxial cable’, *i.e.*, a carbon NT filled with iron ‘core’ and containing dielectric boron–nitrogen nanotubulenes as the housing. It was confirmed by EELS that the carbon and boron–nitrogen layers in such heterostructures are separated from each other.

Studies on dichalcogenide NT were continued. Thermal decomposition of $(\text{NH}_4)\text{Mo}_{1-x}\text{W}_x\text{S}_4$ in an inert atmosphere or in hydrogen gave single-layer and multilayer NT with ‘mixed’ composition $\text{Mo}_{1-x}\text{W}_x\text{S}_2$ ($x < 0.1$)²⁹⁸ containing new defect types. A method for the synthesis of sulfide NT with the composition $\text{Cu}_{5.5}\text{FeS}_{6.5}$ was suggested.²⁹⁹ Pyrolysis of a mixture of WO_{3-x} with carbon NT in an $\text{N}_2 + \text{H}_2\text{S}$ atmosphere gave new composite structures, *viz.*, single-layer carbon NT encapsulated in multilayer WS_2 -nanotubulenes.³⁰⁰ Problems of hydrogen accumulation in MoS_2 -nanotubulenes were discussed.³⁰¹

Synthesis of silicon NT, both open and closed on the ends, with inner diameters of ~60–80 nm was reported.³⁰² They were obtained by deposition of a mixture of SiCl_4 with hydrogen onto a $\text{Ni}_x\text{Mg}_y\text{O}$ support that served simultaneously as a catalyst.

Interesting results were reported by Bao *et al.*³⁰³ who obtained nano-sized nickel tubes by electrochemical deposition of metallic nickel in pores of an alumina membrane. These nanostructures manifest magnetic properties. Li *et al.*³⁰⁴ were the first to obtain gallium-nitride NT.

Progress was also achieved in methods for the synthesis of oxide nanotubulenes. New schemes for the preparation of vanadium-oxide NT were discussed.^{305, 306} Doble *et al.*³⁰⁶ were the first to obtain mixed NT with the composition $\text{Mn}_{0.1}\text{VO}_{2.5+\delta}$ by ion-exchange reactions. A method for the synthesis of TiO_2 , ZrO_2 , Nb_2O_5 and Ta_2O_5 metal-oxide nanotubulenes using organic crystallites as templates was discussed.³⁰⁷ Reactions of crystalline TiO_2 (anatase or rutile) with a NaOH solution gave a multilayer titanium-oxide NT with distances of ~ 0.75 nm between the adjacent layers.³⁰⁸ The chemical compositions of the tubes (*viz.*, the Ti:O ratio) vary widely. A compacted set of titanium oxide-based NT was found in a product of anodic oxidation of pure titanium.³⁰⁹ The NT diameters range within 25–65 nm; their ends closed on the support side form a barrier layer resembling porous Al_2O_3 .

GeO_2 nanorods of 50–150 nm diameters and a few hundred micrometres long were obtained.³¹⁰ Studies of the photoluminescent properties of these nanostructures showed that they are promising as materials for optoelectronic nanodevices. The sol–gel method was used to obtain semiconducting Ga_2O_3 and In_2O_3 nanotubulenes with ~ 100 nm diameters.³¹¹

Maurin *et al.*³¹² studied the electrochemical doping of carbon electrodes built of NT with lithium; a number of other issues of the electrochemistry of lithium-doped carbon NT were considered elsewhere.^{313, 314} The positron annihilation method was used to study multilayer carbon NT doped with potassium, rubidium and cesium.³¹⁵ A review paper³¹⁶ discussed methods for the synthesis of composites containing metal atoms intercalated in carbon NT and the role of metal atoms as NT growth catalysts, as well as the results of studies of these composites by molecular dynamics and quantum-chemical methods.

A new composite material consisting of multilayer carbon NT in amorphous SiO_x has been obtained.³¹⁷ Furthermore, the SiO_x/NT structure was simulated by a strong-bond DFT method. The sol–gel method was used to obtain yet another new composite containing vanadium pentoxide and carbon NT, which may be promising as lithium battery electrodes.³¹⁸

Studies on $\text{C}_n@C$ -nanotubulene hybrid systems (fullerenes in nanotubes) were continued.^{319–321} The local electronic states of the $\text{C}_{60}@C$ -nanotubulene system were studied by scanning tunnelling microscopy³¹⁹ and EELS.³²⁰ It was concluded³²⁰ that fullerene–NT interactions occur due to weak van der Waals forces. The methodological aspects of the use of EELS spectroscopy for studies on the optical and electronic structures of $\text{C}_n@C$ -nanotubulenes were analysed.³²¹

Interesting results were obtained in theoretical simulation of the systems in question.³²² For example, calculations for a set of hypothetical SiC-nanotubulenes by DFT made it possible to suggest that they can be synthesised by injection of holes.³²³ The type of the interband transition in these metastable tubular structures (*i.e.*, whether direct or indirect transitions occur) depend on their chirality. The E_{str} of these NT were found to be smaller than the E_{str} of the corresponding carbon NT.

Much attention is paid to the development of microscopic models of ‘hybrid’ nanostructures. Based on calculations of the potential energies for systems containing spherical and ellipsoid fullerenes inside carbon NT, the ‘optimum’ sizes for the fullerenes to be incorporated were discussed.³²⁴ The molecular dynamics method was used to calculate the energy states and the elastic and tribological parameters of fullerenes in (n,n) -C-nanotubulenes (where $n = 5 - 10$).³²⁵ A very interesting problem was considered by Liu *et al.*³²⁶ they optimised model ‘hybrid’ nanostructures in the form of carbon NT containing a monoatomic ‘fibre’ of carbon atoms inside (along the axis). It was shown that for the NT with

diameters larger than ~ 0.43 nm the fibre turns into a spiral along the NT axis.

Non-empirical DFT calculations of the energy states of C_{60} fullerene in boron–nitrogen NT were carried out.³²⁷ It was estimated that incorporation of fullerenes into (9,9)- and (10,10)-NT is exothermic, which implies that such ‘hybrid’ structures can actually be synthesised. It was shown that they would be semiconductors.

The formation mechanism of yet another type of ‘hybrid’ structure, *viz.*, small-size ionic KI crystallites inside carbon NT, was studied by molecular dynamics methods.³²⁸

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^a — *Physics-Uspekhi (Engl. Transl.)*

^b — *Russ. J. Inorg. Chem. (Engl. Transl.)*

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^d — *Russ. J. Struct. Chem. (Engl. Transl.)*

^e — *Chem. Phys. Rep. (Engl. Transl.)*

^f — *Theor. Exp. Chem. (Engl. Transl.)*

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

Captodative aminoalkenes

A Yu Rulev

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Abstract. Procedures for the synthesis of captodative aminoalkenes, which were developed primarily over the last 15 years, are systematised. The influence of the structural and stereoelectronic effects of the substituents both at the nitrogen atom and at the double bond on the reactivity of these systems is considered. Particular emphasis is given to regio- and stereoselectivity of electrophilic, nucleophilic and radical reactions of captodative aminoalkenes as well as to processes of the construction of carbo- and heterocyclic compounds based on these aminoalkenes. A special section is devoted to the chemistry of methylidene- and arylmethylidenequinuclidin-3-ones. The bibliography includes 327 references.

I. Introduction

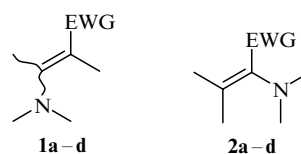
Two decades ago, Viehe^{1–4} proposed the concept of the captodative effect. Later on, the notion of captodative alkenes was introduced for compounds characterised by the simultaneous presence of electron-withdrawing (captive) and electron-donating (dative) substituents at the same carbon atom of the double bond. Alkenes containing the electron-donating and electron-withdrawing substituents in the vicinal position are termed push-pull.

Among captodative alkenes, enamines containing the geminal electron-withdrawing group (EWG) attract the most attention. Since these alkene derivatives possess special chemical properties, they were regarded as a separate group of organic compounds. Recent studies demonstrated that cross-conjugated isomers exhibit specific and much more versatile reactivities as compared to fully conjugated push-pull aminoalkenes.

Many captodative aminoalkenes have already found wide application. It will suffice to mention that these compounds are structural fragments of bioorganic molecules and serve as building blocks in the synthesis of various biologically active heterocycles and analogues of natural compounds. In the solution of some natural-science problems of the prebiotic chemistry and philosophical questions about the origin of life on Earth, much attention has been focused on the simplest representatives of captodative

alkenes (see, for example, the studies^{5–9} devoted to 2-aminoacrylonitrile).

However, while the chemistry of push-pull aminoalkenes **1** has been studied in sufficient detail and its various aspects were surveyed in a series of fundamental reviews,^{10–16} captodative aminoalkenes **2**, on the contrary, remained poorly studied until recent years.



EWG = CN (**a**), CO₂R (**b**), C(O)R (**c**), CHO (**d**).

The first effort to systematise the main procedures for the preparation of 2-aminocycloalk-2-enones and consider their most remarkable properties was made in the review,¹⁷ which covered the data published up to 1983. In the review¹¹ devoted to the chemistry of β -aminoenones, a special section was concerned with the data on the chemical behaviour of captodative aminoalkenes (mainly, cyclic), which have been reported only in 30 scientific sources. In the last 15 years, some important aspects of the chemistry of captodative aminoalkenes were developed substantially owing, primarily, to elaboration of simple and efficient procedures for the synthesis of such systems. The present review generalises the data on the chemistry of captodative aminoalkenes. The first section of the review is dedicated to procedures for the preparation of captodative alkenes containing an unsubstituted, mono- or disubstituted amino group and one electron-withdrawing group (carbonyl, alkoxy carbonyl or cyano group) at the same centre. In the second section, the spectroscopic characteristics of captodative aminoalkenes are analysed, including the data on their structures. In the third section, the major types of transformations characteristic of these compounds are classified. A special section is devoted to the chemistry of 2-methylidene- and 2-arylmethylidenequinuclidin-3-ones belonging to bicyclic captodative aminoalkenes, which do not exhibit properties of enamines due to their structural characteristic features. Quinoid structures, which formally contain the $C=C(NR_2)CO$ fragment, and activated alkenes bearing the geminal acylamino group are beyond the scope of the present review. Data on some compounds of this type (in particular, dehydroamino acids) were surveyed in a number of publications (see, for example, the review¹⁸).

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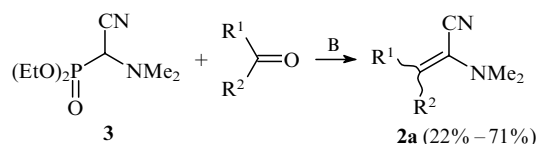
Uspekhi Khimii **71** (3) 225–254 (2002); translated by T N Safonova

II. Synthesis of captodative aminoalkenes

1. Insertion of the double bond into systems containing geminal amino and electron-withdrawing groups

a. Olefination of carbonyl compounds

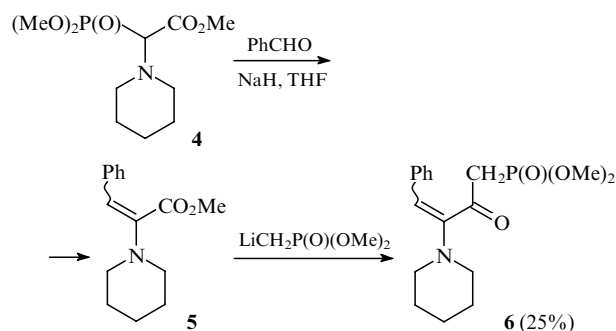
One of the classical ways for inserting a double bond into a molecule involves Wittig-type olefination of aldehydes and ketones. Various captodative aminoalkenes were successfully prepared according to this procedure. Costisella and Gross demonstrated that cyanophosphonate **3** reacted with aromatic or aliphatic aldehydes and ketones in the presence of a strong base (BuLi, THF;¹⁹ NaH, dioxane or DMSO²⁰) to form 1-cyanoenamines **2a** in moderate yields.



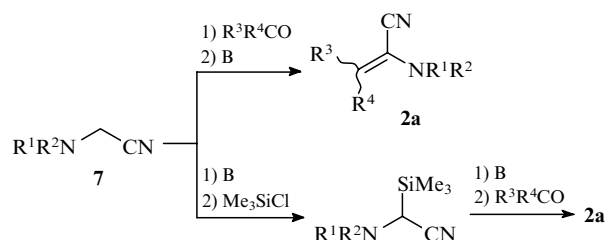
$\text{R}^1 = \text{H, Me, Et, Pr}^i, \text{n-C}_6\text{H}_{13}, \text{Ph, 4-NO}_2\text{C}_6\text{H}_4, (\text{EtO})_2\text{P(O)CH}_2, \text{2-furyl};$
 $\text{R}^2 = \text{H, Ph; B is a base.}$

Later on, it was found that this reaction could be performed by electrolysis of phosphonates **3** on platinum or glassy-carbon electrodes,²¹ the carbanion being generated on the cathode. This carbanion reacts with the carbonyl compound to give finally the target alkenes **2a** in satisfactory yields.

In addition to the aminonitriles **3**, the reactions were successfully performed with esters. Thus methyl (dimethoxyphosphoryl)piperidinoacetate (**4**) reacted with benzaldehyde to form unstable methyl 3-phenyl-2-piperidinoacrylate (**5**), which was transformed into β -ketophosphonate **6** without isolation.²²



The 1-cyanoenamines **2a** were also prepared from aminoacetonitriles **7** and aliphatic (including α,β -unsaturated) or aromatic aldehydes by the Peterson reaction^{23–27} or condensation in the presence of a strong base (KH, KOH–K₂CO₃).^{24, 28} Both procedures appeared to be extremely sensitive to the nature of the amino group in the starting substrate **7**. In the case of dimethylamino-, diethylamino- or pyrrolidinoacetonitriles, the reactions either did not take place at all or proceeded in very low



$\text{R}^1 = \text{Me, CH}_2=\text{CHCH}_2, \text{MeCH}=\text{CHCH}_2; \text{R}^2 = \text{Ph, Bn};$
 $\text{R}^3 = \text{H, Me, Pr}^n, \text{Pr}^i, \text{n-C}_5\text{H}_{11}, \text{Ph, 4-MeOC}_6\text{H}_4, \text{MeCH}=\text{CH},$
 $\text{EtCH}=\text{CH, PhCH}=\text{CH, 2-thienyl, 1-naphthyl};$
 $\text{R}^4 = \text{H, Me, Et, Ph; B = KH, LDA or KOH–K}_2\text{CO}_3\text{–Bu}_4\text{NBr.}$

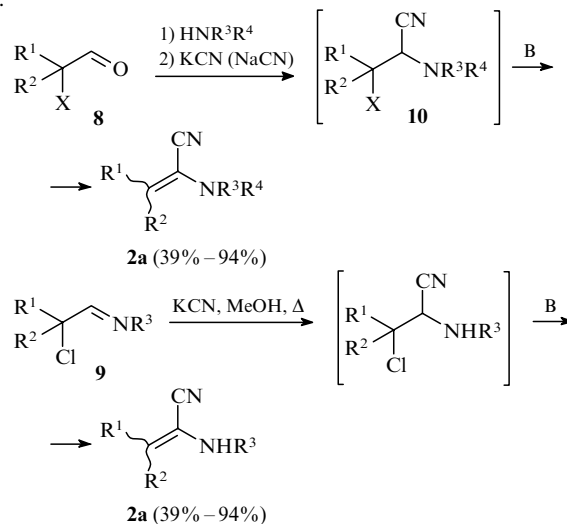
yields.²⁴ (*N*-Methylanilino)acetonitrile [**7**, $\text{NR}^1\text{R}^2 = \text{N(Me)Ph}$] proved to be the only substrate, which was almost quantitatively transformed into the corresponding 1-cyanoenamine.

Aldol condensation of α -aminoketones bearing the active methylene group with aromatic aldehydes afforded the corresponding captodative aminoalkenes **2c**.^{29, 30}

b. Elimination

A wide range of captodative aminoalkenes were prepared by elimination reactions, which very readily proceed in the case of β -heterosubstituted ketones, aldehydes, nitriles and esters.

Elimination of hydrogen halide from α -amino- β -haloketones or derivatives of carboxylic acids is a valuable approach, provided that the corresponding starting compounds are readily accessible. The idea of the use of haloaldehydes as building blocks in the synthesis of captodative aminoalkenes has long been known. More than 40 years ago, Temin³¹ developed an original synthesis of α -morpholinoacrylonitrile from chloroacetaldehyde (**8**, $\text{R}^1 = \text{R}^2 = \text{H, X} = \text{Cl}$), which was generated *in situ* from dimethylacetal.^{32, 33} This classical procedure (with small modifications) continues to be used for the preparation of the 1-cyanoenamines **2a**.^{34–36}



$\text{R}^1 = \text{H: R}^2 = \text{Pr}^n, \text{Pr}^i, \text{Ph; R}^1 = \text{Me: R}^2 = \text{Et, Ph; R}^1 = \text{R}^2 = \text{H, Me, Et, Cl; R}^1 - \text{R}^2 = (\text{CH}_2)_4, (\text{CH}_2)_5, \text{CH}_2\text{CH}=\text{CHCH}_2; \text{X} = \text{Cl, Br};$

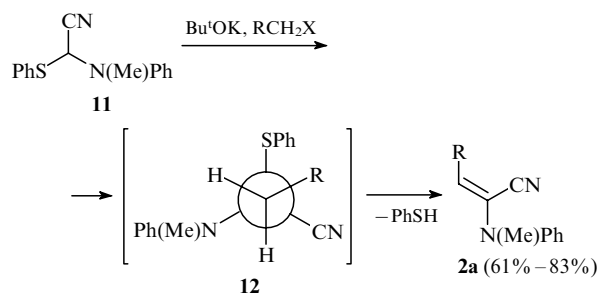
$\text{NR}^3\text{R}^4 = \text{NH}_2, \text{NMe}_2, \text{NEt}_2, \text{pyrrolidino, piperidino, morpholino, N(Me)Ph, N(Me)C}_6\text{H}_{11}\text{-cyclo};$
 $\text{R}^4 = \text{H: R}^3 = \text{Me, Et, Pr}^i, \text{Bu}^t,$
 $\text{cyclo-C}_6\text{H}_{11}, \text{CH}_2\text{Bn; B} = \text{Et}_3\text{N or NaOH.}$

De Kimpe *et al.*^{37, 38} extended the scope of application of this method using α -chloroaldehydes **9** as the starting compounds. The latter are prepared from aliphatic aldehydes by successive imination with primary amines and chlorination with *N*-chlorosuccinimide. The reactions of the aldehydes **9** with KCN in methanol afford the 1-cyanoenamines **2a** in high yields. It was assumed^{37, 38} that the synthesis proceeded through 2-(*N*-alkylamino)-3-chloro-substituted nitriles as intermediates, which were readily dehydrochlorinated under the reaction conditions.

There are also other examples where the resulting 2-amino-3-halopropionitriles **10** were subjected to dehydrohalogenation to give the corresponding 1-cyanoenamines **2a**, including those with the unsubstituted,³⁹ mono-⁴⁰ or disubstituted amino group.^{41, 42} For these reactions, Et₃N^{32–36, 39–41} or NaOH³¹ are the reagents of choice.

An elegant preparative procedure proposed recently for the synthesis of various 1-cyanoenamines **2a** is based on the involvement of (*N*-methylanilino)phenylthioacetonitrile (**11**) in the tandem alkylation–elimination process.^{43, 44} The reaction proceeds stereospecifically to form the *E* isomer, which is accounted for by

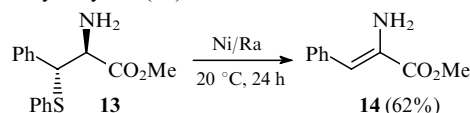
anti-elimination of PhSH from intermediate **12**. The latter was isolated and characterised by spectroscopic methods.⁴³



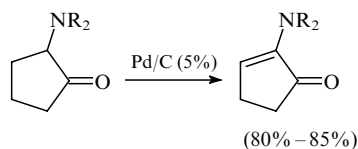
R = H, Me, Pr, Br(CH₂)₂, I(CH₂)₄, Ph, CH₂=CH, PhCH=CH, MeCH=CH, BrCH=CH, PhSCH₂CH=CH, PhSCH=CH;

X = Cl, Br, I.

An attempt to reduce ester **13** with Raney nickel led to unexpected elimination of PhSH giving rise to methyl 2-amino-3-phenylacrylate (**14**).⁴⁵



In my opinion, the above-considered reactions are of considerable synthetic value. In addition, there are other examples of the synthesis of captodative aminoalkenes resulting in elimination of hydrogen halide,⁴⁶ alkanethiol,⁴⁷ amine,⁴⁸ hydrogen cyanide,⁴⁹ water⁵⁰ or alcohol.^{51,52} Dehydrogenation of *N,N*-disubstituted 2-aminocycloalkanones is also worthy of mention. Thus 2-aminocyclopent-2-enones were obtained in high yields by passing gaseous 2-aminocyclopentanones over Pd/C.⁵³

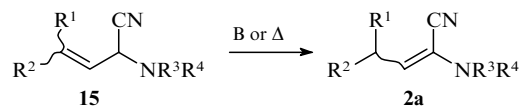


NR₂ = NEt₂, N-piperidyl, N-morpholyl.

c. Rearrangements

In some unsaturated compounds, double-bond migration readily occurs under the action of strong bases. The driving force for this process is the formation of a thermodynamically more stable isomer due to interaction between the π -system of the double bond and the electron-withdrawing group.

Treatment of β,γ -unsaturated α -aminonitriles **15** with strong bases (Bu^tOK or MeONa) under mild conditions afforded the corresponding 1-cyanoenamines **2a**.^{26,27,54–56} It should be noted that the stereochemistry of the reaction product depends both on the conditions of its preparation and the structure of the starting substrate. In addition, thermally initiated isomerisation can take place in these systems, as, for example, upon distillation of the nonconjugated aminonitriles **15**.³⁴

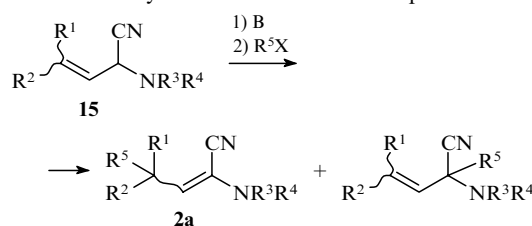


R¹ = H; R² = Me, Pr, Ph; R¹ = R² = H;

NR³R⁴ = N(Me)Ph, N(All)Ph, N(Me)C₆H₄Br-2; B = Bu^tOK, MeONa.

Under the action of strong bases, the β,γ -unsaturated *N,N*-disubstituted α -aminonitriles **15** produce ambident anions, which can undergo alkylation either at the α or γ position.⁵⁷ This property was used for the preparation of various 1-cyanoen-

amines **2a**.^{54,58–63} It was established that regioselectivity of alkylation is determined by different factors, among which are the steric parameters of the electrophilic reagent, the amino group and the γ -substituent in the substrate.⁵⁸ The formation of the captodative aminoalkenes **2a** is favoured by the presence of a bulky amino group in the substrate molecule. For example, alkylation of the nitriles **15** containing the N(Me)Ph or N(cyclo-C₆H₁₁)Ph groups always proceeds regioselectively to form the 1-cyanoenamines **2a**.⁶¹ The stereochemistry of addition depends also on the reaction conditions. Thus the reactions performed at low temperatures (–78 °C) afforded predominantly or even exclusively the *Z* isomers of the compounds **2a**.^{60,61}

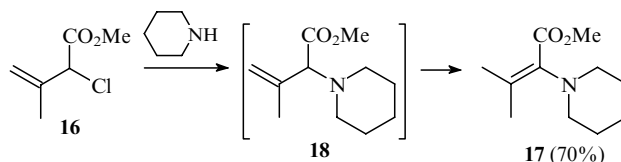


R¹ = H, Me, Ph, MeCH=CH; R² = H, Me; NR³R⁴ = N(Me)Ph, NMe₂,

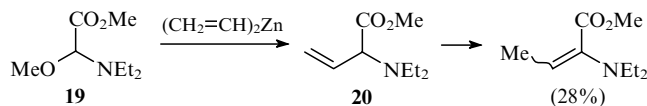
N-piperidyl, N-morpholyl; R⁵ = Me, Et, Prⁱ, Bu, Bn, All, Br(CH₂)₃,

Cl(CH₂)₃, 2-BrC₆H₄CH₂; X = I, Br; B = LDA or Bu^tOK.

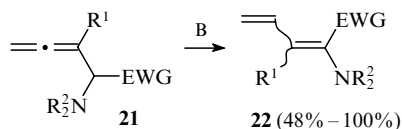
In some cases, the initially formed β,γ -unsaturated α -aminonitriles or esters also undergo double-bond migration to the α,β position with respect to the electron-withdrawing group.^{64–67} For instance, the reaction of methyl 2-chloro-3-methylbut-3-enoate (**16**) with piperidine started with the attack on the allylic carbon atom to give finally the conjugated amino ester **17**.⁶⁵ It is reasonable to assume that intermediate **18** generated through the replacement of the chlorine atom is isomerised to the more stable alkene **17** under the action of the amine.



When developing a general procedure for the synthesis of esters of β,γ -unsaturated α -amino acids using organozinc compounds, the French research team^{66,67} found that the reaction of aminoacetal **19** with divinylzinc afforded amino ester **20**, which underwent isomerisation to give methyl 2-diethylaminobut-2-enoate.



Prototropic isomerisation of β -allenic amino esters, ketones or nitriles **21** under the action of strong bases [MeONa–DMSO,⁶⁸ Bu^tOK–HMPA (HMPA is hexamethylphosphoramide)⁶⁹ or Bu^tOK–THF⁷⁰] proceeded rapidly to give conjugated aminoalkenes **22** in high yields.^{68–70}



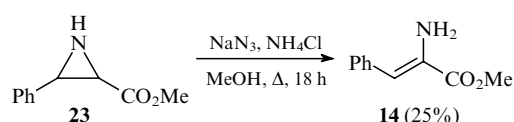
R¹ = H, Me, Et, Pr, Bu, Ph;

NR₂ = NMe₂, NEt₂, N-piperidyl, N-morpholyl;

EWG = CO₂Me, CO₂Et, C(O)Me, CN.

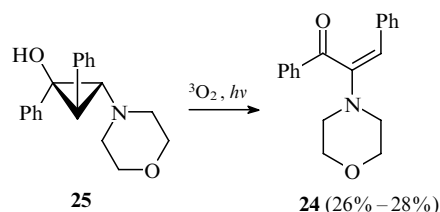
Generally, tautomeric transformations are not considered as preparative reactions. However, unlike simple enamines with unsubstituted or monosubstituted amino groups, which exist predominantly in the imino form, captodative aminoalkenes **2** are much more stable in the enamine form. This allows their isolation either in the individual form or as a tautomeric mixture in which the enamine form dominates. Examples of such syntheses of aminoalkenes containing the activating carbonyl,^{71, 72} alkoxy-carbonyl⁷³ or cyano group⁷⁴ are available in the literature.

A series of captodative aminoalkenes were prepared from the corresponding substituted aziridines.^{45, 75–77} In some cases, their formation was absolutely unexpected. For example, treatment of aziridinecarboxylate **23** with sodium azide in methanol gave rise to the unsaturated ester **14** instead of the expected methyl 2-amino-3-azido-3-phenylpropionate.⁴⁵



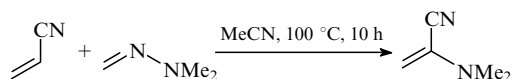
It was reported that 2-amino-3-methoxy-1,3-diphenylprop-1-en-1-one was transformed into α -aminochalcone under the action of strong bases.⁷⁸ The authors assumed that this reaction proceeded through intermediate aziridinoketones. However, the formation of unsaturated α -aminoketones has not subsequently been confirmed.⁷⁹

Recently, α -aminoenone **24** was synthesised by photooxidation of cyclopropanol **25**.⁸⁰ Photolysis was carried out in the presence of photosensitising agents, viz., 9,10-dicyanoanthracene or triphenylpyrylium tetrafluoroborate, for 0.5–5.2 min. It was noted that the enone **24** decomposed when the reaction time was increased.



2. Insertion of the amino group into the conjugated C=C–EWG system

The reaction of acrylonitrile with formaldehyde dimethylhydrazine produced 2-dimethylaminopropenenitrile regardless of the reaction conditions.⁸¹



Apparently, this is the only example of the formal synthesis of captodative aminoalkene from unsubstituted activated alkene.

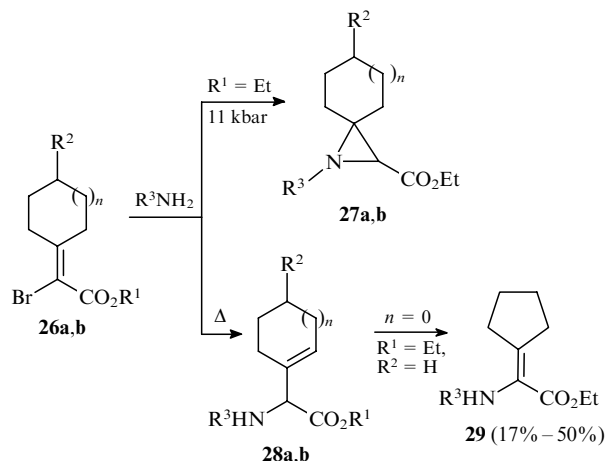
a. Nucleophilic substitution

Nucleophilic substitution of a particular leaving group is most commonly used for the insertion of the amino group into the conjugated C=C–EWG fragment.

Although the replacement of the functional group X in the conjugated C=C(X)EWG system by the amino group seems at first glance to be the shortest pathway to captodative aminoalkenes, the reactions of N-nucleophiles with haloalkenes activated with the geminal electron-withdrawing group are complicated processes and do not necessarily afford the desired products. The results of these studies were critically analysed in the review.⁸²

All the aforesaid is clearly exemplified by the data from the recent study,⁸³ which demonstrated that the results of the reac-

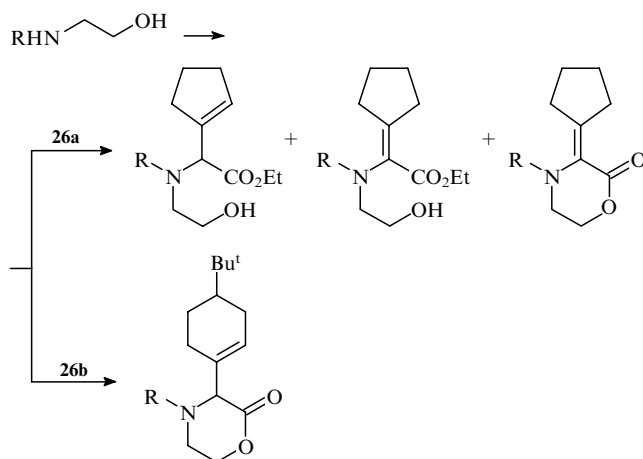
tions of primary amines with bromo(cycloalkylidene)acetates **26a,b** depend substantially on the reaction conditions, the nature of the amine and the size of ring in the starting substrate. Under superhigh pressure, these reactions afforded spiroaziridines **27a,b** in high yields (and with high diastereoselectivity in the case of the derivatives **27b**). Under the same conditions, amines containing an aromatic or bulky substituent at the nitrogen atom produced predominantly α -amino- β,γ -unsaturated esters **28a,b**. Thermal activation of the compounds **26a,b** was accompanied by migration of the exocyclic double bond followed by the replacement of the allylic bromine atom to form exclusively the esters **28a,b**. Only in the case of the derivatives **28a** containing the five-membered ring, back migration of the endocyclic double bond was observed giving rise formally to *ipso*-substitution product **29**.



$n = 0$, $R^1 = \text{Et}$, $R^2 = \text{H}$ (**a**); $n = 1$, $R^1 = \text{Me}$, $R^2 = \text{Bu}^t$ (**b**);

$R^3 = \text{Pr}^n, \text{Pr}^i, \text{Ph}, \text{Bn}, \text{PhCHMe}$.

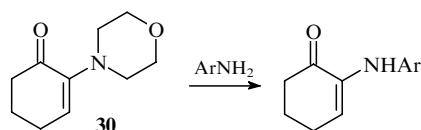
In the reactions with N,N- or N,O-binucleophiles, compounds **26a,b** underwent a cascade of transformations. Both upon thermal activation and under high pressure, the reactions involved double-bond migration and substitution of the halogen atom followed by condensation to form oxazinones (in the case of N,O-dinucleophiles) or piperazinones (in the case of N,N-dinucleophiles).⁸⁴ As in the case of reactions involving primary amines, the captodative system can be constructed only with the use of the bromo(cyclopentylidene)acetate **26a** and aminoethanol derivatives.⁸⁴



$R = \text{Me}, \text{Bn}$.

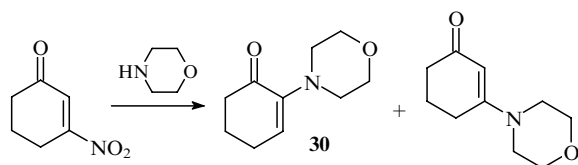
Since the halide ion is one of the best nucleofuges, it is not surprising that this ion is most generally used as the leaving group. Nevertheless, examples of the replacement of other groups at the sp^2 -carbon atom are also available in the literature. These reactions often proceed very readily.

In spite of the ambiguous results of the reactions of 2-amino-cycloalk-2-enones with N-nucleophiles,⁸⁵ 2-morpholinocyclohex-2-enone (**30**) is recognised as a convenient substrate in transamination.¹⁷

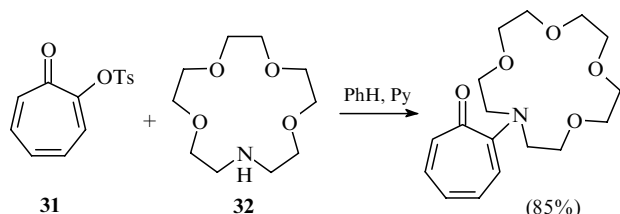


Ar = Ph, 4-MeOC₆H₄, 4-BrC₆H₄, 2-HOC₆H₄, 2-HO₂CC₆H₄.

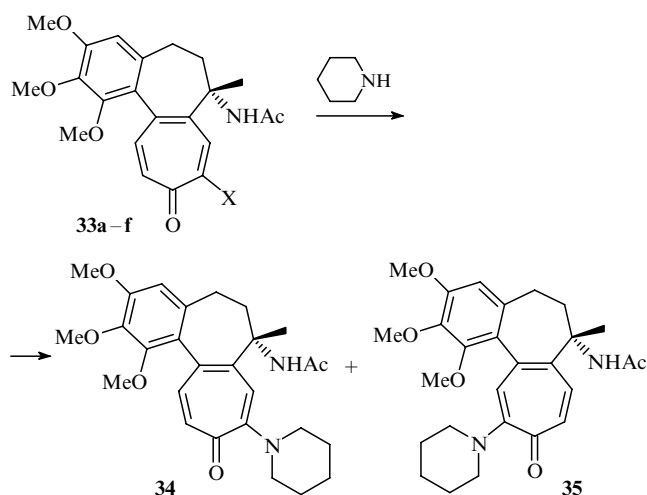
2-Morpholinocyclohex-2-enone (**30**) was prepared by the reaction of 3-nitrocyclohex-2-enone with morpholine, isomeric β-aminoketone being obtained as the minor product.⁸⁶



Refluxing of an equimolar mixture of 2-(*p*-tolylsulfonyloxy)-tropone (**31**) and azacrown ether **32** in benzene in the presence of pyridine afforded the corresponding substitution product.⁸⁷



Competitive *ipso*- and *tele*-substitution of various leaving groups in other troponoid systems has been well studied as well.^{88–90} For example, isocolchicides **33a–f** readily reacted with piperidine, the ratio between the *ipso* (**34**) and *tele* isomers (**35**) being determined by the nature of the leaving group X. The reactions of the compounds **33a–c** afforded exclusively the isomers **34**, whereas the compounds **33d–f** produced the *tele* isomers **35** in 10%–25% yields. In the case of colchicides containing a substituent at position 10, only *ipso*-substitution was observed regardless of the nature of the leaving group.⁹⁰

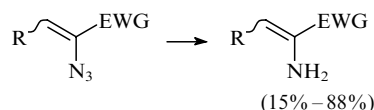


X = Cl (**a**), SOMe (**b**), SMe (**c**), OMe (**d**), F (**e**), OTs (**f**).

Finally, it should be noted that none of the attempts to replace the alkoxy group in α-alkoxyacroleins afforded the α-formyl-substituted enamines **2d**⁹¹ although the reactions of amines with 3-alkoxy- or 3-phenoxypropenals are accepted to be a procedure of choice for the synthesis of their push-pull isomers **1d**.^{12, 92, 93}

b. Synthesis of captodative aminoalkenes bearing the unsubstituted amino group

Undoubtedly, captodative aminoalkenes containing an unsubstituted amino group are of particular interest. The classical approach to their synthesis is based on reduction of the corresponding nitro and azido derivatives. It was recommended to use hydrogen on a metal catalyst,⁹⁴ hydrogen sulfide⁹⁴ or aluminium amalgam^{94–96} for reduction of the azido group. In addition, α-amino-α,β-unsaturated ketones and esters were prepared by electrolysis of solutions of ene azides activated with geminal carbonyl or ester groups.^{97–100} Refluxing of azidoesters in toluene in the presence of catalytic amounts of iodine also afforded esters of unsaturated α-amino acids.^{18, 101, 102}



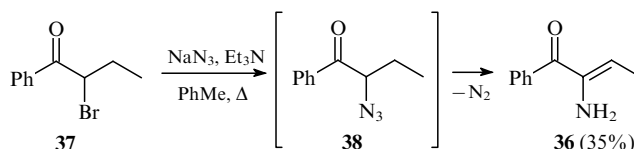
EWG = CO₂Me, CO₂Et, MeCO, 4-MeC₆H₄CO, 4-ClC₆H₄CO;

R = Me, Et, Prⁿ, Prⁱ, Ph, PhCH=CH, 4-MeC₆H₄, 4-HOC₆H₄,

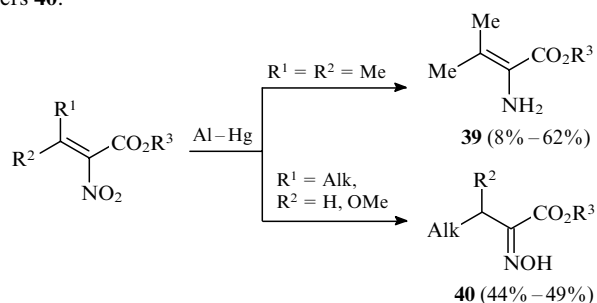
4-MeOC₆H₄, 4-ClC₆H₄, 2,4,6-Me₃C₆H₂, 2-BnC₆H₄, 2-MeC₆H₄,

2-PrⁱC₆H₄, 2-furyl, 2-thienyl, 3-thienyl, 3-indolyl.

An unusual synthesis of α-aminoenone **36** from α-bromo-ketone **37** and sodium azide has been reported.⁷¹ In the first step, the bromine atom was replaced to give azidoketone **38**. Subsequent elimination of N₂ afforded imino ketone, which underwent rapid isomerisation into the unstable alkene **36**.



Nitroalkenes are readily reduced with aluminium amalgam to the corresponding amino derivatives.^{103–107} However, this procedure allows the preparation only of esters of β,β-disubstituted α-amino acids **39**. Reduction of β-methoxy-β-alkyl- or β-alkyl-substituted substrates gave rise predominantly to hydroxyimino esters **40**.^{104, 107}



R¹ = Me, Et, Prⁿ, Prⁱ; R² = H, Me, MeO; R³ = Me, Et, Buⁿ.

Careful removal of various protective groups also made it possible to prepare the captodative aminoalkenes **2a–c** containing the unsubstituted amino group (see, for example, Refs 108–112).

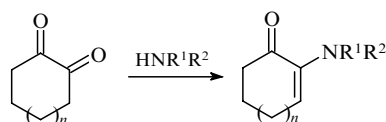
Procedures were developed for the synthesis of captodative aminoalkenes containing the unsubstituted amino group along with the keto, ester or cyano group. The exceptions are the formyl derivatives **2d**. Recent attempts to synthesise these compounds based on 2-haloalk-2-enals and hexamethyldisilazane or (diphenylmethylidene)amine failed.¹¹³ Admittedly, the question about the possibility of the existence of the aminoalkenes **2d** containing the unsubstituted amino group as well as of all aminoaldehydes with the unprotected amino group^{114, 115} remains open.

3. Simultaneous insertion of the double bond and the amino group

a. Syntheses based on diketones and ketoesters

One of the most general methods for the synthesis of captodative aminoalkenes is based on condensation of primary and secondary amines with readily enolizable 1,2-dicarbonyl compounds. As a rule, the reactions are carried out at room temperature or on refluxing of equimolar amounts of the reagents in an appropriate solvent (benzene, toluene, more rarely, chloroform or alcohol) in the presence or absence of a base or acid catalyst. The liberated water is removed either by azeotropic distillation or using molecular sieves.

Examples of the syntheses of 2-aminocycloalk-2-enones containing the disubstituted amino group were given in the review¹⁷ and in a number of recent publications.^{116–119} The use of chiral pyrrolidines in reactions with five–eight-membered cyclic 1,2-diketones allowed the preparation of optically active α -aminoenones.¹²⁰ Primary amines can also produce α -aminoenones in the reactions with cyclic diketones.^{121–124} Along with usual alkyl- and arylalkylamines [BuNH₂, cyclo-C₆H₁₁NH₂, Ar(CH₂)₂NH₂], esters of some α -amino acids, such as glycine, alanine and tyrosine, were also successfully used in these reactions.^{125, 126}

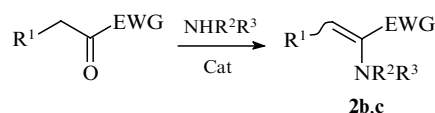


$n = 0, 1, 2, 3$; $R^1 = \text{H, Alk, All, Ar}$; $R^2 = \text{Alk, All, CH}_2\text{CO}_2\text{Et, CH(Alk)CO}_2\text{Et}$.

Since acyclic analogues of aminoketones are much less stable, the structures of the starting substrate and the reaction conditions are of particular importance in their synthesis. Acyclic α -aminoenones containing the internal or terminal double bond were prepared from α -diketones according to a classical procedure,¹²⁷ the yields being at most 30%. All attempts to purify the products led to their resinification.^{128, 129}

Conventional procedures for the preparation of enamines containing the geminal alkoxy carbonyl group offered considerable promise.

It appeared that prolonged refluxing of 2,2-diethoxyethylamine with ethyl (3-chloro-2-nitrophenyl)pyruvate in toluene actually afforded the corresponding enamine in quantitative yield.¹³⁰ Taking into account the high sensitivity of alkyl pyruvates both to acidic and basic reagents, Arnold¹³¹ improved this procedure. He proposed that TiCl₄, which is traditionally used in the synthesis of enamines, should be changed for softer AsCl₃. In essence, this modification allowed the first synthesis of the terminal aminoalkenes **2b** ($R^1 = \text{H}$). In spite of low stability, all products were prepared in the pure form in high yields.



EWG	R ¹	NR ² R ³	Catalyst	Yield (%)	Ref.
MeCO	H		TiCl ₄	—	128, 129
EtCO	H		TiCl ₄	30	129
EtCO	Me		TiCl ₄	25	129
PhCO	Ph		TiCl ₄	—	129
CO ₂ Me	H	NMe ₂	AsCl ₃	82	131
CO ₂ Me	H		AsCl ₃	73	131

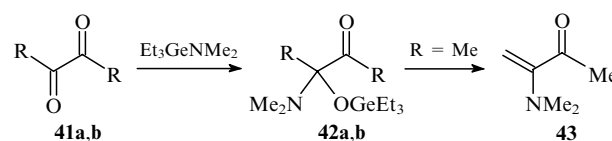
EWG	R ¹	NR ² R ³	Catalyst	Yield (%)	Ref.
CO ₂ Me	H		AsCl ₃	75	131
CO ₂ Bu ^t	H	NMe ₂	AsCl ₃	68	131
MeCO	H		AsCl ₃	100	133

The sole exception is the pyrrolidine derivative, which was not isolated by the author. It should be noted that methyl α -piperidinoacrylate has been obtained previously from the corresponding chlorine-substituted ester and piperidine¹³² in very low yield (5%–10%). Later on, the procedure proposed by Arnold¹³¹ was successfully used for the synthesis of optically active acyclic α -aminoenone, viz., 3-[(*S*)-2-(methoxymethyl)pyrrolidino]but-3-en-2-one.¹³³

The reaction of *o*-phenylenediamine with pyruvic acid in a 0.1 M HCl solution at 20 °C gave rise to a mixture of the corresponding α -amino derivative of acrylic acid and its tautomer with the imine structure.¹³⁴ Both isomers can be isolated in the individual form.

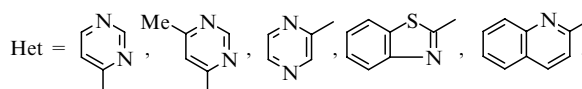
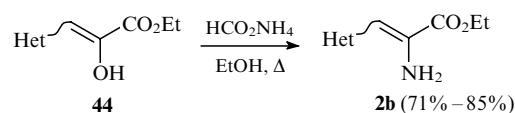
An attempt to prepare the captodative enamines **2d** by direct condensation of methylglyoxal with two equivalents of secondary amine was doomed to failure because the reaction proceeded with the involvement of the more reactive aldehyde group.¹³⁵

Not only amines but also their derivatives serve as N-nucleophiles in condensation with dicarbonyl compounds giving rise to the aminoenones **2c**.^{136, 137} For example, trialkylgermylamines were found to react at one of the carbonyl groups of α -diketones **41a,b** to form α -amino- α -triethylgermyloxy ketones **42a,b**. The latter compounds appeared to be thermally unstable. Thus the compound **42a** decomposed to give aminoenone **43**.¹³⁶



$R = \text{Me (a), Ph (b)}$.

Recently, an ingenious procedure was developed for the synthesis of esters of unsaturated amino acids **2b** from esters of hetarylpyruvic acids **44**.¹³⁸ The esters **44** exist only in the enol form and are very reactive. These compounds are readily transformed to give the unsaturated amino esters **2b** in high yields upon refluxing with ammonium formate in ethanol. However, all attempts to obtain the compounds **2b** from the esters **44** under the action of other aminating reagents (aniline, benzylamine, ammonium chloride or ammonium acetate) failed.



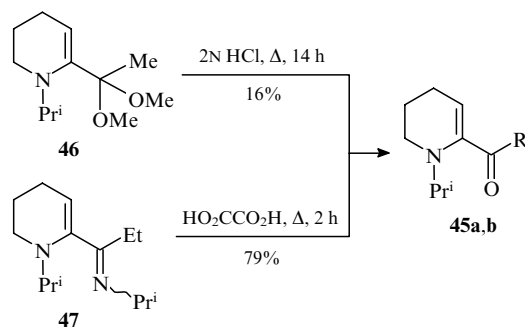
b. Oxirane-ring opening

The oxirane-ring opening under the action of amines is widely used only for the preparation of cyclic aminoenones. These reactions have been surveyed in the review.¹⁷ Since then, no modifications of this procedure were proposed. Noteworthy only are the studies,^{139, 140} which were not included in the cited review, and the investigations^{141, 142} reported at a later time.

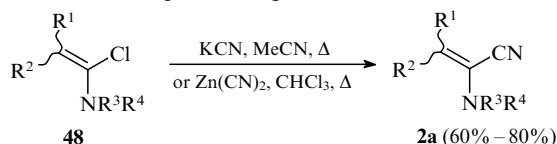
4. Formation of an electron-withdrawing group in aminoalkene

Examples of the insertion or generation of an electron-withdrawing group for the construction of captodative systems are few in number. In addition, these reactions are of limited application and of no particular preparative value.

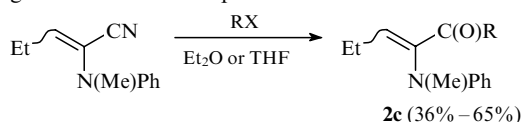
The formation of the aminoalkenes **2c** containing the geminal carbonyl group was observed upon hydrolysis of enediamines,^{143, 144} oxidation of enamines^{145, 146} or aminoalcohols¹⁴⁷ and removal of protective groups.^{148, 149} Thus analogues of one of the natural components of the smell of freshly baked bread, *viz.*, compounds **45a,b**, were synthesised by careful acid hydrolysis of the corresponding ketal **46**¹⁴⁸ or azomethine derivative **47**.¹⁴⁹



A more general and efficient procedure for the synthesis of the 1-cyanoenamines **2a** is based on the nucleophilic substitution of the halogen atom by the cyanide ion.^{150, 151} For example, prolonged refluxing of 1-chloro-1-(dimethylamino)alkenes **48** with potassium cyanide in acetonitrile or with zinc cyanide in chloroform afforded the 1-cyanoenamines **2a** in good yields.¹⁵⁰ Unfortunately, this procedure is inapplicable to the synthesis of β-monosubstituted analogues of the compounds **2a** (R¹ = H) because the starting chloro derivatives are much less accessible and, in addition, they readily undergo dechlorination under the action of bases or upon heating.



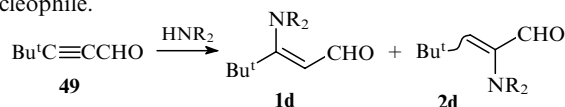
Finally, one activating function in compounds of the type **2** can be transformed into another one. Thus 2-(*N*-methylanilino)-pent-2-enitrile was transformed into the enamines **2c** containing the geminal carbonyl group under the action of organolithium, -magnesium or -zinc compounds.⁵⁴



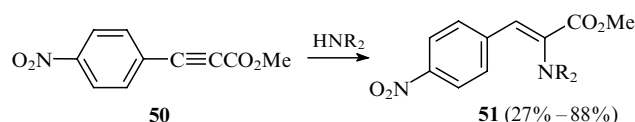
5. Other procedures

Other reactions giving rise to the captodative aminoalkenes **2a–d** have also been described in the literature. The results of investigations for a series of activated alkynes were the basis of several publications. It is known that the reactions of ethynylcarbonyl compounds with N-nucleophiles are among procedures most commonly used for the preparation of amino derivatives of the push-pull type **1**.¹² However, it was unexpectedly found that dialkylamines containing bulky substituents added not only at the β position but also at the α position with respect to the aldehyde group of 4,4-dimethylpent-2-ynal (**49**) to give a mixture of the unsaturated aminoaldehydes **1d** and **2d**.¹⁵² Thus the

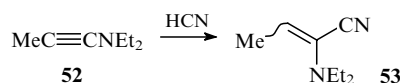
proportion of the isomer **2d** reached 50% and 10% in the reactions of PrⁱNH and BuⁿNH, respectively. The authors related the regioselectivity of the addition to the spatial structure of the nucleophile.



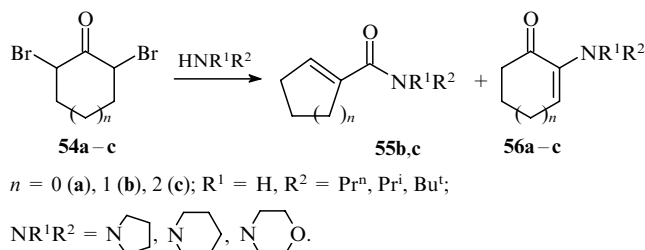
Analogously, the reactions of methyl 4-nitrophenylpropiolate (**50**) with some secondary amines afforded the corresponding α-amino derivatives **51**.¹⁵³



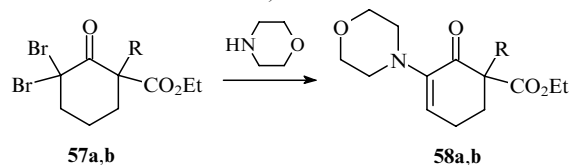
In the synthesis of pyrimidine derivatives from triazines and 1-diethylaminoprop-1-yne (**52**), HCN, which was eliminated in the course of the reaction, added to the starting alkyne to produce 2-diethylaminocrotononitrile (**53**) in yields of up to 76%.¹⁵⁴



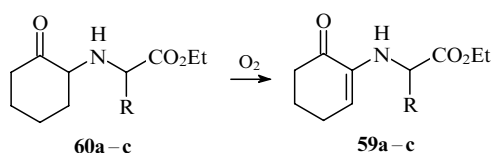
Cyclic α,α'-dibromoketones **54a–c** reacted with primary¹⁵⁵ and secondary amines^{17, 156} to give either Favorskii rearrangement products **55b,c** or the corresponding 2-aminocycloalk-2-enones **56a–c** depending on the ring size of the ketone and the structure of the nucleophile. The ratio of the reaction products is substantially affected by the nature of the solvent. The formation of the enamines **56a–c** is favoured by polar aprotic solvents.



In spite of the fact that treatment of α,α-dihaloketones with amines generally afforded the corresponding diamino derivatives,¹⁵⁷ the reactions of ethyl 1-alkyl-3,3-dibromo-2-oxocyclohexanecarboxylates **57a,b** with a tenfold excess of morpholine gave rise to aminoalkenes **58a,b**.¹⁵⁸

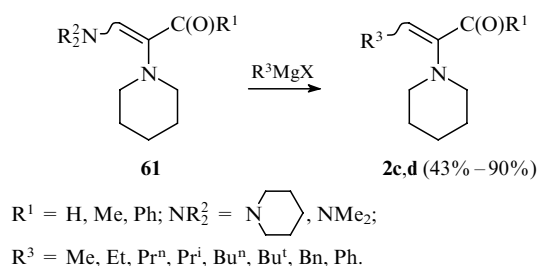


Recently, 2-aminocyclohex-2-enones **59a–c** were prepared¹²⁶ by oxidation of saturated ketones **60a–c**. Oxidation proceeded

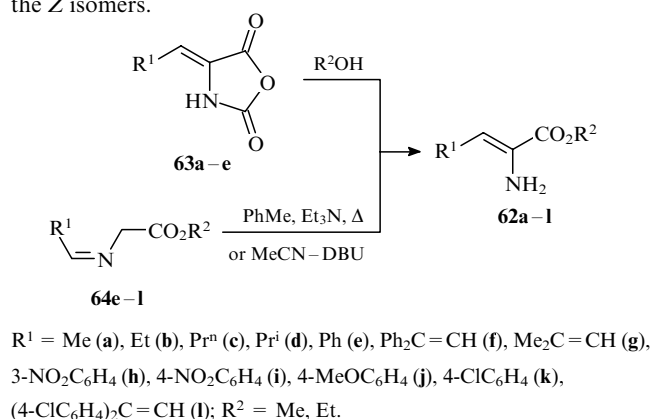


even upon storage of the starting substrates without a solvent in air. The same results were obtained by bubbling oxygen through a solution of the ketones **60** in chloroform.

The most reactive captodative aminoalkenes **2d** were first synthesised by L Duhamel and co-workers.^{159, 160} The reactions of Grignard reagents with formylated or acylated enediamines **61** produced the corresponding aminoalkenes **2c,d** in good yields.



Ingenious methods were proposed for the synthesis of esters of dehydroamino acids with the free amino group.^{161–164} Alkyl 2-aminoalk-2-enoates **62a–e** were prepared by alcoholysis of anhydrides **63a–e** under mild conditions.^{161, 162} In the studies,^{163, 164} aldimines **64e–l** (which were prepared by condensation of glycine esters with aldehydes) were used as the starting reagents, which were transformed into the target compounds **62e–l** upon refluxing in toluene in the presence of triethylamine or upon storage in the MeCN–DBU system (DBU is 1,8-diazabicyclo[5.4.0]undec-7-ene) at room temperature. Spectral analysis demonstrated that the esters **62a–l** were always generated only as the *Z* isomers.

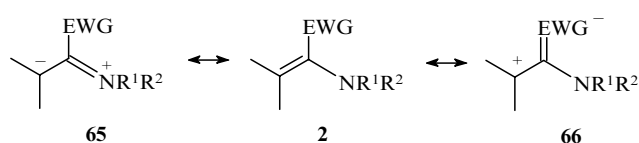


Other reactions giving rise to captodative aminoalkenes have also been reported. However, they are of limited application, cannot be used for preparative purposes, and hence, are beyond the scope of the present review.

III. Structures and spectroscopic characteristics of captodative aminoalkenes

In the analysis of the structures of captodative aminoalkenes, one should first of all answer the question of how the combination of the electron-withdrawing and electron-donating groups is reflected in the degree of *p*, *π*- and *π*, *π*-conjugation in such systems.

Captodative aminoalkenes can be represented by superposition of the structural fragments of enamines, on the one hand, and of α,β -unsaturated aldehydes, ketones or derivatives of carboxylic acids, on the other hand. This approach assumes that three canonical structures must be taken into account in the description of the reactivities of these compounds.



If the structure **65** makes a larger contribution to the total electronic state of the molecule compared to that of the resonance form **66**, the β -carbon atom would be expected to possess higher

nucleophilicity. In contrast, if the structure **66** predominates, captodative aminoalkenes must approach the corresponding activated alkenes in their chemical properties.

It is well known that the degree of conjugation between the π -electrons of the double bond and the lone electron pair of the nitrogen atom or the π -system of the activating group is manifested by the chemical shift of the olefinic proton in the ^1H NMR spectrum.^{165–167} Apparently, this correlation can be made only if the steric parameters of the substituents at the nitrogen atoms are identical or similar to those at the β -carbon atom, whereas the differences in their chemical shifts are rather large. The ^{13}C NMR spectra are less dependent on the influence of the medium and the anisotropic effects and directly reflect the state of both the π and σ electron density in the molecule. For a series of push-pull alkenes, the difference in the chemical shifts of two adjacent carbon nuclei was used for estimating the degree of polarisation of the double bond.^{165–167} However, it should be emphasised that ^{13}C NMR spectroscopy provides only qualitative estimates of the degree of polarisation of the double bond in the captodative aminoalkenes **2**. An effort to perform spectral analysis of 2-aminocycloalk-2-enones was made in the studies.^{17, 168}

The spectroscopic characteristics of captodative aminoalkenes containing the terminal double bond are given in Table 1. In the ^1H NMR spectra of these compounds, the signals for the

Table 1. Chemical shifts of the vinyl protons (in CDCl_3) in captodative

aminoalkenes $\text{=C(EWG)NR}^1\text{R}^2$ (a–o).				
Compound	EWG	NR^1R^2	Chemical shifts of the vinyl protons /ppm	Ref.
a	CN	NH_2	4.67, 4.74	39
b	CN	NMe_2	4.33, 4.53 ^a	20
c	CN	$\text{N}(\text{cyclohexyl})_2$	4.55, 4.75	33, 169
d	CN	$\text{N}(\text{cyclohexyl})\text{S}$	4.63, 4.83	170
e	CN	$\text{N}(\text{cyclopentyl})_2$	4.15, 4.42	33
f	CN	$\text{N}(\text{cyclohexyl})\text{Ph}$	4.62, 4.80	170
g	CN	$\text{N}(\text{cyclohexyl})\text{NPh}$	4.67, 4.87	170
h	CN	$\text{N}(\text{cyclopentyl})\text{S}$	4.63, 4.83	170
i	CN	$\text{N}(\text{cyclohexyl})\text{N}(\text{cyclohexyl})\text{C}_6\text{H}_4\text{CF}_3$	4.71, 4.92	170
j	CN	$\text{N}(\text{Me})\text{Ph}$	4.64, 4.80	23
k	CO_2Me	NMe_2	4.43, 5.04	131
l	CO_2Me	$\text{N}(\text{cyclohexyl})_2$	4.54, 5.11	131
m	CO_2Me	$\text{N}(\text{cyclohexyl})\text{O}$	4.63, 5.26	131
n	$\text{C}(\text{O})\text{Me}$	$\text{N}(\text{cyclohexyl})_2$	4.48, 4.87	see ^b
o	$\text{C}(\text{O})\text{Me}$	$\text{N}(\text{cyclohexyl})\text{O}$	4.80, 5.20	128

^a In CCl_4 . ^b The author's own data.

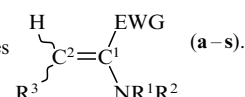
protons of the $\text{H}_2\text{C}=\text{}$ group are observed in the ‘olefinic region’ between the signals typical of vinylamines ($\delta = 3.40\text{--}3.78$)¹⁷¹ and the corresponding activated alkenes ($\delta = 5.75\text{--}6.36$).^{172–174} It should be noted that the chemical shifts of the olefinic protons depend on the nature of the captodative substituents. For example, the shifts $\delta(\text{H}_2\text{C}=\text{})$ in the spectra of α -aminoacrylonitriles bearing the nitrogen-containing heterocycles with similar steric parameters (see Table 1, the compounds **c–i**) are changed as the electron-donating ability of the amino group changes. As in the series of unsubstituted enamines,¹⁷⁵ the strongest orbital interaction between the lone electron pair of the nitrogen atom and the double bond is observed in the pyrrolidine derivative **e**.

The insertion of the alkyl or aryl substituent at the β position enhances deshielding of the olefinic proton and provides the possibility for the existence of the geometric isomers (Table 2).

As in the case of unsubstituted enamines,¹⁷⁵ the signal for the olefinic proton of the *E* isomers of captodative aminoalkenes is always observed at higher field. The results of the study⁴⁸ showed that this regularity is violated by some formyl-substituted enamines. However, I thoroughly checked the molecular geometry by NMR spectroscopy using the Overhauser effect and found that the assignment of the signals made in the cited study⁴⁸ was incorrect. To a first approximation, the larger value of $\delta(\text{HC}=\text{})$ for the *Z* isomers can be considered a result of strengthening of π,π -conjugation with a simultaneous decrease in p,π -conjugation due to the steric interaction between the β -substituent and the tertiary amino group. For this reason, the *Z* isomer is generally thermodynamically more stable.

Factors other than the structural characteristics of the molecule are also responsible for the ratio between the *E* and *Z* isomers.

Table 2. Chemical shifts of the olefinic protons and the carbon nuclei (in CDCl_3) in captodative aminoalkenes



Compound	EWG	NR^1R^2	R^3	Isomer	Chemical shifts of the olefinic protons /ppm	Chemical shifts of the carbon nuclei /ppm		Ref.
						C^2	C^1	
a	CHO		Me	<i>E</i>	5.15	122.7	148.8	176
				<i>Z</i>	5.48	140.4	151.8	
b	CHO		Me	<i>E</i>	5.80	124.2	147.4	176
				<i>Z</i>	6.20	141.8	150.3	
c	CHO	NEt_2	Me	<i>Z</i>	6.50	146.6	149.2	176
d	CHO		Ph	<i>E</i>	6.50 ^a	—	—	48
				<i>Z</i>	6.75 ^a	—	—	
e	CHO		Ph	<i>E</i> ^b	6.10	—	—	48
				<i>Z</i>	6.50	—	—	
f	CHO	NEt_2	Ph	<i>E</i>	6.66	—	—	see ^c
				<i>Z</i>	6.77	139.3	146.9	
g	C(O)Me		Me	<i>E</i>	4.80	—	—	129
h	C(O)Et		Me	<i>E</i>	4.90	106.9	150.6	129
i	C(O)Me	N(Me)Ph	Et	<i>Z</i>	6.55	116.9	147.2	54
j	C(O)Ph		Ph	<i>E</i> ^b	5.70	—	—	177
k	C(O)Ph		Ph	<i>E</i>	5.90	107.0	146.9	129
				<i>Z</i> ^b	6.06	—	—	
l	C(O)Ph	NEt_2	Ph	<i>E</i>	5.57	103.40	145.75	see ^c
				<i>Z</i>	6.12	—	—	
m	CO_2Me		Me	<i>E</i>	4.54	102.2	140.4	178
				<i>Z</i>	6.08	127.8	—	
n	CO_2Me	$\text{N(Me)C}_6\text{H}_{11}\text{-cyclo}$	Me	<i>Z</i>	6.50	141.9	133.9	178
o	CO_2Me	N(Me)Ph	Et	<i>Z</i>	6.94	143.9	135.9	178
p	CO_2Me	N(Me)Ph	Pr	<i>Z</i>	6.89	142.5	136.6	178
q	CN	NMe_2	Me	<i>E</i>	5.08	113.5	—	20
				<i>Z</i>	5.82	133.3	—	
r	CN	NMe_2	Ph	<i>E</i>	5.82	115.3	—	20
				<i>Z</i>	6.18	129.8	—	
s	CN	N(Me)Ph	Et	<i>E</i>	5.81	135.6	121.3	179
				<i>Z</i>	6.15	146.4	146.3	

^a In CCl_4 . ^b The assignment to the *E* and *Z* isomers was made based on the author's own data. ^c The author's own data.

Example of *E,Z* isomerisation of captodative aminoalkenes, which proceeded rather readily either in the course of the reactions^{48, 128, 129, 177} or upon subsequent purification (for example, upon distillation)¹⁷⁹ and even upon storage over a short period at room temperature,¹²⁹ are available in the literature.

For captodative aminoalkenes bearing the internal double bond, the chemical shift of the olefinic proton is also sensitive to variations in the nature of the electron-donating and electron-withdrawing substituents. Generally (although not necessarily), the stronger are the electron-withdrawing properties of the activating group and the weaker are the electron-donating properties of the amino group, the more substantial is the downfield shift of the signal for the olefinic proton. If the nitrogen atom possesses substituents capable of being involved in conjugation with the lone electron pair of the nitrogen atom, the chemical shift of the olefinic proton is increased further by 0.3–0.8 ppm. This fact also indicates that in these compounds conjugation between the double bond and the electron-withdrawing group typical of activated alkenes is virtually completely restored.

In the ¹³C NMR spectra of captodative *N,N*-disubstituted aminoalkenes, the signal for the C² atom is observed at a higher field as compared to the signal for the C¹ atom. It should be noted that this regularity is also true for the series of enamines bearing such a powerful electron-withdrawing substituent as the formyl group.¹⁷⁶ The difference in the chemical shifts of the adjacent carbon atoms of the alkene fragment observed in these systems is comparable with that for unsubstituted enamines (30–45 ppm). These data are unambiguously indicative of high polarisation of the double bond and are a strong argument in favour of the predominant contribution of the structure **65** to the ground electronic state of the molecule.

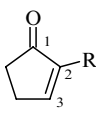
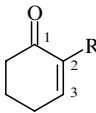
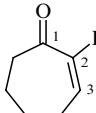
In the case of *N*-methylaniline derivatives containing the geminal electron-withdrawing group, an inversion of the usual order of the chemical shifts of the C¹ and C² nuclei is observed. The difference $\delta(C^2) - \delta(C^1)$ reaches +14.3 ppm (see Table 2, compounds **o**, **p** and **s**). The exceptions are enamines bearing the carbonyl group for which the positions of the resonance signals for the carbon nuclei are less dependent on the nature of the amino group (see Table 2, compounds **h**, **i**, **k** and **l**). A satisfactory explanation for this phenomenon is lacking.

The presence of conjugation in the C=C–EWG system of the carbonyl-containing captodative aminoalkenes **2d** is evidenced by the presence of intense absorption bands at 1655–1690 (C=O) and 1585–1620 cm^{−1} (C=C) in their IR spectra.¹⁸⁰ The former spectral region is close to the stretching vibration frequencies characteristic of the conjugated carbonyl group, whereas the frequencies belonging to the latter region are somewhat lower than the vibration frequencies of the double bond in the corresponding unsubstituted enals and enones and are noticeably lower than the vibration frequencies of the C=C bond in simple enamines.

Analysis of the IR spectra of captodative carbonyl-containing enamines by comparing the intensities of the absorption bands of the C=C and C=O groups led Arnould *et al.*¹⁷⁷ to the conclusion that the *E* isomer in the ground state adopts the *s-cis* conformation, whereas the *Z* isomer has the *s-trans* conformation.

Finally, the efficiency of *p,π*-conjugation in 2-aminocycloalk-2-enones depends dramatically on the ring size (Table 3). For example, the shifts $\delta(HC=)$ in the ¹H NMR spectra of piperidine and morpholine derivatives of cycloalkenones increase substantially on going from seven- to six- and then to five-membered rings. As in the spectra of acyclic enamines bearing the geminal carbonyl group, the resonance signals for the C³ atom in the spectra of 2-aminocycloalk-2-enones containing mono- and disubstituted amino groups are shifted upfield as compared to the signals for the C² atom. The difference between the chemical shifts

Table 3. Chemical shifts of the olefinic protons in 2-aminocycloalk-2-enones.

Compound	R	Chemical shifts of the olefinic protons /ppm	Solvent	Ref.
	NHPr ⁱ	5.98 ^a	CDCl ₃	155
	NHBu ^t	5.83 ^b	CDCl ₃	155
		5.91	CCl ₄	181
		6.42	CDCl ₃	182
		5.70 ^c	CCl ₄	156
		5.86 ^d	CDCl ₃	86
		5.23	CCl ₄	183
		5.13	CCl ₄	183

The chemical shifts of the carbon nuclei: ^a $\delta(C^3) = 120.61$, $\delta(C^2) = 145.13$ (see Ref. 155); ^b $\delta(C^3) = 121.04$, $\delta(C^2) = 142.62$ (see Ref. 155); ^c $\delta(C^3) = 126.1$, $\delta(C^2) = 148.1$ (see Ref. 146); ^d $\delta(C^3) = 133.7$, $\delta(C^2) = 150.8$ (see Ref. 146).

of the β - and α -sp²-hybridised carbon atoms varies between −22 and −27 ppm, whereas this difference for unsubstituted cyclic α,β -unsaturated ketones ranges from 21 to 33 ppm. Undoubtedly, this effect should be related to the fact that *p,π*-conjugation between the nitrogen atom and the double bond dominates over the π,π -interaction between the double bond and the carbonyl group. All the aforesaid send one in the critical review of the conclusion made previously¹⁷ that the canonical structure **66** is more appropriate for the description of the ground state of 2-aminocycloalk-2-enones.

Hence, the spectroscopic data provide evidence for the presence of competitive *p,π*- and π,π -conjugation in the captodative aminoalkenes **2a–d**, the efficiency of the conjugation being determined by the nature of the functional groups. In the general case, the compounds under consideration are intermediate between unsubstituted enamines and α,β -unsaturated aldehydes, ketones or derivatives of carboxylic acids. What this means is these systems would be expected to exhibit dual reactivity with respect to nucleophilic and electrophilic reagents.

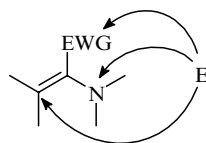
IV. Reactions of captodative aminoalkenes

Being polyfunctional systems, the captodative aminoalkenes **2a–d** are not only valuable starting reagents for organic synthesis but are also excellent models for solution of some problems of alternative reaction centres. Analysis of the data available in the literature shows that insignificant (at first glance) changes in the structure of the substrate or the reagent and variations in the reaction conditions can give rise to radically different reaction products. In addition, the polyfunctional properties of the compounds under consideration are often responsible for their unexpected and surprising cascade transformations.

1. Reactions with electrophilic reagents

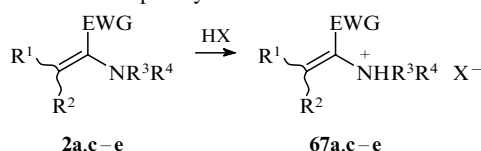
a. Protonation and hydrolysis

Apparently, the nitrogen atom, the β -carbon atom and the heteroatom of the activating group serve as the nucleophilic centres in captodative aminoalkenes. Consequently, the regioselectivity of the electrophilic attack is the central problem of the reactions of the compounds **2a–d** with electrophilic reagents.



Protonation serves as the simplest test for the reactivity of such systems. Unlike simple enamines generating stable immonium salts¹⁷⁵ and the push-pull aminoenones **1c**, which are protonated predominantly at the oxygen atom,¹⁰ the captodative aminoalkenes **2a,c,d** can add the proton at each of three major nucleophilic centres depending on the structure of the substrate, the nature of the protonating reagent and the reaction conditions.

Thus the reactions of mineral or strong carboxylic acids with the aminoalkenes **2**, which are activated by the geminal cyano,¹⁸⁴ carbonyl,¹⁸⁵ formyl^{186,187} or azomethine group,¹⁸⁸ generally afford the corresponding enammonium salts **67a,c–e**. It should be emphasised that the hydrochlorides **67a,c,d** ($X = \text{Cl}$) were isolated and completely characterised.

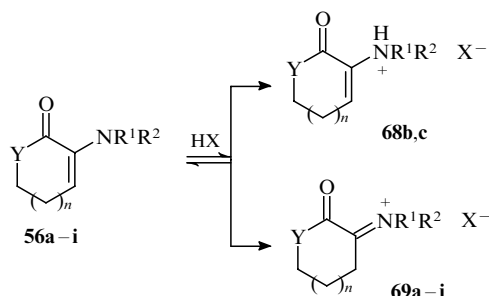


EWG = CN (**a**), C(O)Ph (**c**), CHO (**d**), CH = NMe (**e**);

$R^1 = \text{H}$, $R^2 = \text{Me}$, Ph; $R^1-R^2 = (\text{CH}_2)_5$;

$\text{NR}^3\text{R}^4 = \text{NHBu}^t$, NEt_2 , , ; $X = \text{Cl}$, CF_3CO_2 , CCl_3CO_2 .

The regioselectivity of protonation of the 2-aminocycloalk-2-enones **56a–i** is determined by the ring size and the nature of the amino group.^{121,189} For example, the reaction of a solution of trifluoroacetic acid in CDCl_3 with morpholinocyclohexenone **30** afforded exclusively enammonium salt **68b** (NR^1R^2 is morpholino), whereas the reaction with the seven-membered homologue **56c** (NR^1R^2 is morpholino) performed under the analogous conditions led to protonation both at the heteroatom to give compound **68c** (NR^1R^2 is morpholino) and at the β -carbon atom to generate the corresponding immonium salt **69c**.¹²¹ Protonation of aminocyclopentenones (**56a**) as well of the cyclohexenone **56b** containing the monosubstituted amino group ($\text{NR}^1\text{R}^2 = \text{NHC}_6\text{H}_4\text{Me-4}$) afforded immonium salts **69a,b**, which underwent subsequent enolisation.¹²¹ The dependence of the regioselectivity



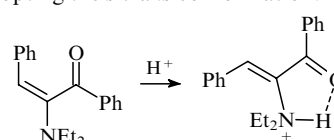
$Y = \text{CH}_2$: $n = 0$ (**a**), **1** (**b**), **2** (**c**); $Y = \text{CHMe}$: $n = 0$ (**d**), **1** (**e**), **2** (**f**);

$Y = \text{NH}$: $n = 0$ (**g**), **1** (**h**), **2** (**i**); $\text{NR}^1\text{R}^2 = \text{NHBn}$, $\text{NHC}_6\text{H}_4\text{Me-4}$,

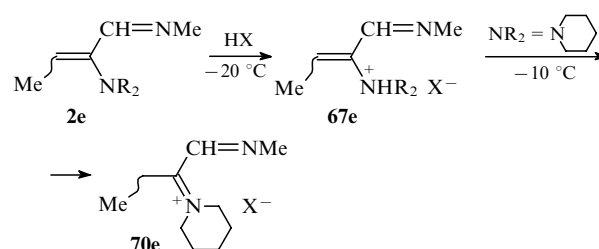
, NMe_2 , ; $X = \text{CF}_3\text{CO}_2$, Cl .

of protonation on the ring size was also observed in the case of the enammonolactams **56h,i**.^{190,191}

The formation of nitrogen-protonated captodative aminoalkenes is a rare example of the existence of enammonium salts, which, as a rule, readily undergo isomerisation to the corresponding immonium salts.¹⁷⁵ A rather stable enammonium salt was first synthesised in 1976.^{192,193} However, really stable compounds with the enammonium structure were prepared only upon protonation of the captodative aminoalkenes **2c,d**. Apparently, their stability is associated with the powerful influence of the electron-withdrawing geminal substituent and the stabilising effect of the intramolecular hydrogen bond that is formed.[†] This assumption is supported by the fact that protonation of (*s-cis*-diethylamino)-benzylideneacetophenone gave rise to the enammonium salt adopting the *s-trans* conformation.¹⁸⁵



The salts **67d** are so stable that they were not transformed into immonium salts at all.^{186,187} As shown in the previous section, a decrease in the electron-withdrawing ability of the activating group in the captodative aminoalkenes **2** leads to an increase in the proportion of the resonance form **65** bearing a negative charge on the β -carbon atom. As a consequence, these aminoalkenes exhibit properties of simple enamines. Actually, unlike the formyl-substituted enamines **2d**, their azomethine analogues **2e** generated the enammonium salts **67e**, which underwent slow isomerisation in CDCl_3 solution to give the more stable C-protonated derivatives **70e**.¹⁸⁸



$\text{NR}_2 = \text{N} \begin{smallmatrix} \diagup \text{O} \diagdown \end{smallmatrix} \text{O}$, ; $X = \text{CF}_3\text{CO}_2$, CCl_3CO_2 .

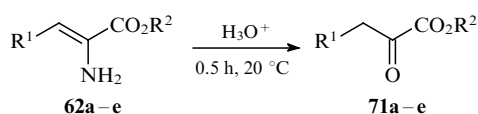
The result of the reaction of the acyclic aminoenones **2c** with acids depends substantially on the nature of the protonating reagent and the reaction conditions. Thus the reaction with anhydrous HCl was accompanied predominantly by protonation at the nitrogen atom, whereas the formation exclusively of immonium salts was observed in a solution of trifluoroacetic acid.¹⁸⁵ The difference in the behaviour of inorganic and carboxylic acids is accounted for by the bifunctional catalytic action of carboxylic acids in the course of proton transfer from the nitrogen atom to the carbon atom.¹⁹⁴

In the enammonium salts **67**, *p*, π -conjugation becomes impossible. Moreover, the donor fragment NR^3R^4 is transformed into the acceptor $\text{N}^+\text{HR}^3\text{R}^4$ upon quaternisation. The formation of the system with the geminal electron-withdrawing substituents results in the essential electron density redistribution. This is the reason that the multiplicity of the C=C bond is somewhat decreased and, as a consequence, the barrier to rotation about this bond is substantially lowered. Examples of *E,Z* isomerisation of enammonium salts (**67c–e**), which proceeded very readily, were cited in Refs 185–188.

In spite of the fact that enammonium salts do not necessarily undergo tautomeric transformations into immonium salts, the

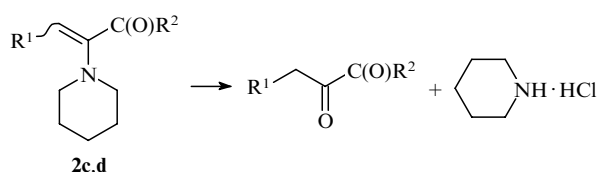
[†] The author's own data.

captodative aminoalkenes **2b–d** are hydrolysed to give the corresponding α -dicarbonyl compounds. For example, the aminoesters **62a–e** were virtually quantitatively transformed into esters of 2-oxocarboxylic acids **71a–e** in a 1 M solution of hydrochloric acid at room temperature during 0.5 h.¹⁶²



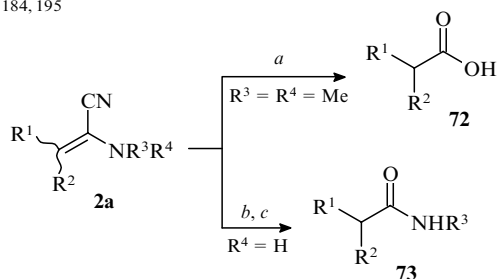
$\text{R}^1 = \text{Me}$ (**a**), Et (**b**), Pr^n (**c**), Pr^i (**d**), Ph (**e**); $\text{R}^2 = \text{Me}$, Et .

The acyl- and formyl-substituted enamines **2c,d** are also hydrolysed in an acidic medium.^{160, 186} Various α -diketones can be prepared from the compounds **2c** by varying the substituents in the starting substrate.



$\text{R}^1 = \text{Alk}$, Ar ; $\text{R}^2 = \text{H}$, Alk , Ar .

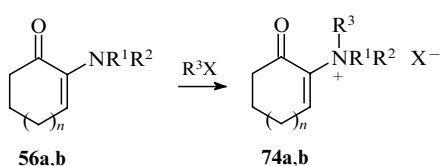
Protonation and hydrolysis of the captodative aminoalkenes **2** are used in a number of simple and efficient synthetic procedures. An example is hydrolysis of the 1-cyanoenamines **2a** containing the unsubstituted, mono- or disubstituted amino group to give the corresponding carboxylic acids **72**.^{20, 110, 150} The reactions of the cyanoenamines **2a** with Lewis acids (AlCl_3 or ZnCl_2) in ethanol followed by hydrolysis gave rise to monosubstituted amides **73**.^{184, 195}



$\text{R}^1 = \text{H}$, Me , Et ; $\text{R}^2 = \text{Me}$, Et , Ph , $4\text{-MeOC}_6\text{H}_4$; $\text{R}^1-\text{R}^2 = (\text{CH}_2)_5$;
 $\text{R}^3 = \text{R}^4 = \text{Me}$; $\text{R}^4 = \text{H}$: $\text{R}^3 = \text{H}$, Me , Pr^i , Bu^t , $\text{cyclo-C}_6\text{H}_{11}$.
 (a) H_2O , H^+ ; (b) AlCl_3 , EtOH or HCl , PhH ; (c) H_2O .

b. Alkylation and acylation

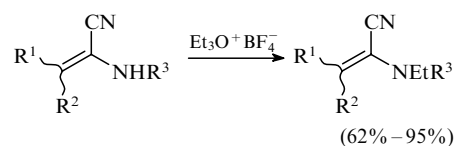
Alkylation of captodative aminoalkenes requires more drastic conditions and affords the corresponding enammonium salts regardless of the nature of the alkylating reagent. It is not surprising that the nature of the amino group exerts a pronounced effect on the ease of the reaction. Thus prolonged refluxing of 2-aminocycloalk-2-enones **56a,b** with alkyl halides afforded *N*-alkyl derivatives **74a,b**.^{181, 189}



$n = 0$ (**a**), 1 (**b**); $\text{NR}^1\text{R}^2 = \text{NMe}_2$, $\text{N}(\text{C}_6\text{H}_{11})_2$, $\text{N}(\text{C}_6\text{H}_5)_2$; $\text{R}^3 = \text{Me}$, Et ;
 $\text{X} = \text{I}$, Cl , BF_4 .

The cyanoenamines **2a** containing a bulky substituent on the monosubstituted amino group do not react with alkyl halides or alkyl *p*-toluenesulfonates. However, aminoalkenes bearing the disubstituted amino group can be prepared with the use of

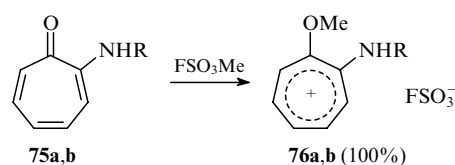
stronger alkylating reagents, for example, of dialkyl sulfates, alkyl fluorosulfonates or triethyloxonium tetrafluoroborate.¹⁹⁶ In the latter case, alkylation proceeded under mild conditions and was not accompanied by side processes.



(62%–95%)

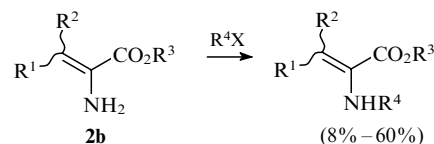
$\text{R}^1 = \text{Me}$, Et ; $\text{R}^2 = \text{Me}$; $\text{R}^1-\text{R}^2 = (\text{CH}_2)_5$; $\text{R}^3 = \text{Me}$, Pr^i , Bu^t , $\text{cyclo-C}_6\text{H}_{11}$.

'Magic methyl' was successfully used for quantitative *O*-alkylation of 2-aminotropone (**75a**) and 2-methylaminotropone (**75b**).¹⁹⁷ It is reasonable to assume that the driving force for this reaction is the formation of the aromatic system of tropylium cation **76a,b**.



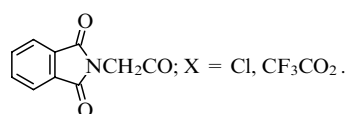
$\text{R} = \text{H}$ (**a**), Me (**b**).

The primary, secondary and tertiary captodative aminoalkenes **2** are difficult to acylate. Thus attempts to perform the reactions of the primary aminoalkenes **2b** with acetyl chloride or acetic anhydride failed.¹³⁸ However, some reactions of the compounds **2b** with acid chlorides or anhydrides of strong carboxylic acids produced *N*-acylated products in moderate yields.^{95, 96, 104, 105, 107, 198–200} These reactions were used in the peptide synthesis.^{200–204}

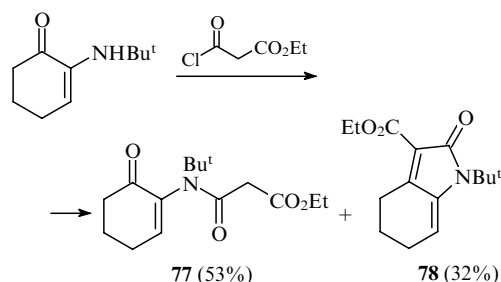


(8%–60%)

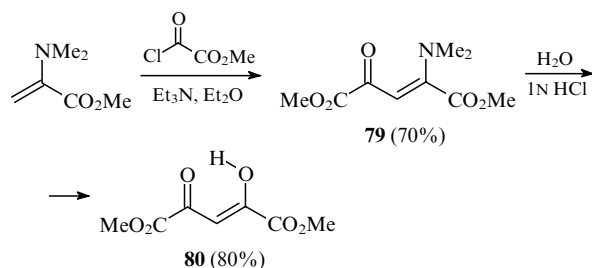
$\text{R}^1 = \text{H}$, Me ; $\text{R}^2 = \text{Me}$, Et , Pr^n , Pr^i , Ph , $\text{MeOCH}_2\text{OC}_6\text{H}_4$, Het ;
 $\text{R}^3 = \text{Me}$, Et ; $\text{R}^4 = \text{ClCH}_2\text{CO}$, BnOCO , $4\text{-MeC}_6\text{H}_4\text{SO}_2$, CF_3CO ,



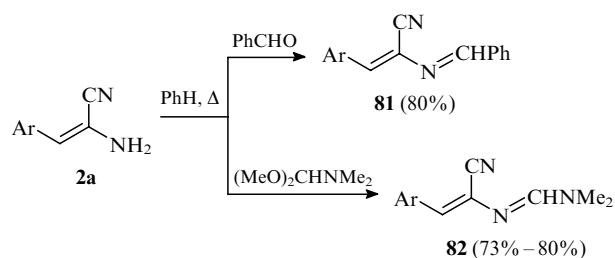
N-Acylation of 3-aminocoumarin derivatives was successfully carried out under the action of phthalic anhydride and 2-chloronicotinoyl chloride.^{205, 206} Perfluoroacyl fluorides proved to be excellent acylating reagents for the formyl-substituted aminoalkenes **2d**.²⁰⁷ The reaction of 2-*tert*-butylaminocyclohex-2-enone with ethyl chlorocarbonylacetate in the presence of pyridine and 4-dimethylaminopyridine afforded a mixture of *N*-acylated derivative **77** and the product of its subsequent intramolecular condensation **78**.²⁰⁸



The formation of diester **79** in the reaction of methyl 2-dimethylaminoacrylate with methoxalyl chloride is a rare example of C-acylation of captodative aminoalkenes. The compound **79** is readily hydrolysed to the symmetrical ester of dioxo acid **80**.¹³¹

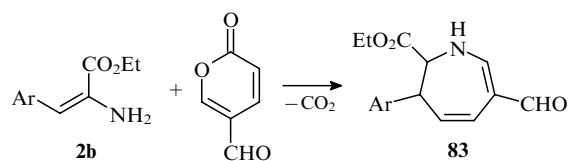


Unsymmetrical amino groups in captodative aminoalkenes are sufficiently basic and nucleophilic that they can be subjected to condensation with carbonyl compounds. These aminoalkenes smoothly react with aldehydes or dimethylformamide dimethyl acetal to form the corresponding azomethines.^{94, 106, 110, 138, 209} Even the unstable cyanoenamines **2a** were readily transformed into 2-aza-3-cyanobuta-1,3-dienes **81** and **82** upon refluxing in benzene with azeotropic distillation of water.¹¹⁰



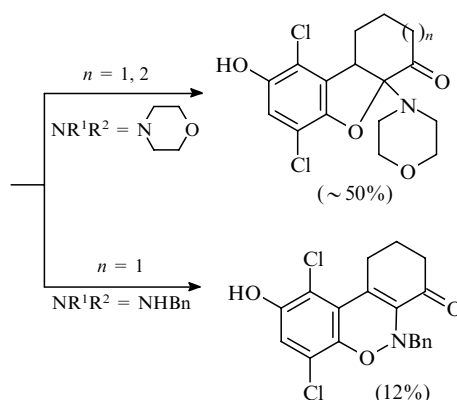
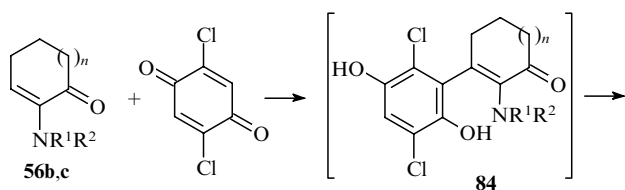
$\text{Ar} = \text{Ph}, 4\text{-MeOC}_6\text{H}_4$.

The reactions of the aminoalkenes **2b** with 5-formylpyran-2-one, which begin with the ring opening, provide the convenient means for preparing dihydroazepines **83**.²¹⁰

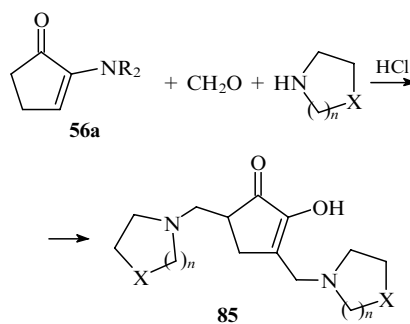


$\text{Ar} = \text{Ph}, 4\text{-ClC}_6\text{H}_4$.

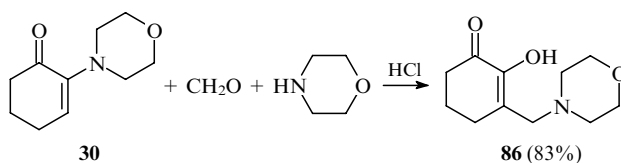
In reactions with some carbonyl compounds, captodative aminoalkenes containing mono- and disubstituted amino groups act as C-nucleophiles. For example, the reactions of the 2-aminocycloalk-2-enones **56b,c** with quinones afforded various heterocyclic compounds.¹²² Their structures depend on the ring size and the nature of the amino group of the substrate. It was believed^{11, 122, 211, 212} that the first step of the reaction gave rise to derivative **84**.



The first investigations into the involvement of the captodative aminoalkenes **2** in aminomethylation demonstrated that the structure of the resulting Mannich base depends dramatically on the ring size of the substrate and the reaction conditions.^{181, 213} Thus the 2-aminocyclopent-2-enones **56a** produced bis-aminomethylated compounds **85** in moderate yields,¹⁸¹ whereas the reaction of the aminoalkene **30** gave rise only to monoaminomethylated product **86** even in the presence of a twofold excess of paraformaldehyde and morpholine hydrochloride.²¹³

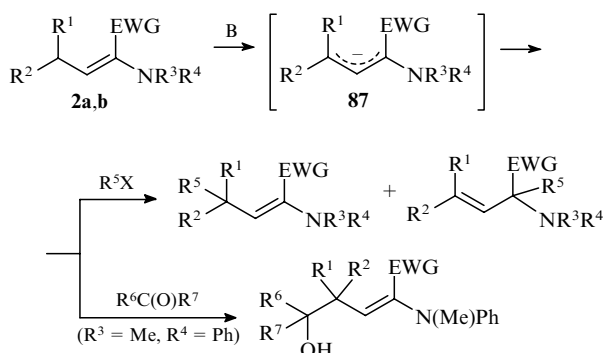


$n = 1, \text{X} = \text{CH}_2$; $n = 2, \text{X} = \text{CH}_2, \text{O}$.



c. Reactions of electrophilic reagents with carbanions generated from captodative aminoalkenes

As mentioned above, the β -substituted captodative aminoalkenes **2a,b** are capable of being deprotonated under the action of strong bases to give allylic anions **87**, which can react with various electrophilic reagents (alkyl halides, aryl halides and carbonyl compounds) either exclusively at the γ -carbon atom or simultaneously at the α - and γ -carbon atoms.^{34, 57, 151, 178, 214–218} The fact that the attack proceeds predominantly at the γ -position is attributed primarily to the steric characteristics of the substrate and the electrophile. These reactions are preparatively valuable because they allow modifications of captodative aminoalkenes to obtain compounds, which are used in the synthesis of various polyfunctional systems.

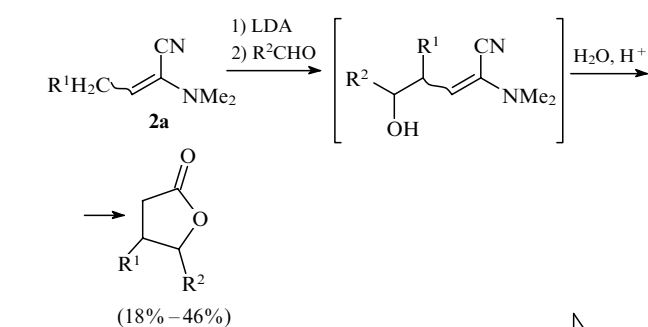


EWG = CN (**a**), CO₂Me (**b**); R¹ = H, Me, PhS, PhSO₂; R² = H, Me;

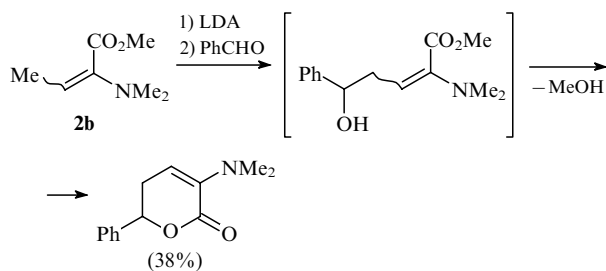
NR³R⁴ = NMe₂, NEt₂, , N(Me)C₆H₁₁-cyclo, N(Me)Ph;

R⁵ = Me, Et, Prⁱ, Buⁿ, n-C₅H₁₁, Ph, Bn, CH₂=CHCH₂, MeCH=CHCH₂,
Me₂C=CHCH₂; X = Hal; R⁶ = H, Me; R⁷ = Me, Prⁱ, Ph;
R⁶-R⁷ = (CH₂)₅; B = BuⁿLi, LDA, Bu^tOK.

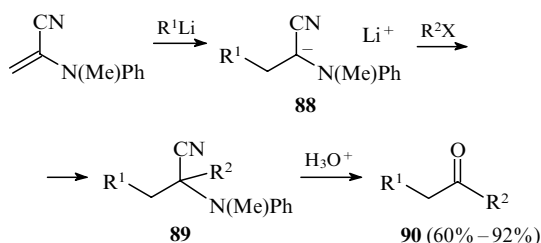
Some tertiary enamines **2a,b** react with aldehydes in the presence of strong bases to give five- or six-membered lactones depending on the nature of the activating group.^{20, 214}



R¹ = H, Me; R² = Ph, Me(CH₂)₃, Me(CH₂)₅, MeCH=CH, , , .



The Michael addition of various anions to 2-(*N*-methylanilino)acrylonitrile afforded initially anions **88**.^{23, 35, 58} Their subsequent reactions with electrophiles gave rise to bifunctional

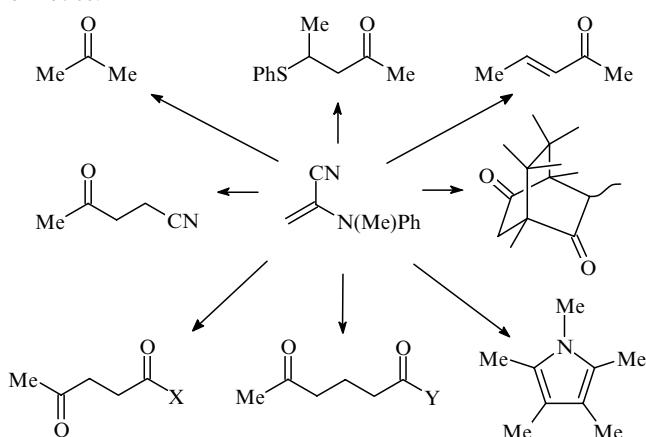


R¹ = Bu^t, Ph, PhCOCH₂CH₂, PhCH=CHCHPh, Bu^tC(O)CH₂;

R² = H, Me, Et, Bn; X = OH, I, Br.

derivatives **89**, which were hydrolysed to the corresponding carbonyl compounds **90**.^{23, 35, 58}

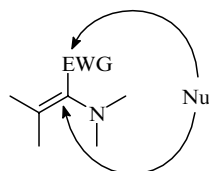
When developing this methodology and varying the nature of the electrophile and the organolithium derivative, Ahlbrecht and co-workers unveiled the considerable synthetic potential of one of the simplest captodative aminoalkenes, viz., 2-(*N*-methylanilino)acrylonitrile. This compound proved to be a versatile and readily accessible starting reagent for the one-pot synthesis of ketones,²³ β-, γ- and δ-diketones,^{179, 219–221} γ- and δ-oxoaldehydes,^{221, 222} β-phenylthioketones, which were transformed into α,β-unsaturated carbonyl compounds²²³ upon pyrolysis, as well as of derivatives of oxocarboxylic acids (nitriles,^{224, 225} esters and amides²²⁶). The efficient syntheses of bicyclic diketones²²⁰ and pyrroles¹⁷⁹ based on 2-(*N*-methylanilino)acrylonitrile are worthy of notice.



X = H, Alk, Ar, OR, NR₂; Y = H, Alk, Ar.

2. Reactions with nucleophilic reagents

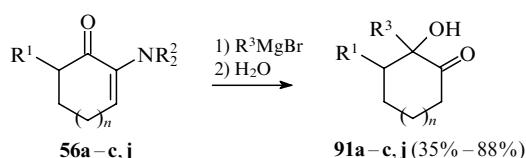
Taking into account the electronic structure of captodative aminoalkenes, one would expect that these compounds will act as poor Michael acceptors and the attack of nucleophilic reagents will proceed predominantly either at the electrophilic centre of the activating group or at the α-carbon atom.



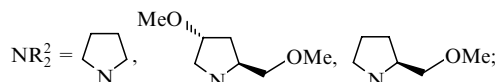
Actually, attempts to perform the 1,4-addition of some C- and N-nucleophiles to 2-aminocycloalk-2-enone have not met with success. Only nitroalkanes produced Michael adducts in moderate yields (see Ref. 17).

In the study on the cyanoenamines **2a**,⁵⁴ it was concluded that the direction of the addition of nucleophiles generally follows the rule of hard and soft acids and bases (HSAB). However, some of nucleophilic reactions of captodative aminoalkenes do not obey the HSAB principle.

The 1,2-addition of organometallic compounds to form a new C–C bond is the most extensively used nucleophilic reaction of captodative aminoalkenes. The reactions of the 2-aminocycloalk-2-enones **56a–d** with Grignard reagents proceeded regioselectively to produce 2-hydroxycycloalkanones **91a–d** in good yields.^{120, 227–230}



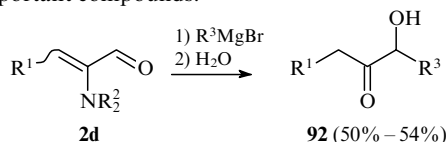
$n = 0$ (a), 1 (b), 2 (c), 3 (j); $\text{R}^1 = \text{H}, \text{Me}$;



$\text{R}^3 = \text{Me}, \text{Et}, \text{Ph}, \text{CH}_2=\text{CH}, \text{CH}_2=\text{CMe}$.

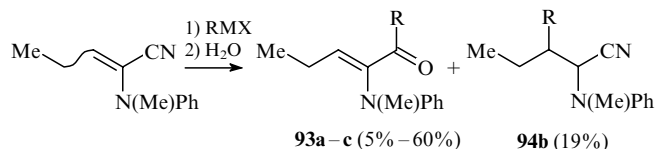
1,4-Adducts were detected in no cases. The reactions with the use of chiral substrates afford hydroxyketones with high enantioselectivity, which depends on the solvent used. Thus the enantiomeric excess (*ee*) achieved in the reaction of the aminoenone **56a** [$\text{R}^1 = \text{H}$, NR_2^2 is (2*S*)-2-methoxymethylpyrrolidino] with $\text{CH}_2=\text{CHMgBr}$ in tetrahydrofuran was only 33%, whereas it reached 84% in a $\text{Et}_2\text{O}-\text{THF}$ mixture (9:1).²³⁰ Interestingly, the absolute configuration of the optically active α -hydroxycycloalkanones **91** depends on the nature of the substituent R^2 . For example, the aminoenone **56b** [$\text{R}^1 = \text{H}$, NR_2^2 is (2*S*)-2-methoxymethylpyrrolidino] reacted with methyl- or ethylmagnesium bromide to give the compounds (2*R*)-**91b** ($\text{R}^3 = \text{Me}$ or Et) with an optical purity of 92%–95%, whereas the hydroxyketones **91b** ($\text{R}^3 = \text{CH}_2=\text{CH}, \text{Ph}$), which were obtained by the reactions of the same substrate with vinyl- or phenylmagnesium bromide, adopt an opposite configuration (*ee* 58%–95%).¹²⁰ The authors attributed these stereochemical results to the difference in the structure of an intermediate complex of the organometallic compound with the aminoenone.

Like 2-aminocycloalk-2-enones, acyclic captodative aminoalkenes react with organometallic compounds to form predominantly 1,2-adducts. Thus the formyl-substituted enamines **2d** are readily transformed into acylins **92**, which provides the basis for a new efficient procedure for the preparation of these synthetically important compounds.[‡]



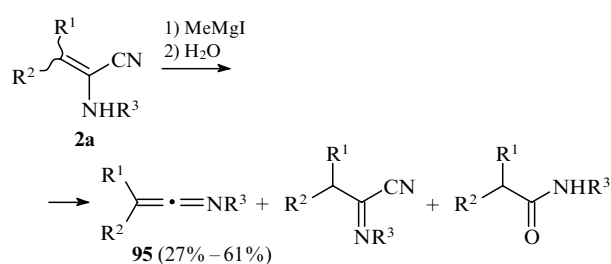
$\text{R}^1 = \text{Me}, \text{Ph}$; $\text{R}^2 = \text{Alk}, \text{Het}$; $\text{R}^3 = \text{Et}, \text{Ph}$.

Analogously, the reactions of 2-(*N*-methylanilino)pent-2-enonitrile with organomagnesium and organozinc reagents proceed as the 1,2-addition. However, the reaction of the same substrate with benzylmagnesium bromide gave rise to 1,4-addition product **94b** along with 1,2-adducts **93b** in comparable amounts.⁵⁴



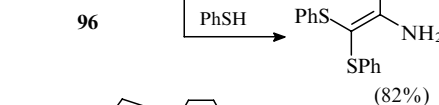
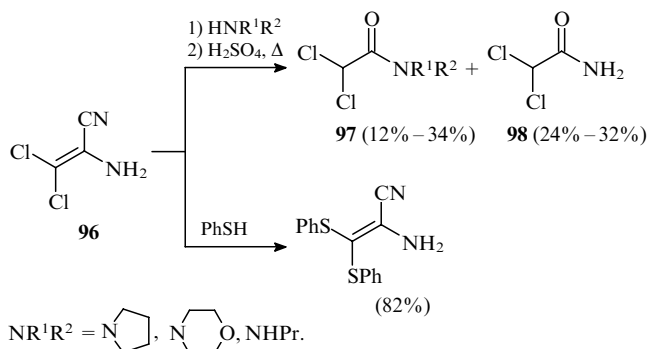
$\text{RMX} = \text{MeMgI}, \text{BnMgCl}, \text{AlI}_2\text{ZnBr}$; $\text{R} = \text{Me}$ (a), Bn (b), Al (c).

In the case of the secondary cyanoenamines **2a**, Grignard reagents serve as strong bases. These reactions afford trialkylketenimines **95** as the major reaction products.²³¹



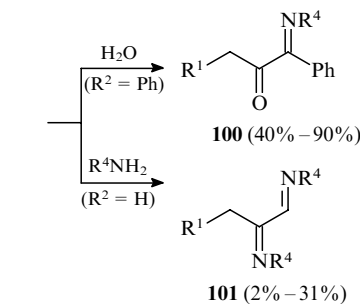
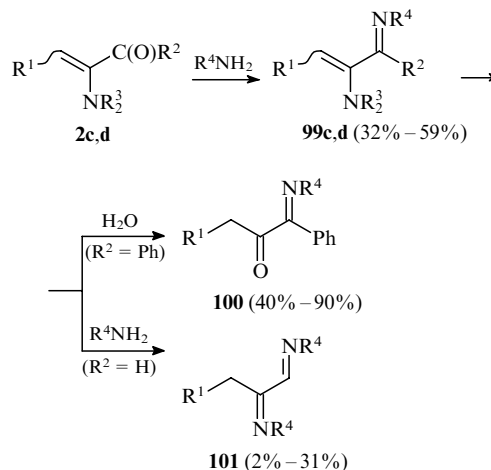
$\text{R}^1 = \text{R}^2 = \text{Me}, \text{Et}$; $\text{R}^3 = \text{Pr}^i, \text{Bu}^i$.

In the reactions with captodative aminoalkenes, N-nucleophiles attack either the electrophilic centre of the activating group or the α -olefinic carbon atom. For example, 2-amino-3,3-dichloroacrylonitrile (**96**) reacted under mild conditions with primary and secondary amines to give amides **97** and **98**.²³² The mechanism of formation of these compounds involves the nucleophilic attack at the carbon atom bound to the cyano group followed by hydrolysis of the amidines generated in the first step. Curiously, the chlorine atoms were not replaced even in the presence of a fourfold excess of the amine (*cf.* Ref. 82). At the same time, the reaction of the substrate **96** with more nucleophilic thiophenol proceeded regioselectively with the replacement of both chlorine atoms.²³²



$\text{NR}^1\text{R}^2 = \text{N-pyrrolidine}, \text{N-piperidine}, \text{NHPy}$.

Condensation of primary amines and hydrazine derivatives with the captodative aminoalkenes **2c,d** proceeded exclusively at the carbonyl group. Under the action of the liberated water, the initially formed azomethinoenamines **99c** were hydrolysed in a basic medium to give oxo derivatives **100**.²³³ Under these conditions, the compounds **99d** were converted into bis-azomethines **101**. The ratio **99d**:**101** depends on the reaction conditions and the nature of the starting reagents.²³⁴ Under analogous conditions, guanidine and thiourea did not react with the aminoalkenes **2c**.²³³

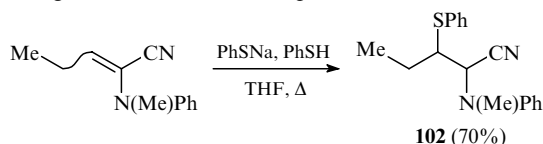


$\text{R}^1 = \text{Me}, \text{Ph}$; $\text{R}^2 = \text{Ph}$ (c), H (d); $\text{NR}_2^2 = \text{NEt}_2$, N-pyrrolidine , N-piperidine ; $\text{R}^4 = \text{Me}, \text{Bu}, \text{NH}_2, \text{NHEt}$.

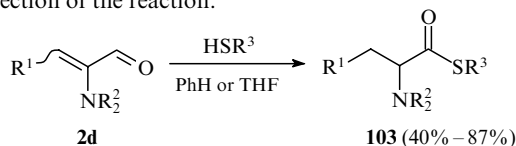
[‡] The author's own data.

2-Morpholinocyclohex-2-enone (**30**) undergoes condensation with ethanolamine acting as a N-nucleophile to give the corresponding azomethine derivative.²³⁵ As mentioned in Section II.2.a, 2-aminocycloalkenones are involved in *ipso*-substitution reactions under the action of primary aromatic amines and even ammonia.^{17, 88}

Unlike N-nucleophiles, S-nucleophiles can be involved in the intra- or intermolecular conjugated addition to captodative aminoalkenes. For example, prolonged refluxing of 2-(*N*-methylamino)pent-2-enonitrile with sodium thiophenoxide and thiophenol in THF gave rise to 1,4-addition product **102**.⁵⁴



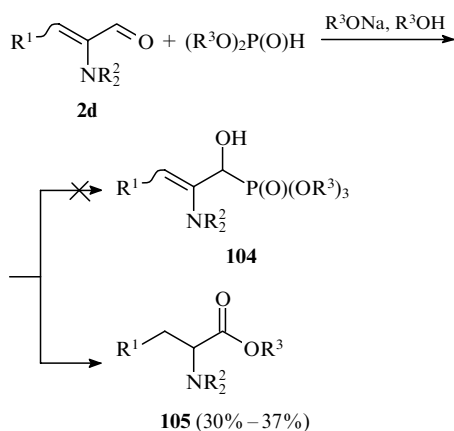
The reactions of the aminoalkenes **2d** with alkane- or arene-thiols or dithiols afforded neither 1,2- nor 1,4-adducts; instead, the compounds **2d** were unexpectedly transformed into the corresponding thiol esters of α -amino acids **103** in yields of up to 87%.²³⁶ Neither changes in the structures of the reagents nor variations in the reaction conditions have an effect on the direction of the reaction.



$R^1 = \text{Me, Ph; } NR_2^2 = \text{NEt}_2, \text{N-morpholinyl; } R^3 = \text{Et, Bu, Ph, CH}_2\text{CH}_2\text{SH.}$

This methodology, which allows the construction of the $\text{CH}(NR_2)\text{CO}$ fragment, was further developed in the synthesis of esters of α -amino acids containing the disubstituted amino group. It is well known that these compounds are important precursors for the design of new pharmaceuticals and for the preparation of polyfunctional compounds.

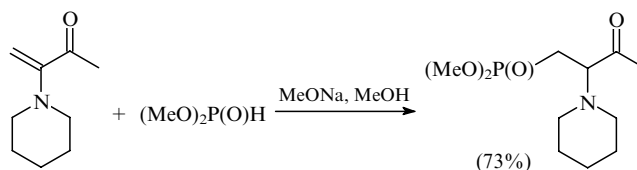
It appeared that the reactions of the formyl-substituted enamines **2d** with an equimolar amount of dialkyl phosphonate in the presence of sodium alkoxide afforded esters of *N,N*-disubstituted α -amino acids **105** rather than the expected phosphonates **104**.^{237–239} The moderate yields of the esters **105** were accounted for by competitive anionic polymerisation of the starting substrate or one of the intermediates under the action of sodium alkoxide. In the absence of the catalyst, the reaction of the phosphonate with the aminoalkene **2d** did not take place.



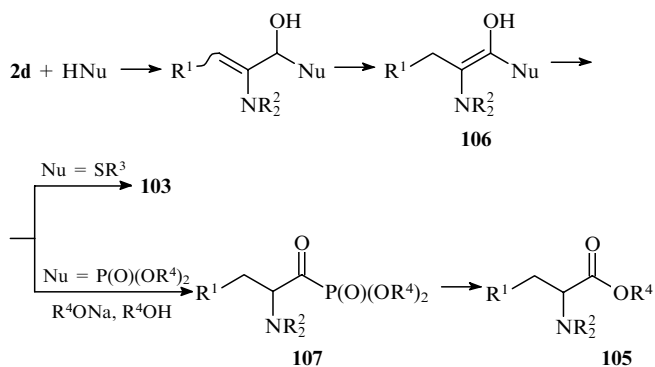
$R^1 = \text{Me, Pr, Ph; } NR_2^2 = \text{NEt}_2, \text{N-morpholinyl, N-piperidinyl; } R^3 = \text{Me, Et.}$

Unlike the formyl-substituted enamines **2d**, the aminoenones **2c** containing the terminal double bond are involved in the regioselective 1,4-addition to dimethyl phosphonate. Thus 3-piperidinobut-3-en-2-one smoothly produced the Michael adduct.²³⁹

The 1,2-adduct was not detected even in trace amounts. 2-Diethylaminobenzylideneacetophenone did not react with dimethyl phosphonate.



The scheme providing an explanation for the generation of the amino acid derivatives **103** and **105** was proposed in the studies.^{236–240} Undoubtedly, the first step involves the addition of the nucleophile to the formyl group of the aminoalkene **2d**. The key step of the scheme involves isomerisation of the initially formed 1,2-adduct to give thermodynamically more stable tetrasubstituted alkene **106**, which is rapidly transformed into the thiol ester **103** (in the case of S-nucleophiles) or ketophosphonate **107** (in the case of P-nucleophiles). Heterolysis of the C–P bond in the intermediate **107** readily proceeds under the action of alkoxides to give the ester of α -amino acid **105**.

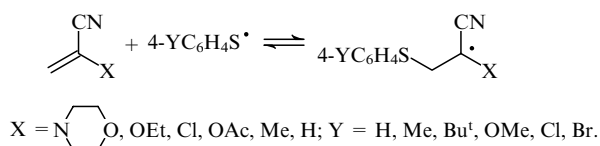


The proposed hypothesis was strongly supported by isolation of the enol **106** [$\text{Nu} = \text{P}(\text{O})(\text{OMe})_2$] as a stable silyl ether generated in the reaction of the α -formyl-substituted enamine **2d** ($R^1 = \text{Ph}$, $\text{NR}_2^2 = \text{NEt}_2$) with dimethyl trimethylsilyl phosphite.²³⁹ The above-described reaction of the substrates **2d** with dialkyl phosphonates is one of the first examples of the vicarious nucleophilic addition. From the practical standpoint, the reactions of soft nucleophiles with the aminoalkenes **2d** provide a new convenient procedure for the one-pot synthesis of derivatives of *N,N*-disubstituted α -amino acids.

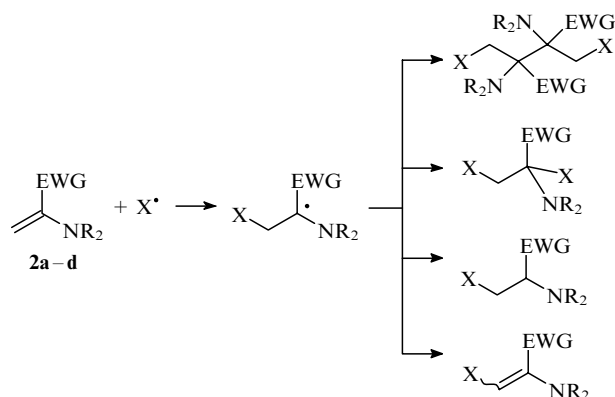
3. Radical reactions

Aminoalkenes containing a geminal activating group are excellent radicalophiles. The stabilising effect of captodative substituents on the radical centre has been postulated more than 20 years ago¹ and was subsequently confirmed by numerous experiments.

Ito *et al.*²⁴¹ carried out the kinetic study of the addition of arylthiyl radicals to acrylonitriles bearing the electron-donating group X at the α position. It appeared that the rate constant of this reaction decreases in the series $\text{NR}_2 > \text{OR} > \text{Cl} > \text{OAc} > \text{Me} > \text{H}$. This sequence correlates well with their electron-donating ability and indicates that captodative substituents exert the synergistic effect on stability of the radical. It should be noted that the relative activity of amino derivatives is ~ 20 times higher than that of their alkoxy analogues and ~ 550 times higher than the reactivity of unsubstituted acrylonitrile. Consequently, the aminoalkenes **2** proved to be the most efficient radical traps of all the known compounds.



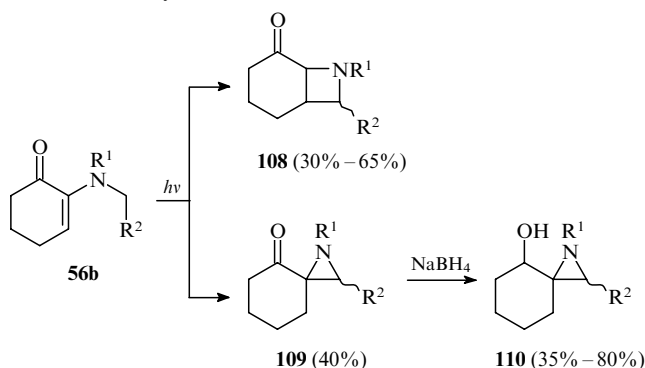
This ability of captodative systems finds versatile synthetic applications.^{4, 132, 242} Below are given the possible pathways of transformations of the radical intermediate giving rise to various polyfunctional compounds with high selectivity.



EWG = CN (**a**), CO₂R (**b**), C(O)R (**c**), CHO (**d**); R = Alk, Ar.

The behaviour of captodative aminoalkenes in photolysis is very sensitive to insignificant structural changes in the substrate and primarily to the nature of the substituents at the nitrogen atom. Conceivably, that is why it is difficult to make generalisations and predict the direction of the reaction based on the available data.

In most cases, photolysis of the 2-aminocyclohex-2-enones **56b** [$R^1 = \text{Et}$, $R^2 = \text{Me}$; $R^1 - R^2 = (\text{CH}_2)_4$, $(\text{CH}_2)_2\text{OCH}_2$] containing the α -hydrogen atoms in the substituents at the nitrogen atom is accompanied by elimination of one of these hydrogen atoms. Subsequent cyclisation of the resulting biradical intermediate affords bicyclic azetidine derivatives **108**.^{189, 243} Analogues of the compounds **56b** bearing the methyl group at position 3 produced the azetidines **108** in low yields.¹⁸⁹ In some cases, the reactions of the aminoalkenes **56b** performed under the same conditions unexpectedly gave rise to spiroaziridines **109**, which were isolated as alcohols **110** after reduction of the carbonyl group.^{119, 244} It is believed that the aziridines **109** were formed through α -hydrogen abstraction followed by the rearrangement of unstable azabicyclooctenol.¹¹⁹

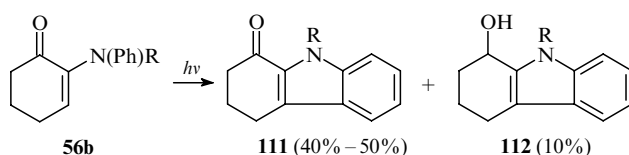


108: $R^1 = \text{Et}$, $R^2 = \text{Me}$; $R^1 - R^2 = (\text{CH}_2)_4$, $(\text{CH}_2)_2\text{OCH}_2$;

109, 110: $R^1 = \text{H}$, $R^2 = \text{Ph}$; $R^1 = \text{Bn}$, $R^2 = \text{Ph}$;

$R^1 = \text{Me}$, All, $R^2 = \text{CH}=\text{CH}_2$.

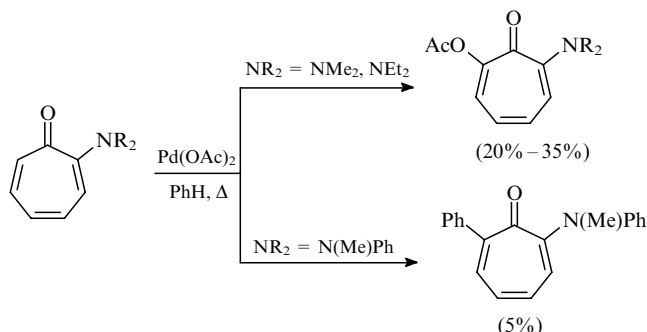
Photochemical cyclisation of *N*-arylaminoalkenones afforded carbazole derivatives **111** and **112**.¹⁴⁰



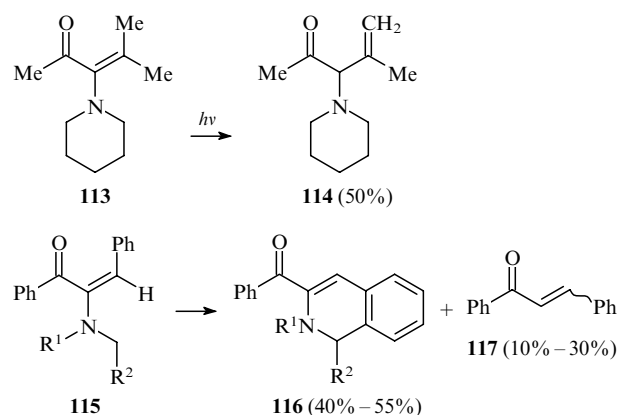
R = Me, Et.

Radical cyclisation of 2-(haloarylethyl)aminocycloalk-2-enones proceeds both at the C² atom of the enone fragment to form aminoalkenes, which are azepine derivatives, and at the nitrogen atom to produce compounds of the indole series.²⁴⁵

The reactions of 2-aminotropones with palladium acetate, which are considered to be a catalytic radical process, differ essentially from the reactions of other troponoid compounds performed under the same conditions.²⁴⁶ Depending on the substituents at the nitrogen atom, either acetoxylation ($\text{NR}_2 = \text{NMe}_2$, NEt_2) or arylation [$\text{NR}_2 = \text{N}(\text{Me})\text{Ph}$] were observed.



The photochemical behaviour of the acyclic aminoalkenones **2c** differs from that of the 2-aminocyclohex-2-enones **56b**. Thus in photolysis of aminoalkenone **113** in ether or pentane, allylic hydrogen abstraction proceeded more efficiently to give isomeric nonconjugated alkene **114** as the only reaction product.¹⁷⁷ In the absence of the allylic hydrogen atom, for example, in aminoalkene **115**, the substrate underwent rapid *E,Z* isomerisation followed by slow formation of a mixture of compounds consisting primarily of cyclisation product **116** and elimination product **117**.¹⁷⁷



$R^1 = \text{Et}$, $R^2 = \text{Me}$; $R^1 - R^2 = (\text{CH}_2)_4$, $(\text{CH}_2)_2\text{OCH}_2$.

Intramolecular photocyclisation of 2-anilinoalkenonitriles gave rise to 2-cyano-1-methyl-3-*R*-indoles ($R = \text{Me}$, Ph , $\text{CH}=\text{CHMe}$). Under the action of Bu_3SnH in the presence of azoisobutyronitrile, radical cyclisation of 2-anilinoacrylonitriles containing the haloalkyl (alkenyl) substituent at position 3 gave rise to substituted cycloalkanes or cycloalkenes.^{63, 247}

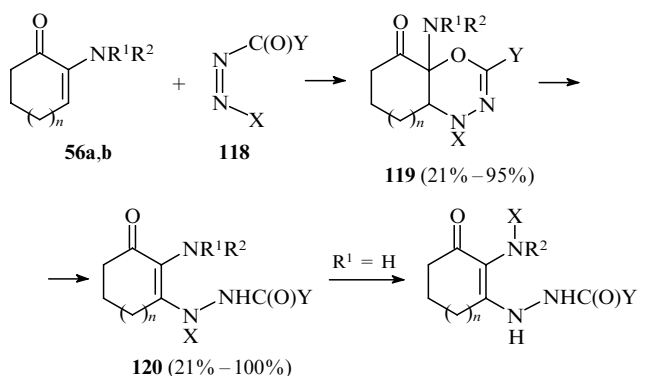
4. Captodative aminoalkenes in the synthesis of carbo- and heterocyclic compounds

Due to the presence of multiple carbon–carbon and carbon–heteroatom bonds, captodative alkenes can be used in the synthesis of carbo- and heterocyclic compounds. Cycloaddition reactions are apparently the most important transformations of captodative aminoalkenes. These reactions have been extensively studied in the last decade. The aminoalkenes **2a–c** can be involved in [2 + 2]-, [3 + 2]- and [4 + 2]-cycloaddition reactions, the latter reactions being most common.

It is well known that dienophiles containing electron-withdrawing substituents are readily involved in the Diels–Alder

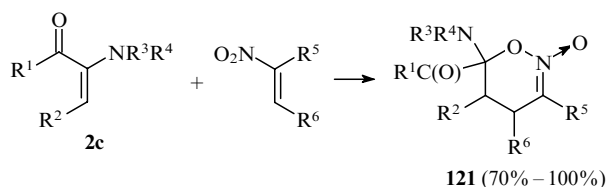
reactions with electron-rich dienes. It is not surprising that [4 + 2]-cycloaddition of simple enamines to nonactivated dienes occurs very rarely. Unlike simple enamines, captodative aminoalkenes successfully react with various dienes, including nonactivated compounds.

The reactions of the 2-aminocycloalk-2-enones **56a,b** with electrophilic diazenes **118** are formally classified as [4 + 2]-cycloaddition.^{248–253} Stability of 1,3,4-oxadiazines **119** thus formed depends both on the nature of the amino group and the ring size of the substrate as well as on the presence of the functional groups in the diazene **118**. Generally, aminoenones bearing a disubstituted amino group form rather stable cyclic derivatives **119**, which are slowly transformed into acyclic isomers **120** at room temperature or upon heating.^{248–250} Analogous [4 + 2]-adducts were also obtained from *N*-aryl-substituted aminocycloalkenones.²⁵² In other cases, the formation of the heterocycles **119** is not necessarily detected and the enediamines **120** are the only reaction products, which are readily rearranged into more stable isomers.^{251–253} Benedetti *et al.*²⁵¹ assumed that the compounds **120** can also be formed immediately from the starting substrates.

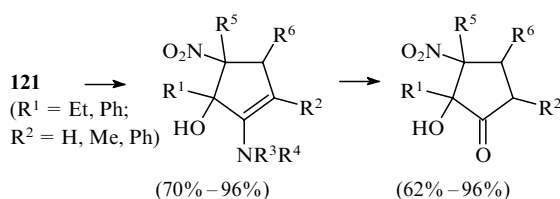


$n = 0$ (**a**), 1 (**b**); $R^1 = H$; $R^2 = Bu^n, Bu^t, Ph$; $NR^1R^2 = N$ (cyclopentyl), N (morpholinyl); $X = Ph, 4-NO_2C_6H_4, PhCO, CO_2Me, CO_2Et$; $Y = Ph, 4-NO_2C_6H_4, OEt$.

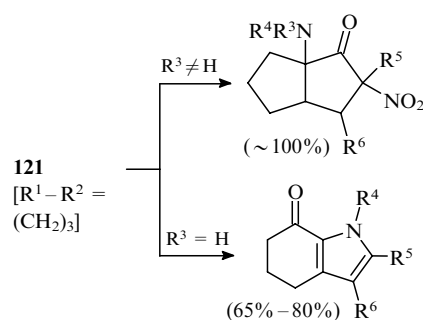
The reactions of the cyclic and acyclic aminoalkenones **56b** and **2c** (as dienophiles) with nitroalkenes (as heterodienes) were used for the synthesis of various carbo- and heterocyclic systems, *viz.*, tetrahydroindoles,¹⁴¹ polyquinanes^{254,255} and pentalenes.^{129,256–258} In most cases, the authors of the cited studies postulated that 1,2-oxazine *N*-oxides **121** were formed as intermediates whose subsequent transformations depend primarily on the nature of the substituents and the reaction conditions. Some heterocyclic derivatives **121** were so stable that they can be isolated in quantitative yields.^{141,257–259} In a number of studies,^{129,141} [2 + 2]-cycloaddition products or Michael adducts were detected along with the compounds given below.



$R^1 = Et, Ph$; $R^2 = H, Me, Ph$; $R^1-R^2 = (CH_2)_3$; $NR^3R^4 = NHBu^n, NHBu^t, NHPh, N$ (cyclopentyl), N (morpholinyl), N (piperidinyl); $R^5, R^6 = H, Me, Ph$.

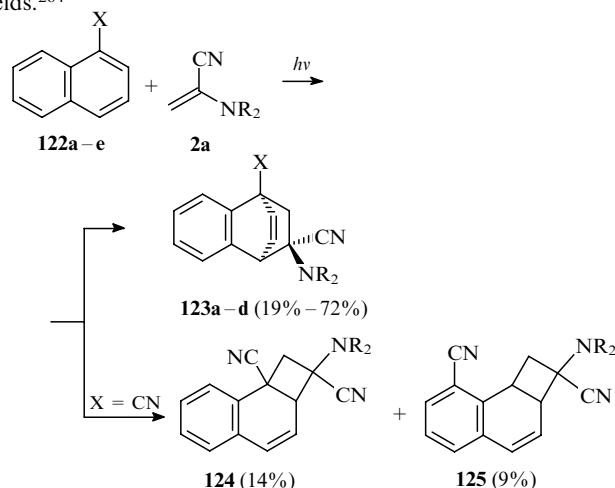


$R^5 = H, Me, Ph$; $R^6 = H, Me$.



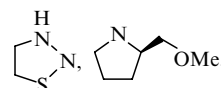
$R^5 = H, Me, Ph$; $R^6 = Me, Ph$.

Döpp and co-workers^{260–264} performed extensive studies on cycloaddition of various captodative alkenes to unsaturated systems over many years. The Diels–Alder reactions of the cyanoenamines **2a** with 1-naphthaldehyde (**122a**), 1-acetonaphthone (**122b**), 1-naphthophenone (**122c**) or methyl 1-naphthoate (**122d**) proceeded with high regio- and stereoselectivity to form adducts **123a–d**.^{36,170,261–263} By-products of [2 + 2]-cycloaddition were obtained in negligible yields (< 1%) (in some cases, these compounds were not detected at all). In contrast, the cyanoenamine **2a** (NR_2 is morpholino) is involved in [2 + 2]-cycloaddition with naphthalene-1-carbonitrile **122e** to give a mixture of isomeric polycyclic compounds **124** and **125** in low yields.²⁶⁴



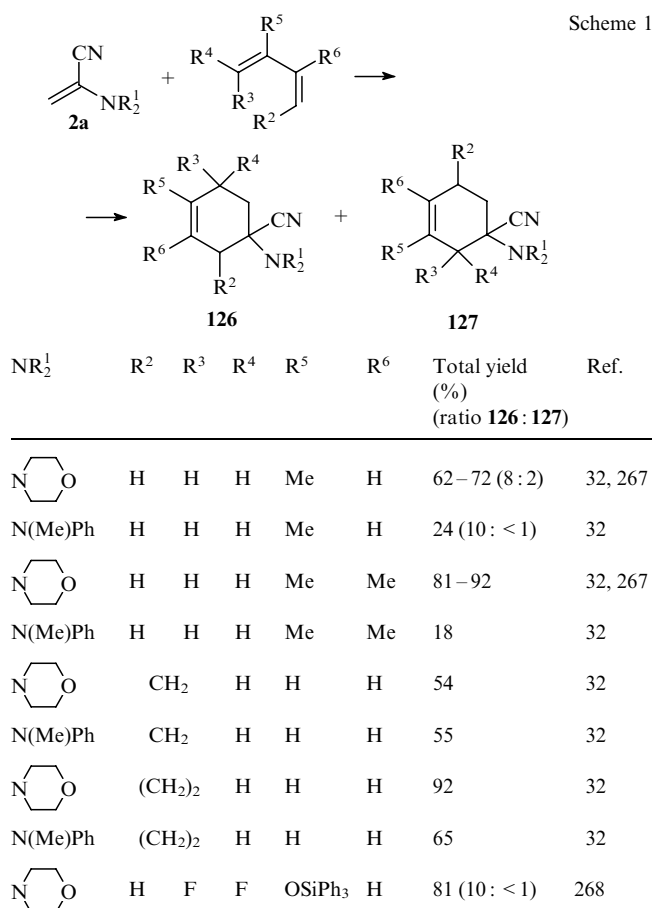
$X = CHO$ (**a**), $C(O)Me$ (**b**), $C(O)Ph$ (**c**), CO_2Me (**d**), CN (**e**);

$NR_2 = N$ (morpholinyl), N (piperidinyl), N (piperidinyl)- Ph , N (piperidinyl)- NPh , N (piperidinyl)- $NC_6H_4CF_3$ -3,



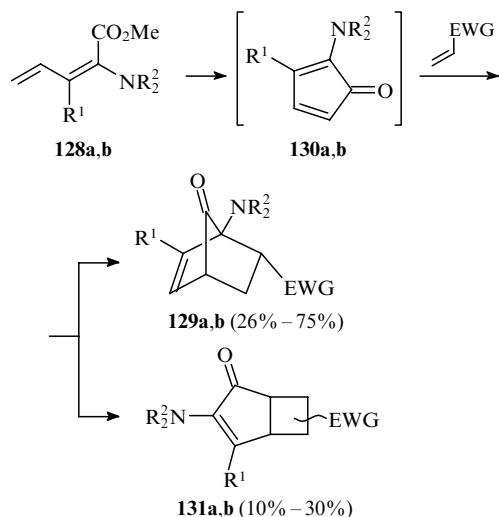
The reactions of the aminoalkene **2a** (NR_2 is morpholino) with substituted 1-acetonaphthones afford the [2 + 2]- and [4 + 2]-cycloaddition products in a ratio which depends on the position of the substituent. The reaction with 2-methoxy-1-acetonaphthone produced only the [2 + 4]-adduct, whereas derivatives bearing a substituent at position 4 gave rise to [2 + 2]-cycloaddition products.²⁶⁵ Under the conditions of photolysis, 2-morpholinoacrylonitrile was involved in the [2 + 2]-cycloaddition reaction with 3-acetylthianaphthene.²⁶⁶

Unlike unsubstituted enamines, the cyanoenamines **2a** react with a number of nonactivated conjugated dienes to give [4 + 2]-cycloaddition products **126** and **127** (Scheme 1). The acrylonitrile **2a** (NR_2 is morpholino) proved to be more reactive as a dienophile than its analogue containing the aromatic amino group, the regioselectivity of the addition being dependent on the nature of the substituents in the diene (see Scheme 1).



The above-considered reactions clearly demonstrate that captodative aminoalkenes are good dienophiles, which are much superior to the corresponding alkoxy and thio analogues in reactivity.²⁶⁹ These compounds are equally efficient as dienes provided that the β -substituent contains one or several multiple bonds.^{25, 26, 270}

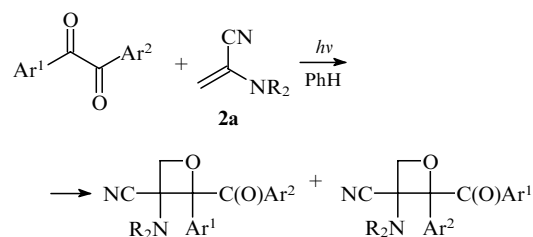
The reactions of dienes **128a,b** with derivatives of acrylic acid afforded unexpected cyclisation products.^{69, 271} Aminonorbornones **129a,b** were formed through the [4 + 2]-cycloaddition of methyl acrylate or acrylonitrile to aminocyclopentadienones **130a,b** generated upon intramolecular condensation of the dien-amino esters **128a,b**. The [2 + 2]-cycloaddition products **131a,b** were obtained as by-products. The proportion of the [4 + 2]-cycloaddition products **129a,b** depends on the nature of the



EWG = CO₂Me, CN; R¹ = Me (**a**), Et (**b**); NR₂² = NMe₂, NEt₂, .

amino and activating groups, *viz.*, the highest yields were achieved in the case of the dienes **128a,b** containing the piperidine substituent.

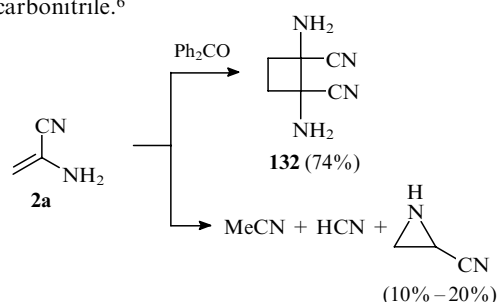
The captodative alkenes **2a–d** are excellent substrates in [2 + 2]-cycloaddition. The reactions of these compounds with substituted alkenes or carbonyl compounds produced respectively cyclobutanes²⁷² or oxetanes (the Paterno–Büchi reaction).^{273, 274} Thus the addition of symmetrical 1,2-diketones to the cyanoenamines **2a** proceeded regio- and stereospecifically to give head-to-head [2 + 2]-adducts with the *cis*-oriented amino and aryl groups (the configuration of the resulting diastereomer determined in the study²⁷³ is, apparently, in error). Under irradiation of a mixture of unsymmetrical diones and the cyanoenamines **2a**, the addition at the carbonyl groups proceeded with comparable rates to give a mixture of isomeric oxetanes in 9%–90% yields.²⁷⁴



Ar¹ = Ar² = Ph, 4-MeC₆H₄, 4-MeOC₆H₄, 4-ClC₆H₄, 4-CF₃C₆H₄, 2-C₁₀H₇; Ar¹ = Ph: Ar² = 4-MeOC₆H₄; 2-C₁₀H₇;

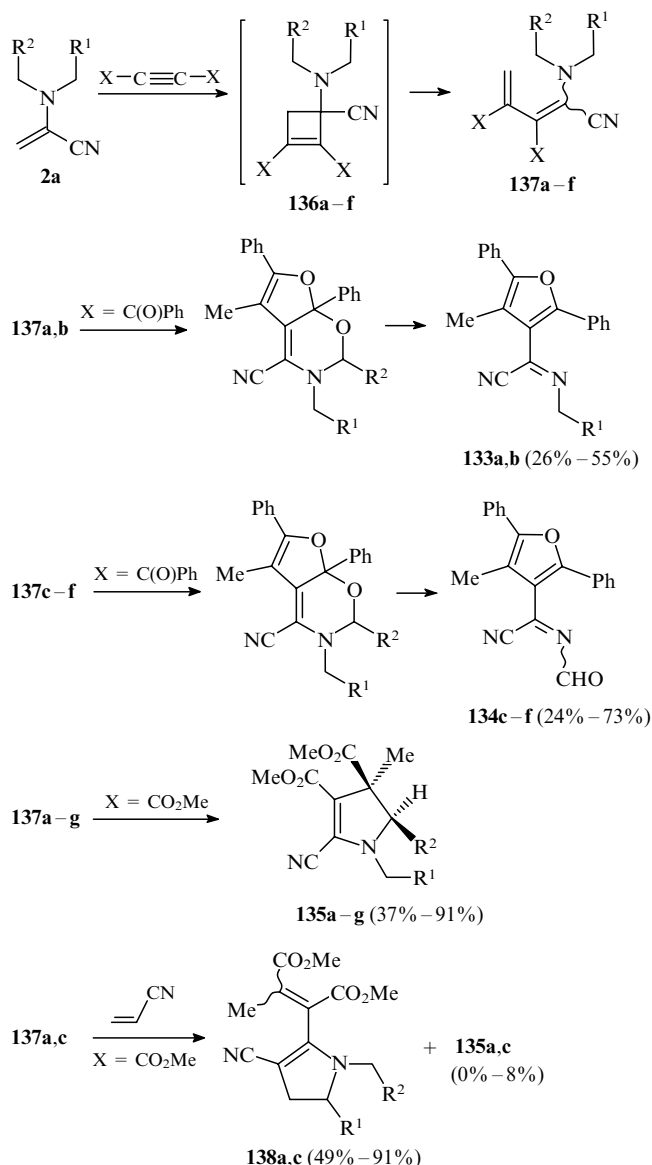
NR₂ = , , , , .

Examples of head-to-head and head-to-tail photochemical dimerisation of captodative aminoalkenes are available in the literature,^{5, 6, 275} the type of dimerisation being dependent on the structure of the substrate. The result of the reaction depends also on the reaction conditions. For instance, 2-aminoacrylonitrile underwent dimerisation in the presence of benzophenone as a photosensitising agent to form a mixture of diastereomers **132**.⁵ However, the formation of the cyclobutanes **132** was not observed in the absence of Ph₂CO. In the latter case, the main reaction involved fragmentation of the starting substrate to yield HCN and MeCN accompanied by competitive isomerisation into aziridine-2-carbonitrile.⁶



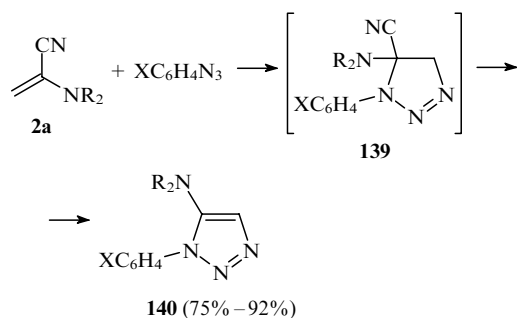
The captodative aminoalkenes **2a** are much more reactive than their push-pull isomers **1a**. These compounds react with dimethyl acetylenedicarboxylate or dibenzoylacetylene by being involved in the so-called ' α -cyclisation of tertiary amines'.^{276–278} Depending on the nature of the amino group in the aminoalkenes **2a** and the activating group in the acetylene derivative, either furans **133a,b** and **134c–f** or dihydropyrroles **135a–g** were obtained as the final reaction products. The preparation of dihydropyrroles, which were formed with high stereoselectivity, required more drastic conditions (refluxing in acetonitrile or DMSO).^{276, 279} The reaction mechanism includes [2 + 2]-cycloaddition and rapid recyclisation of adducts **136** into dienes **137**, which are the key intermediates for all products. The dienes **137a,c** are involved in 1,3-dipolar addition reactions with dipolarophiles, such as acrylonitrile, yielding finally a mixture of cycloadducts **138a,c** and the dihydropyrroles **135a,c** (Scheme 2).²⁷⁸

Scheme 2



$R^1 = R^2 = H$ (a), Me (b); $R^1 - R^2 = (CH_2)_2$ (c), $(CH_2)_3$ (d), $(CH_2)_4$ (e), $(CH_2)_5$ (f), CH_2OCH_2 (g); $X = C(O)Ph$, CO_2Me .

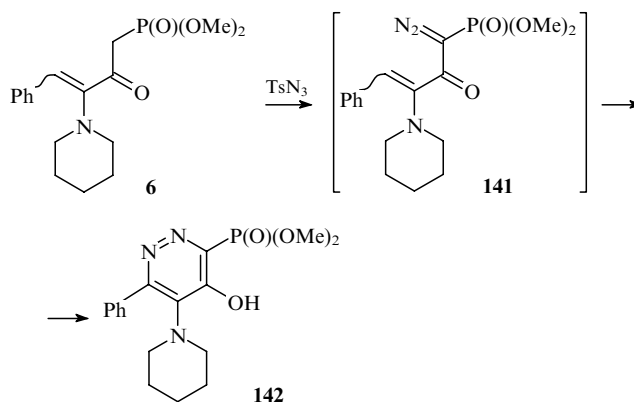
In [3 + 2]-cycloaddition, captodative aminoalkenes behave analogously to common enamines. Like enamines,¹⁷⁵ these compounds add aryl azides to give the corresponding dihydrotriazoles.^{11, 33, 280, 281} However, some of these cyclic derivatives are unstable and cannot be isolated. For example, dihydrotriazoles **139** formed in the reactions of the cyanoenamines **2a** underwent



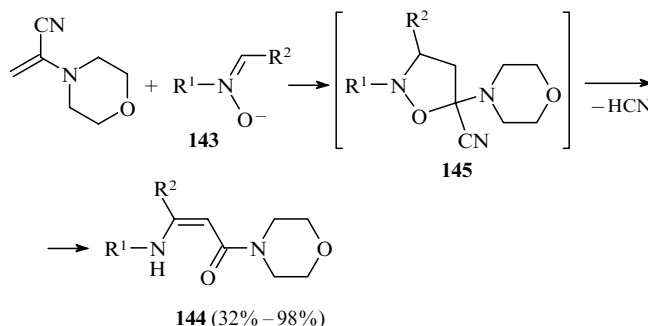
$NR^2 = N$ (pyrrolidine), N (piperidine), N (morpholine); $X = H$, 4-Me, 3- NO_2 , 4-Br, 3-Cl.

spontaneous HCN elimination to generate 1,2,3-triazoles **140**.^{3, 280} The reactions always proceed regiospecifically to yield the only isomer.

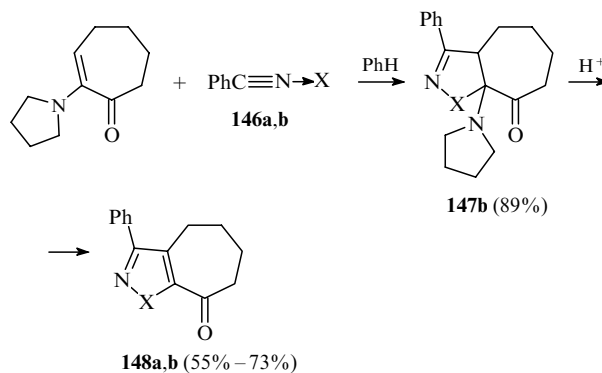
Like enamines, the β -oxophosphonate **6** reacted with tosyl azide to give diazo compound **141**, which underwent cyclisation into pyridazine **142**.²²



In spite of the fact that the reactions of 2-morpholinoacrylonitrile with aldonitrone **143** afforded morpholides **144**, Döpp and Walter²⁸² considered these reactions as 1,3-dipolar cycloaddition. Actually, the formation of the amides **144** can be attributed to elimination of HCN from intermediate isoxazolidine **145** followed by the ring opening. Hence, this cycloaddition reaction is also regiospecific, the terminal carbon atom of the starting aminonitrile being nucleophilic. Keto nitrones did not react with 2-morpholinoacrylonitrile.²⁸²



Cycloaddition of 1,3-dipolar compounds **146a,b** to 2-pyrrolidino-cyclohept-2-enone afforded initially compound **147b**, which lost amine upon acid treatment to form pyrazolone derivative **148a** or isoxazolone derivative **148b**.²⁸³



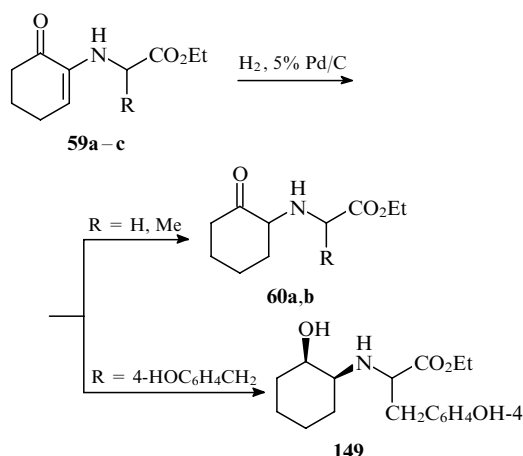
$X = NPh$ (a), O (b).

5. Other reactions most typical of captodative aminoalkenes

The captodative aminoalkenes **2a–c** are involved in some reactions, which cannot be unambiguously classified with the above-considered types. The most typical reactions, which are not

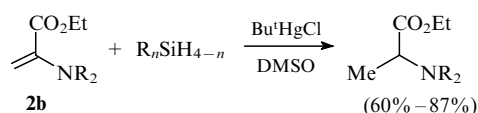
associated with the presence of a particular specific substituent, are considered in this section.

The aminoalkenes **2a–c** are rather readily subjected to hydrogenation. Under traditional conditions of heterogeneous catalysis, selective reduction of the C=C double bond generally takes place.^{17, 126, 284} In some cases, the reactions are accompanied by simultaneous reduction of the activating group. For example, the addition of hydrogen to the enamines **59a,b** afforded the corresponding 2-aminocyclohexanones **60a,b**. However, hydrogenation of the substrate **59c** performed under the same conditions gave rise to a mixture of diastereomers of *cis*-1,2-aminoalcohols **149** in quantitative yield.¹²⁶



R = H (**a**), Me (**b**), 4-HOC₆H₄CH₂ (**c**).

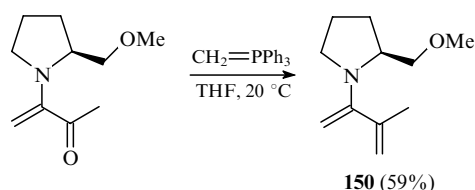
Of a wide variety of different activated alkenes, only the captodative aminoalkenes **2b** appeared to react with hydrosilanes with reduction of the C=C double bond.²⁸⁵



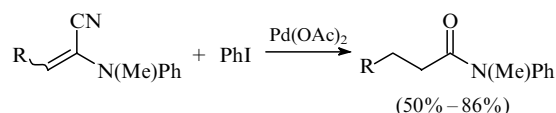
NR₂ = NEt₂, N(CH₂)_nO; n = 1–3.

The reactions with the use of metal aluminium hydride or borohydride as reducing agents either proceeded only at the activating group (C=O or CN)^{17, 150} or resulted in simultaneous reduction of both functional groups.¹⁵⁹

Wittig olefination of optically active 2-(methoxymethyl)pyrrolidinobut-3-en-2-one afforded chiral 2-amino-substituted buta-1,3-diene **150**. This compound is the first representative of the compounds, which have previously been difficult to access.¹³³



Noteworthy are the palladium-catalysed reactions of 2-(*N*-methylanilino)alkenenitriles with iodobenzene.²⁸⁶ Owing to the studies performed by De Kimpe and co-workers,^{184, 195} this transformation of cyanoenamines became an efficient procedure for the synthesis of the corresponding amides.



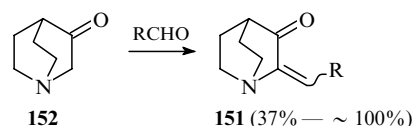
Captodative aminoalkenes readily undergo isomerisation. As mentioned above, the aminoenones **2c** and the aminoenals **2d** can be very readily subjected to *Z,E* isomerisation, which either occurs in the course of their preparation or subsequent transformations or takes place upon storage. In addition to *Z,E* isomerisation, examples of rearrangements of these compounds under the action of both acidic²⁸⁷ and basic reagents¹⁸³ are available in the literature.

Analysis of the most typical transformations of the captodative aminoalkenes **2a–d** shows that these compounds can exhibit the properties of either enamines or activated alkenes depending on various factors. The balance in favour of the canonical structure of enamine can be rather easily disturbed upon insignificant changes in the nature of the activating or amino group.

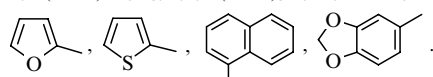
V. Methylidene- and arylmethylidene-quinuclidin-3-ones

Methylidene- and arylmethylidenequinuclidin-3-ones **151** not only serve as the key intermediates in the design of new pharmaceuticals but are also of interest in theoretical organic chemistry. These compounds can formally be considered as bicyclic captodative aminoalkenes. However, they cannot exhibit properties of enamines because of the fixed spatial orientation of the lone electron pair of the nitrogen atom. This is the essential distinction between the compounds **151** and the above-considered systems.

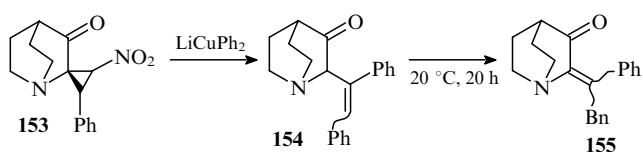
The 2-arylmethylidenequinuclidin-3-ones **151** are generally prepared by base-catalysed condensation of quinuclidin-3-one **152** with various arene- or hetarenecarbaldehydes.^{288–299} The compounds **151** are obtained as individual isomers or as mixtures of geometric isomers in yields from moderate to quantitative. The same methodology was successfully applied to the synthesis of ferrocenylmethylidene-substituted³⁰⁰ and tricyclic analogues of quinuclidinone.³⁰¹



R = Ph, 2-PhC₆H₄, 2-HOC₆H₄, 2-MeOC₆H₄, 2-FC₆H₄, 2-ClC₆H₄, 3-HOC₆H₄, 4-HOC₆H₄, 4-MeOC₆H₄, 4-ClC₆H₄, 4-NO₂C₆H₄, 4-Me₂NC₆H₄, 4-PhOCH₂CH₂OC₆H₄, 2,4-(MeO)₂C₆H₃, 3,4-(MeO)₂C₆H₃, 3,4,5-(MeO)₃C₆H₂, BnOC₆H₄, C₅H₅FeC₅H₄,

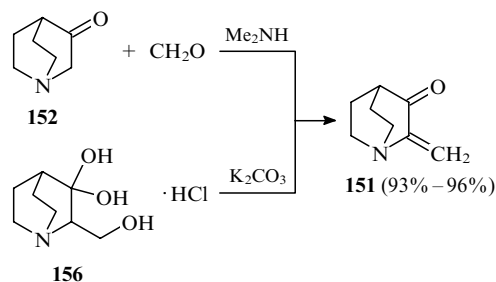


The cyclopropane-ring opening in spirocyclic quinuclidinone derivative **153**, which occurs under the action of C-, N- or O-nucleophiles, provides an interesting example of the preparation of β,β-disubstituted methylidenequinuclidones.³⁰² Thus the reaction of the compound **153** with lithium diphenylcuprate afforded a mixture of isomers **154** and **155**. The compound **154** was completely transformed into the quinuclidinone **155** during 20 h (the ratio *Z* : *E* = 3 : 1).³⁰²

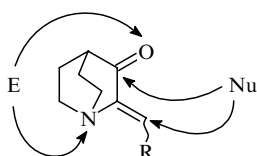


The quinuclidinone **151** (R = H) containing the terminal double bond was smoothly generated from the ketone **152** under the conditions of the Mannich reaction³⁰³ as well as by dehydra-

tion of 2-hydroxymethyl-3,3-dihydroxyquinuclidine hydrochloride (**156**).³⁰⁴

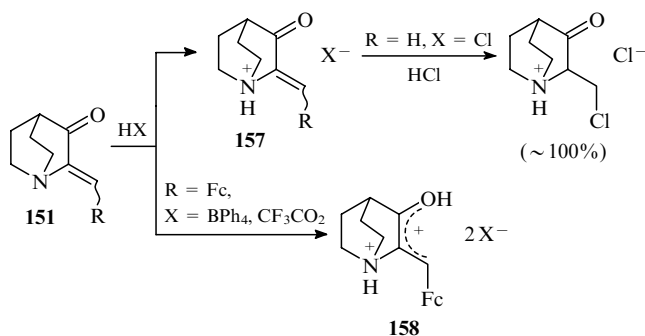


The orthogonal arrangement of the lone electron pair of the nitrogen atom hinders p,π -conjugation as a result of which the amino group exerts only the inductive effect on the double bond. This characteristic feature of the arylmethylidenequinuclidinones **151** is reflected in the observed downfield shifts of the signals for the olefinic proton ($\delta = 6.80\text{--}7.50$) in the ^1H NMR spectra and for the β -carbon atom ($\delta = 125\text{--}146$) in the ^{13}C NMR spectra as compared to the signals of the above-considered captodative aminoalkenes **2c** or **56b**. Hence, the quinuclidinones **151** would be expected to exhibit properties of strong amines in reactions with electrophilic reagents and properties of Michael acceptors in reactions with nucleophiles.



Like captodative aminoalkenes, the arylmethylidene- and ferrocenylmethylidenequinuclidinones **151** are protonated and alkylated at the nitrogen atom.^{299, 305–307} However, the same regioselectivity of the electrophilic attack is accounted for by different reasons. Thus enammonium salts of captodative aminoalkenes are highly stable due primarily to the stabilising effect of an intramolecular hydrogen bond, whereas N -protonation (alkylation) of the quinuclidinones **151** is associated only with the basicity of the nitrogen atom.

Bubbling of dry HCl through a solution of methylidenequinuclidinone led to quaternisation of the nitrogen atom to form compound **157** ($R = \text{H}$) along with the anti-Markovnikov addition of hydrogen halide to the double bond.³⁰⁵ In the case of the ferrocenylmethylidenequinuclidinones **151** ($R = \text{Fc}$), two heteroatoms are simultaneously protonated. The formation of the dications **158** was confirmed by NMR spectroscopy.^{299, 307}

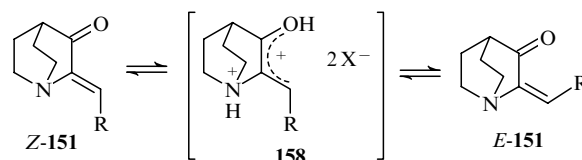


$R = \text{H, Ph, 4-FC}_6\text{H}_4, 2,4\text{-(MeO)}_2\text{C}_6\text{H}_3, \text{Fc}$;

$X = \text{Cl, BPh}_4, \text{PhCO}_2, \text{CF}_3\text{CO}_2$.

Under the action of gaseous HCl in chloroform^{288, 290, 295, 308} or of NaBPh_4 in acetic acid,^{299, 307} the compounds **151** underwent reversible Z,E isomerisation. For example, Z -2-aryl-methylidene- and Z -2-ferrocenylmethylidenequinuclidinones are readily (often

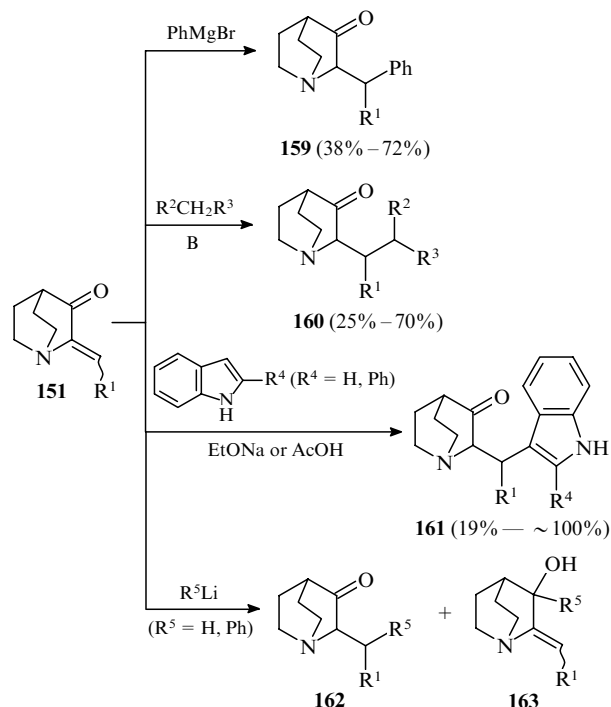
quantitatively in a matter of minutes) transformed into the corresponding E isomers.^{295, 299, 307} In this case, there is the evident analogy with enammonium salts of captodative aminoalkenes, *viz.*, isomerisation becomes possible due to a decrease in the double-bond character of the alkene fragment.²⁹⁹ These transformations of the quinuclidinones **151** provide the means of performing the selective synthesis of their individual geometric isomers, which is of importance in studying the structure–properties relationships (including, the structure–biological activity relationships).



The fact that the quinuclidinones **151** cannot exhibit the properties of enamines is reflected in their reactions with nucleophilic reagents. For example, the majority of the reactions of the compounds **151** and their tricyclic analogues with various C-nucleophiles proceed as conjugated 1,4-addition.^{294, 301, 302, 309–314} In some cases, Michael adducts **159–162** are obtained in moderate yields, which is attributable to competitive 1,2-addition giving rise to compounds **163**. The latter compounds were obtained as the major products in the reactions of the quinuclidinones **151** with aryl- or alkyl lithium derivatives (Scheme 3).^{299, 300, 307, 315, 316} As mentioned above, numerous attempts to perform the Michael addition to captodative aminoalkenes failed almost without exception (see Section IV.2).

Alcohols serve as O-nucleophiles in the Michael addition reactions with methylidenequinuclidin-3-one, the reactions pro-

Scheme 3



$R^1 = \text{H, Ph, 2-ClC}_6\text{H}_4, 4\text{-MeOC}_6\text{H}_4, \text{Fc}$; $R^2 = \text{CO}_2\text{Me}$, $R^3 = \text{CN}$;

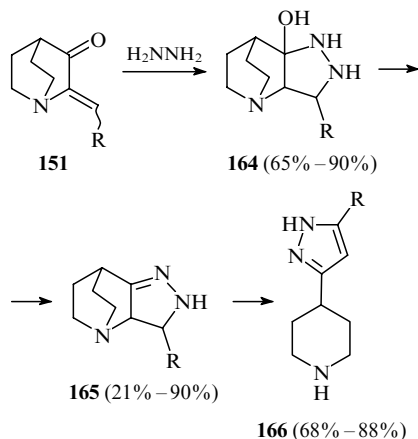
$R^2 = \text{Ph}$, $R^3 = \text{CN}$; $R^2 = \text{Ph}$, $R^3 = \text{N=CHPh}$; $R^2 = \text{H}$, $R^3 = \text{NO}_2$;

$R^2 = \text{C(O)Me}$, $R^3 = \text{CO}_2\text{Et}$; $R^2 = \text{C(O)Me}$, $R^3 = \text{C(O)Ph}$;

$R^2 = R^3 = \text{C(O)Me}$, $R^2R^3\text{CH}_2 =$; $B = \text{NaOH, MeOH, BuLi}$.

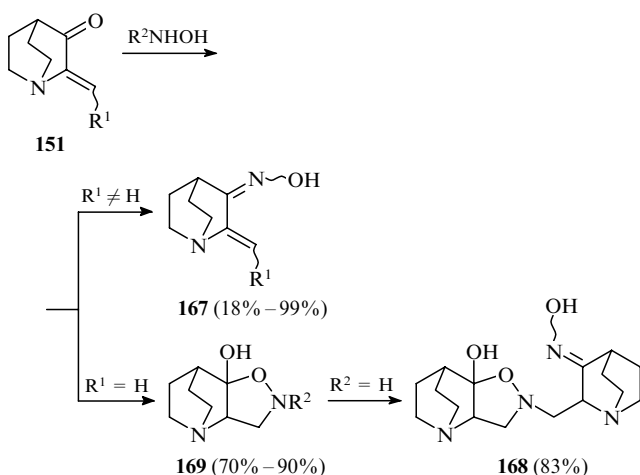
ceeding slowly.³⁰⁶ As expected, aniline forms the corresponding Schiff's base with the latter compound.³¹⁷

The presence of two electrophilic centres, *viz.*, the carbon atom of the carbonyl group and the β -carbon atom of the double bond, allows the use of the quinuclidinones **151** for the construction of various heterocyclic systems. For example, the reactions of the ketones **151** ($R = H, Ph$ or Fc) with hydrazine afforded quinuclidine derivatives **164** or **165** depending on the reaction conditions. Under the action of basic reagents (KOH or an excess of hydrazine), the latter compounds were decomposed upon heating to give pyrazoles **166**.^{290–292, 296, 297, 300, 317, 318} Analogous transformations were observed in the reactions of the compounds **151** with thiosemicarbazide.³¹⁸ Phenylhydrazine reacts analogously to primary amines to produce phenylhydrazone.²⁹⁰



$R = H, Ph, Fc$.

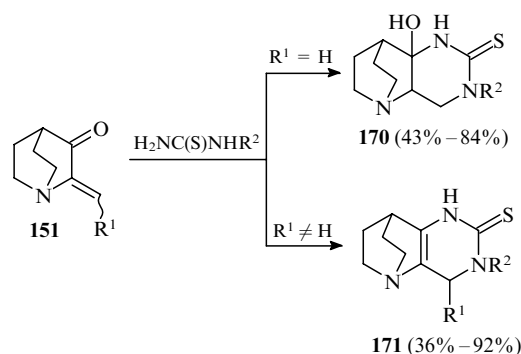
The reactions of hydroxylamines with the arylmethylidenequinuclidinones **151** bearing a substituent at the double bond afforded oximes **167**,^{298, 319, 320} whereas the reaction of the unsubstituted methylidenequinuclidin-3-one **151** ($R^1 = H$) with hydroxylamine gave rise to oxime **168**, which was isolated as dihydrochloride.³²¹ It was assumed that this reaction proceeded through the intermediate formation of 4a-hydroxyisoxazolidino[4,5-*b*]quinuclidine **169**. The *N*-substituted derivatives of the isoxazolidine **169** were prepared in high yields by the reactions of quinuclidinone **151** ($R^1 = H$) with *N*-arylhydroxylamines.³²¹



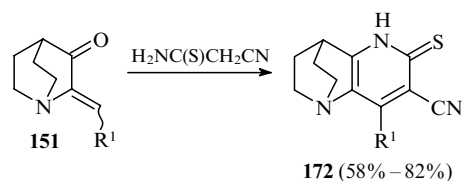
$R^1 = H, Ph, 2-HOC_6H_4, 3-HOC_6H_4, 4-HOC_6H_4, 2-MeOC_6H_4, 4-MeOC_6H_4, 4-Me_2NC_6H_4, 4-NO_2C_6H_4$;

$R^2 = H, Ph, 4-MeC_6H_4, 4-ClC_6H_4, 3-ClC_6H_4$.

The compounds **151** equally readily reacted with thiourea and phenylthiourea to produce pyrimidinethiones **170**³¹⁸ or **171**.^{290, 300, 322} Finally, cyclisation of the ketones **151** with cyanothioacetamide gave rise to the corresponding thiones **172**.³²³

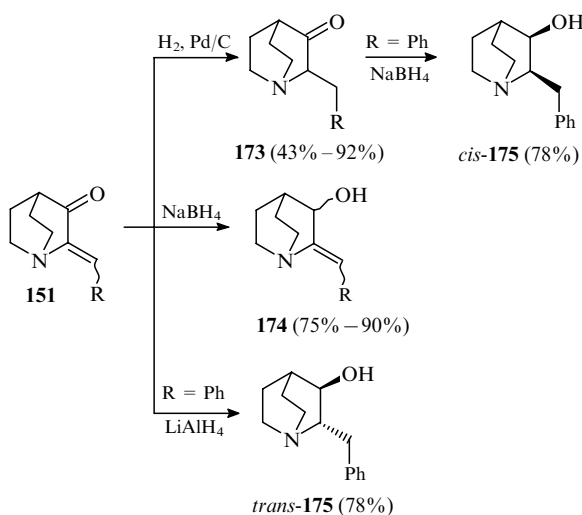


$R^1 = H, Ph, 4-MeOC_6H_4, Fc$; $R^2 = H, Ph$.



$R^1 = Ph, 4-FC_6H_4$.

As in the case of captodative aminoalkenes, reduction of methylidene- and arylmethylidenequinuclidinones can be directed with high selectivity toward either the $C=C$ double bond or the carbonyl group by varying the nature of the reducing agent. When subjected to platinum- or palladium-catalysed hydrogenation, methylidene- and arylmethylidenequinuclidinones were transformed into saturated ketones **173**.^{288, 291, 292, 298, 305} The corresponding allylic alcohols **174** were selectively obtained with the use of $NaBH_4$.^{288, 308, 324, 325} Stereospecific reduction of both functional groups in the benzylidenequinuclidinone **151** ($R = Ph$) with lithium aluminium hydride afforded benzylquinuclidinol *trans*-**175** ($R = Ph$).³²⁶ Catalytic hydrogenation of the same compound **151** ($R = Ph$) followed by reduction with $NaBH_4$ gave rise to *cis*-**175** ($R = Ph$).³⁰⁸



$R = H, Ph, 2-ClC_6H_4, 4-MeOC_6H_4, 3,4-(MeO)_2C_6H_3$.

VI. Conclusion

Recent progress in the chemistry of captodative alkenes allows the preparation of many aminoalkenes containing the geminal activating group, which can be considered as polyfunctional building blocks. Various transformations characteristic of this type of compounds, such as electrophilic or nucleophilic addition and, in particular, cyclisation, can be used in organic synthesis. Unlike the push-pull enamincarbonyl compounds **1c** for which a special type of non-cyclic aromatic stabilisation was assumed,³²⁷ the cross-conjugated aminoalkenes **2a–d** act as 'chemical chame-

leons'. The latter compounds are able to exhibit the properties of either enamines or activated alkenes resulting from insignificant changes in the structure of the substrate and the reaction conditions. Owing to these properties, captodative aminoalkenes are unique building blocks and there is reason to hope that they will find increasing use in organic synthesis.

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^f — *Pharm.-Chem. J. (Engl. Transl.)*

Electrochemical activation of reactions involving organometallic compounds

T V Magdesieva, K P Butin

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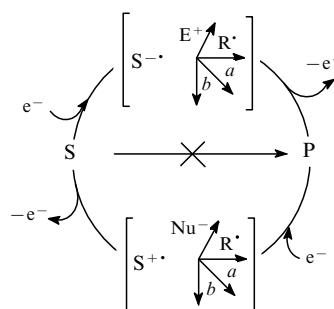
Abstract. Data on the electrochemical activation of various reactions involving organometallic compounds are generalised. Primary attention is devoted to the key types of transformation that can be performed using electrochemical electron transfer, namely, redox activation of 16- and 18-electron complexes of transition metals as the first step of a broad range of reactions, electrocatalysis, mediator processes, and electrosynthesis of compounds containing carbon–metal σ -bonds. The bibliography includes 188 references.

I. Introduction

The problem of increasing the reactivity of compounds arose as soon as chemists became engaged in targeted synthesis. Numerous methods for the increase in the reactivity are currently known, ranging from simple methods (introduction of an appropriate substituent into the molecule) to more complex ones that have become classical (for example, catalysis) and, finally, to the most advanced techniques (in particular, photochemically or electrochemically induced electron transfer). Figure 1 presents classification of the activation processes proposed by Chanon.¹ The diagram axis can be continued without limit because new ways of solving this problem would certainly appear with the progress of science.

Activation through electron transfer is rather effective. In this case, very high process selectivity can be attained because it is possible to specify precisely the potential needed for the generation of a particular active species.

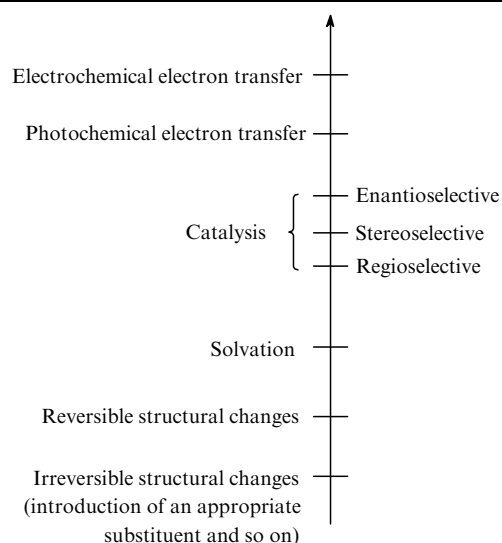
The transformation of a molecule into a reactive radical cation or radical anion (Scheme 1) initiates a wide range of chemical reactions. This is due to the following factors: (1) usually, charged species react with nucleophiles or electrophiles more readily than neutral molecules; (2) the presence of the unpaired electron activates homolytic reaction pathways; (3) further redox processes, disproportionation and so on are also possible.



Scheme 1

S is the substrate, Nu is the nucleophile, E is the electrophile, P is the product; a is a redox reaction; b is dissociation, etc.

Activation of reactions through electron transfer was first employed by Taube² and Basolo and Pearson^{3–6} for inorganic systems. In organic chemistry, the development of this line of research was triggered by Kornblum's discovery^{7,8} of radical nucleophilic substitution ($S_{RN}1$) the mechanism of which has been later studied in detail by Bunnett⁹ and Russel.^{10,11} Saveant¹² was the first to use electrochemical electron transfer for the activation of organic reactions. Since then, the French electrochemical



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Figure 1. Multilevel diagram of the activation methods of reactions.¹

school has held a leading position in the research along this line. A great number of examples in which diverse organic reactions are activated by electrochemical electron transfer have been reported (see, for example, Refs 1, 13).

The intense use of electrochemical electron transfer in reactions involving organometallic compounds started approximately in the early 1980s. Most of the transition metal π -complexes are able to undergo reversible electrochemical redox transitions to give active species with odd numbers of electrons; therefore, electrochemically induced electron transfer can be used efficiently to facilitate ligand exchange, isomerisation, insertion and other reactions.^{14–19}

It is of interest to compare the behaviours of mononuclear metal complexes and supramolecular species containing these complexes as structural units.²⁰ Systems of this type are able to undergo electrochemically induced reversible structural changes, and they can be regarded as prototypes of ‘molecular machines.’ In this case, the electron transfer involving one structural unit entails changes over the whole supramolecular system (for example, electrically induced charge separation, migration of structural fragments, *etc.*).²⁰

A relatively new field in the use of electrochemical electron transfer for changing the reactivity of transition metal complexes is the design of redox-switchable ligands. The introduction into the ligand of ferrocenyl, cobaltocenyl, anthraquinone or other groups prone to reversible redox transitions allows the formation of complexes with switching reactivity.²¹ A change in the redox state of the ‘switch’ induces a change in the electronic properties of the ligand and, hence, the nature of the metal–ligand bond. This promotes various types of reaction, for example, ligand exchange. This approach appears highly promising for the design of ‘redox-switchable’ catalysts. Chiral metal complexes with ‘redox-switchable’ ligands can be used in asymmetric synthesis, for the separation of enantiomers, *etc.*²¹

Yet another extensive field of application of the electrochemical electron transfer in reactions involving organometallic compounds is electrochemical generation of labile complexes of transition metals in low oxidation states and involvement of these species in subsequent chemical transformations *in situ*, most often, as catalysts. The combination of catalysis by metal complexes with the electrochemical electron transfer has opened up almost unlimited scope for performing various mediator processes (see, for example, Refs 22–24).

Numerous examples of reactions activated by electrochemical electron transfer have now been reported in the literature. Since it is impossible to embrace them all within a single review, we intended first of all to show what types of transformations can be accomplished by virtue of the electrochemical electron transfer and how the use of electrochemical methods extends the synthetic capacity of a chemist in the field of organometallic chemistry. Primary attention has been devoted to the studies published during the last decade and not covered in earlier reviews.

II. Reactions of odd-electron complexes of transition metals

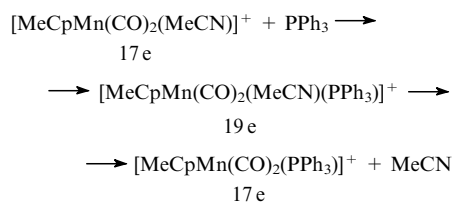
The transfer from relatively stable 16- and 18-electron configurations to 17- and 19-electron configurations of transition metal complexes can be attained *via* electrochemical oxidation or reduction. The odd-electron complexes thus formed are much more reactive; therefore, they can be involved in reactions that either do not proceed at all or proceed too slowly for complexes with 16- and 18-electron configurations. Research into the chemical transformations of odd-electron complexes has been the subject of numerous studies (see, for example, reviews^{15, 18, 22}). If the transformations are classified in terms of the reaction type, the main types are ligand exchange, isomerisation, insertion, extrusion, chelation/dechelation and dimerisation.

1. Ligand exchange

Ligand exchange reactions can be initiated by both oxidation and reduction of mono- or polynuclear metal complexes.

Initiation by oxidation				Initiation by reduction			
ML	$-e^-$	$\rightarrow$	$ML^{+\cdot}$	ML	$+e^-$	$\rightarrow$	$ML^{-\cdot}$
18 e			17 e	18 e			19 e
$ML^{+\cdot} + L'$		$\rightarrow$	$M(L')^{+\cdot} + L$	$ML^{-\cdot} + L'$		$\rightarrow$	$M(L')^{-\cdot} + L$
17 e			17 e	19 e			19 e
$M(L')^{+\cdot} + ML$		$\rightarrow$	$ML' + ML^{+\cdot}$	$M(L')^{-\cdot} + ML$		$\rightarrow$	$ML' + ML^{-\cdot}$
17 e			18 e 18 e 17 e	19 e			18 e 18 e 19 e

Upon reductive activation, an electron passes to an unoccupied orbital; this is accompanied by weakening of the $M-L$ bond. In essence, a similar reaction takes place during oxidation, because an associative mechanism of ligand exchange including the intermediate formation of a 19-electron complex with an additional ligand has been proven for 17-electron complexes by Kochi and coworkers.^{23, 25}

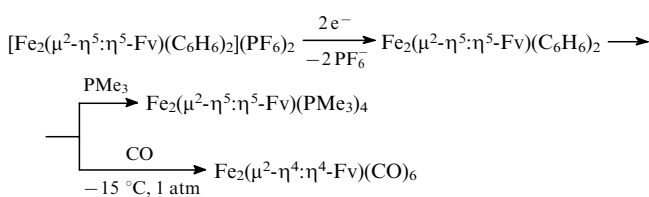


Cp = C₅H₅.

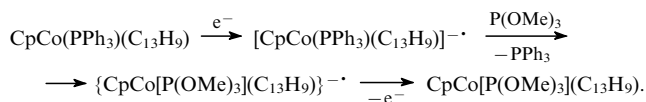
A second ligand present in the solution is coordinated to the 17-electron complex to give a 19-electron intermediate (as in the case of reductive activation) in which cleavage of the $M-L$ bond is facilitated.

A large number of examples of electrochemically activated ligand exchange have been described (see, for example, the reviews^{15–18, 26} and the monographs^{27, 28}). We shall dwell only on some publications that appeared during the last three to four years.

An interesting example of replacement of the arene ligand in binuclear fulvalene (Fv) complexes of iron has been reported.²⁹ The doubly reduced 38-electron complex readily reacts with CO or with different phosphine ligands.

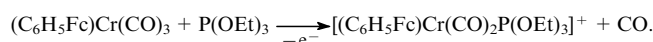


Preparative electrolysis of the fluorenyl complex of cobalt (at a potential of $-2.56\text{ V vs. Fc/Fc}^+$, where Fc is ferrocene) in the presence of various phosphine or phosphite ligands also results in ligand exchange.³⁰

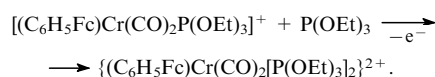


An unusual ligand exchange in the metal coordination sphere accomplished by virtue of a ‘redox switch’ connected to the reaction centre of the molecule has been reported.³¹ The role of the ‘redox switch’ is played by a ferrocenyl fragment linked by a covalent bond to the arene ligand of the chromiumtricarbonyl complex. Since the ferrocene fragment is oxidised first, the reaction takes place at an anodic overpotential substantially lower than that required for oxidation of the chromiumtricarbonyl group. Thus the partial destruction of the complex is avoided and the process selectivity is increased. Although the

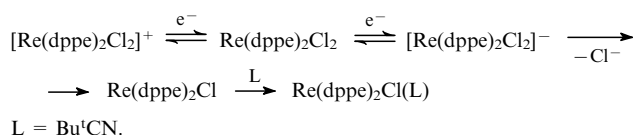
chromium atom has formally an 18-electron configuration, the adjacency of the strong electron acceptor results in easy replacement of the carbonyl group by a phosphorus-containing ligand.



The subsequent transfer of an electron from the Cr atom to the Fe atom turns off the 'redox switch'. Upon further displacement of the potential to the anodic region, the 'redox switch' is actuated once more, the Cr atom is activated again, and the reaction gives a purple complex, which was isolated.

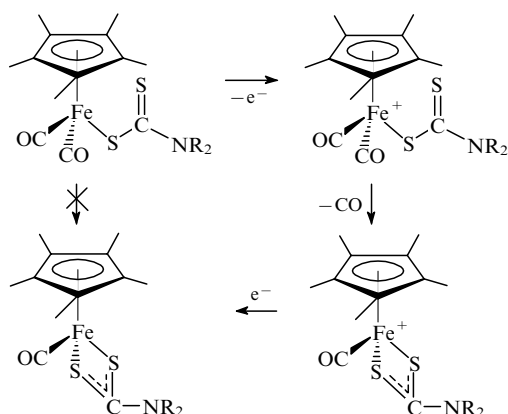


Electrochemical cleavage of the metal–halogen covalent bond with subsequent replacement of the halogen atom by another ligand has been described in detail.³² Upon single-electron reduction of the rhenium complex with diphenylphosphinoethane (dppe) $[\text{ReCl}_2(\text{dppe})_2]^+$ [the $\text{Re}(d^4) \rightarrow \text{Re}(d^5)$ transition], the Re–Cl bond length increases by 0.1 Å; the transfer of one more electron induces cleavage of this bond, and another ligand present in the solution enters the coordination sphere of the metal.



Oxidation of the central metal atom in the complex results in strengthening of bonds with σ -donor ligands (ammonia, amines, pyridine, *etc.*) and weakening of bonds with π -acceptor ligands (CO, nitriles, cyanides, *etc.*); this stipulates the required type of electrochemical activation (cathodic or anodic) in each particular case.

Actually, chelation/dechelation reactions can also be classified as ligand exchange. Some organic groups, for example, the dithiocarbamate group, act as chelating ligands in the coordination sphere of unsaturated complexes. However, they can also occur in the metal coordination sphere as monodentate ligands. It was shown³³ that the monodentate dithiocarbamate ligand can be readily converted into a chelating ligand upon oxidative activation.



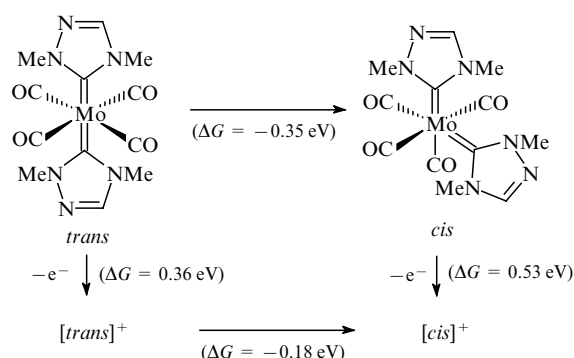
In principle, the inverse problem can also be solved. If it is required to change electrochemically the oxidation state of the central metal atom in a complex but to avoid ligand exchange or coordination of additional ligands, it is expedient to use a so-called cage ligand.²⁰ For example, oxidation of 1,10-phenanthroline complexes of Cu(I) is irreversible because it is accompanied by a structural rearrangement with coordination of solvent molecules to the copper atom giving rise to an octahedral geometry typical of Cu(II) complexes. If 2,9-dimethyl-1,10-phenanthroline is used as the ligand instead of 1,10-phenanthroline, the oxidation of the

Cu(I) complex is completely reversible because the presence of substituents at the α -position relative to nitrogen prevents the coordination of solvent molecules to the metal and, hence, the geometry does not change.³⁴

2. Isomerisation

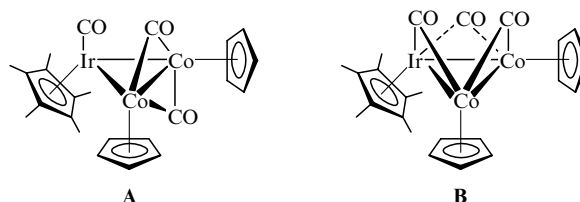
When considering the electrochemically activated isomerisation of transition metal complexes, one can distinguish three main types of transformations encountered most often, namely, *cis*–*trans* isomerisation, change in the hapticity of aromatic π -ligands to the metal in various sandwich and half-sandwich structures and metal migration in complexes with polydentate aromatic ligands.

The first example of electrochemically activated *cis*–*trans* isomerisation was described by Rieke *et al.*³⁵ The reaction follows the scheme



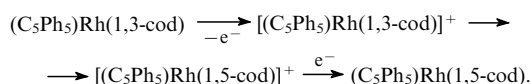
Since then, numerous examples of both cathodically and anodically activated *cis*–*trans* isomerisations have been reported.²⁷ In particular, the rate constants for anodic isomerisation of the thiolate isocyanate complexes *cis*– $[\text{M}(\text{SC}_6\text{H}_2\text{Pr}_3\text{-2,4,6})_2(\text{NCR})_4]$ ($\text{M} = \text{Mo}, \text{W}; \text{R} = \text{Me}, \text{Bu}^+$) have been calculated from the data of cyclic voltammetry.³⁶

Isomerisation can be accompanied by a change in the type of metal bonding to the ligand: the terminal ligand passes to a bridging position or *vice versa*. For example, the 48-electron cluster $\text{Cp}^*\text{IrCp}_2\text{Co}_2(\text{CO})_3$ ($\text{Cp}^* = \text{C}_5\text{Me}_5$) can exist as two isomers, one containing a terminal and two bridging carbonyl groups (A) and one with three bridging CO ligands (B), the second isomer being thermodynamically more stable.



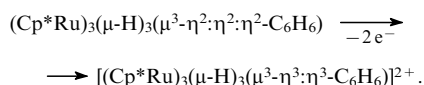
The rate of isomerisation depends appreciably on the number of electrons in the cluster³⁷ and varies in the following sequence: $48e \ll 49e < 47e$ (the ratio of the corresponding rate constants is 1 : 104 : 108). Thus, anodic activation is the most efficient.

Anodically activated isomerisation of diene ligands, for example, cyclooctadiene (cod), is known.³⁸



The trimetallic carbonyl clusters $\text{M}_3(\text{CO})_7(\text{dppm})(\text{tolan})$ ($\text{M} = \text{Os}, \text{Ru}$; dppm is diphenylphosphinomethane; tolan is diphenylacetylene) can also exist as two isomers which differ in the position of the alkyne ligand with respect to the triangle formed by the metal atoms.³⁹ The interconversion of the two isomers can be performed through electrochemical redox isomerisation because one of them is more stable in the reduced form and the other one, in the oxidised form.

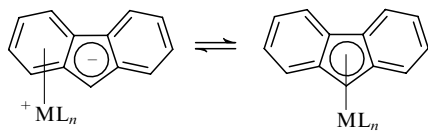
Numerous examples of the change in the type of hapticity of the π -ligand to the metal atom induced by electrochemical electron transfer are known. For example, two-electron oxidation of a trinuclear ruthenium complex induces haptotropic isomerisation giving rise to an unusual μ^3 - η^3 : η^3 -coordination of the benzene ring.^{40, 41}



The structure of the resulting complex was confirmed by X-ray diffraction data.

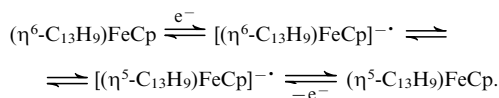
The change in the hapticity upon oxidative or reductive electrochemical activation has also been reported for indenyl, cyclopentadienyl and some other aromatic ligands⁴¹ (see also the review²⁶ and references therein).

Of special interest are redox-induced reactions of complexes with polydentate ligands having, at least, two possible sites of coordination to the metal. In this case, redox switching of the metal from one coordination site to the other has been observed.²⁶



$\text{ML}_n = \text{FeCp}, \text{FeCp}^*, \text{Mn}(\text{CO})_3, \text{Cr}(\text{CO})_3$.

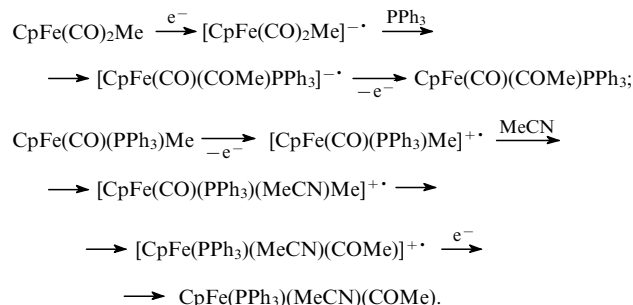
The ring–ring haptotropic isomerisation of 18-electron fluorenyl complexes with the d^6 metal configuration proceeds very slowly even at high temperatures, and the equilibrium is shifted towards the η^5 -isomer. In the case of 19-electron complexes, isomerisation rapidly takes place at -80°C , the equilibrium being shifted towards the η^6 -isomer:



Detailed analysis of the mechanism of ring–ring haptotropic tautomerism and a survey of published examples of these processes have been reported.²⁶

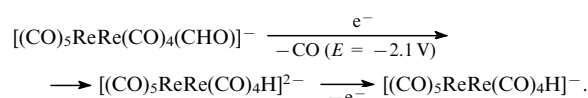
3. Insertion and extrusion

The electrochemical migrational insertion of a carbonyl group into the $\text{Fe}-\text{C}(sp^3)$ bond can be used to synthesise the corresponding acyl complexes; this reaction is carried out with either reductive⁴² or oxidative⁴³ activation.



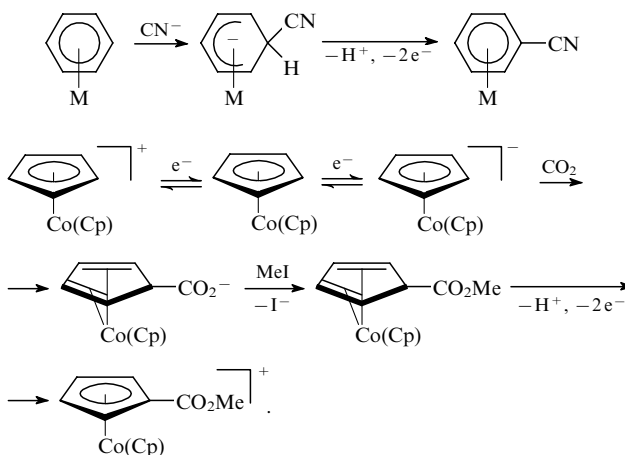
If both anodic and cathodic types of activation are possible, one should prefer the method for which the ratio of the currents of the inverse and forward electrochemical processes ($I_{\text{inv}}/I_{\text{for}}$) in the cyclic voltammogram of the product is closer to unity, *i.e.*, a classical electrochemically reversible process should be the method of choice.¹⁵

The Kochi cathodic activation has provided the possibility of the back reaction, *i.e.*, CO extrusion from formyl metal complexes.⁴⁴

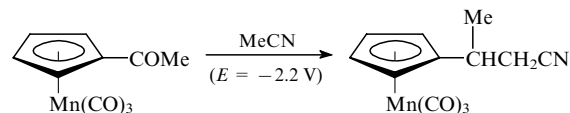


4. Electrochemically activated reactions in the ligand sphere of the metal

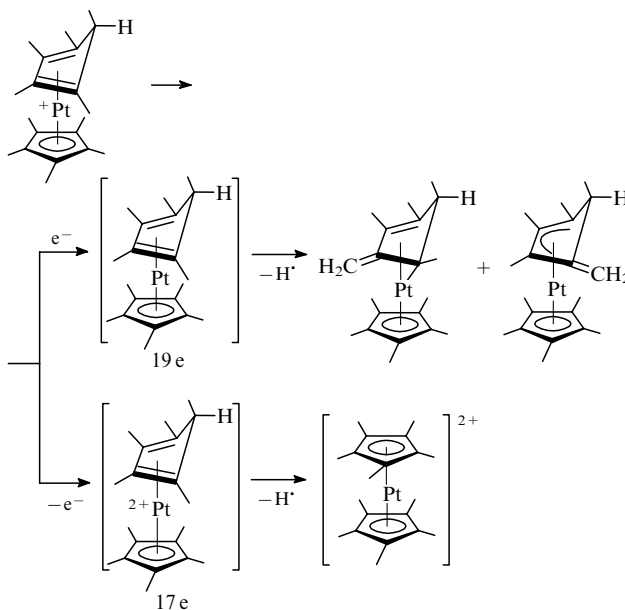
Transition metal complexes tend to undergo reactions accompanied by electrochemical activation of π -bonded ligands, resulting in ligand modification. The activation of C–H bonds followed by substitution in π -coordinated aromatic ligands provides an example.⁴⁵



Examples of reactions of this type can also be found in Walder's monograph.²⁸ A convenient method for building-up the hydrocarbon side chain during electrochemical reduction of acetyl derivatives of ferrocene, cymanthrene and benzenetricarbonylchromium has been proposed.⁴⁶

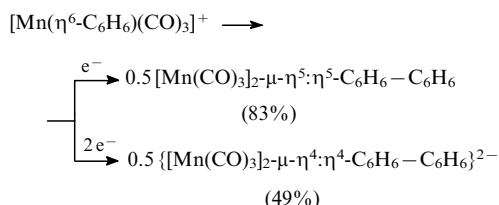


Of recent publications devoted to this topic, a study by Gusev *et al.*⁴⁷ deserves attention. The researchers identified the main regularities of the redox-induced activation of the C–H bonds in Pd and Pt η^4 -pentamethylcyclopentadiene complexes. Single-electron oxidation of these compounds proceeds selectively as homolysis of the C–H bond at the sp^3 -hybridised carbon atom of

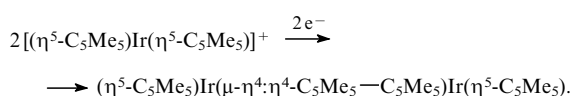


the Cp ring, while its single-electron reduction results in activation of the C–H bonds of the methyl groups.

Dimerisation of organometallic radicals according to the ‘ligand–ligand’ type can also be regarded as a reaction in the ligand sphere of the metal. Reductive dimerisation of the $[\text{Mn}(\eta^6\text{-C}_6\text{H}_6)(\text{CO})_3]^+$ cationic complex, resulting in the formation of a new C–C bond, is an example.⁴⁸

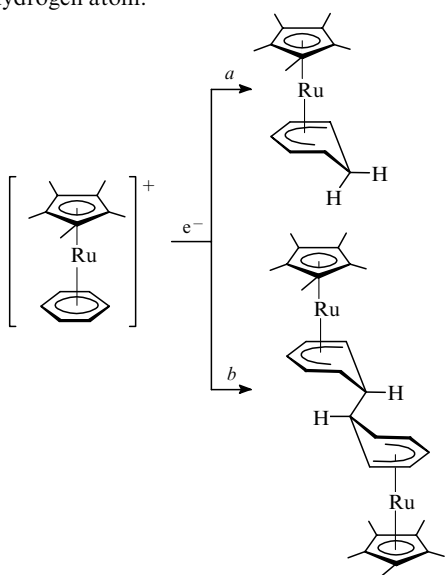


Dimerisation giving a new C–C bond in the ligand sphere of a metal was observed in a two-electron reduction of sandwich iridium complexes.⁴⁹



A similar approach has been used to prepare ‘molecular wires’ consisting of polyyne chains with ferrocenyl and ruthenocenyl groups at the ends.⁵⁰

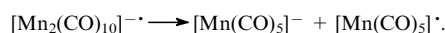
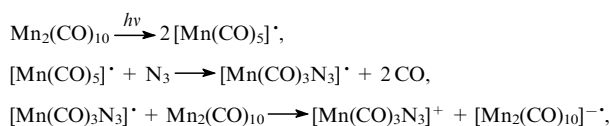
In solutions, 19-electron arenecyclopentadienylruthenium radicals either undergo dimerisation involving the six-membered ring (Scheme 2, pathway *b*) or capture a hydrogen atom from the reaction medium (Scheme 2, pathway *a*). It was found that a decrease in the electron-donating capacity of ligands or an increase in the ligand bulk enhances the stability of radicals and dimerisation becomes the preferential process over the addition of a hydrogen atom.^{51, 52}



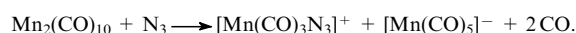
Scheme 2

5. Disproportionation

Disproportionation can also take place with intermediate formation of 19-electron complexes. For example, the $\text{Mn}_2(\text{CO})_{10}$ dimeric complex can disproportionate in the presence of highly electron-donating nitrogen-containing tridentate ligands. This reaction is subject to both electrochemical and photochemical initiation⁵³



The overall reaction is as follows:



III. Electrocatalysis: combination of catalysis by metal complexes with electrochemically induced electron transfer

An important application of the electrochemical electron transfer in reactions involving metal complexes and proceeding *via* organometallic intermediates is electrocatalysis. This line of research has been vigorously developing during the last 15 years and combines the advantages of catalysis by metal complexes and activation through electrochemical electron transfer. When the reaction is carried out at an electrode, electron transfer does not require additional oxidants or reducing agents, and the process is highly selective. Modification of the electrode surface by metal complexes (or the addition of complexes as mediators to the solution) provides the possibility of conducting electrochemically activated reaction at a substantially lower overpotential.

The processes that combine catalysis by metal complexes with electrochemical transfer of an electron can be conventionally classified into two types. One type includes so-called mediator processes in which a complex is first reversibly reduced (or oxidised) at an electrode and then it passes the electron to an organic substrate (S) (or withdraws the electron from it in the case of oxidative activation). In this case, the electron transfer usually follows an outer-sphere mechanism, *i.e.*, no bond between the metal complex and the organic substrate is formed. The mediator electron transfer yields an active form of the organic substrate (either reduced or oxidised form), which is then converted into product (P); as this takes place, the mediator (A) is regenerated.

Reduction	Oxidation
$A + e^- \longrightarrow A^{\bullet-}$	$A - e^- \longrightarrow A^{+\bullet}$
$A^{\bullet-} + S \longrightarrow A + S^{\bullet-}$	$A^{+\bullet} + S \longrightarrow A + S^{+\bullet}$
$S^{\bullet-} \longrightarrow P^{\bullet-}$	$S^{+\bullet} \longrightarrow P^{+\bullet}$
$P^{\bullet-} - e^- \longrightarrow P$	$P^{+\bullet} + e^- \longrightarrow P$

In the second type of process, an electron transfer from the catalyst (Cat) to the organic substrate is an inner-sphere process, *i.e.*, it proceeds *via* the formation of an intermediate activated complex, decomposition and subsequent transformations of which afford product P.

Reduction	Oxidation
$\text{Cat} + e^- \longrightarrow \text{Cat}^{\bullet-}$	$\text{Cat} - e^- \longrightarrow \text{Cat}^{+\bullet}$
$\text{Cat}^{\bullet-} + S \longrightarrow \text{CatS}^{\bullet-}$	$\text{Cat}^{+\bullet} + S \longrightarrow \text{CatS}^{+\bullet}$
$\text{CatS}^{\bullet-} \longrightarrow P^{\bullet-} + \text{Cat}$	$\text{CatS}^{+\bullet} \longrightarrow P^{+\bullet} + \text{Cat}$
$P^{\bullet-} - e^- \longrightarrow P$	$P^{+\bullet} + e^- \longrightarrow P$
or	or
$P^{\bullet-} + \text{Cat} \longrightarrow P + \text{Cat}^{\bullet-}$	$P^{+\bullet} + \text{Cat} \longrightarrow P + \text{Cat}^{+\bullet}$

An advantage of mediator processes⁵⁴ is a decrease in the kinetic barrier to electrochemical reactions; the potential approaches the thermodynamic value. This is valid for processes that include a fast chemical step, $S^{+(-)} \rightarrow P^{+(-)}$. The mediator participating in these reactions should satisfy the following conditions: (1) the ability to undergo reversible oxidation or reduction; (2) $|E_m| \ll |E_s|$ (where E_m and E_s are the potentials of the mediator and substrate, respectively), the optimal potential difference is usually 0.3–0.5 V; (3) structural correspondence between the mediator and the substrate to ensure the electron transfer. The

mediator can occur in the solution or, alternatively, be chemically bound to the electrode (chemically modified electrode).

The inner-sphere electron transfer has a number of advantages over the outer-sphere process.²⁷

1. The redox process does not depend on the potential difference between the mediator and the substrate; therefore, a much more pronounced decrease in the overpotential is possible.

2. The inner-sphere transfer is characterised by a lower activation barrier.

3. An outer-sphere process allows the transfer of only one electron, while in the case of the inner-sphere mechanism, transfer of two or more electrons is possible. (This is especially important for bioelectrocatalysis and for activation of small molecules.)

In real processes, the consumption of electricity is determined by the contributions of various competing reactions involving radical cations or radical anions derived from the catalyst. Moreover, apart from the classical cases in which an inner-sphere or outer-sphere mechanism of electron transfer is regarded as proven, there exist a large number of intermediate processes for which it is difficult to draw a conclusion about the nature of the transition state. In the case of metal complexes with an inner-sphere or a similar mechanism of electron transfer, the activated molecule enters the metal coordination sphere, which increases its reactivity.

Numerous examples of electrocatalytic processes involving transition metal complexes are known.^{55–61} The greatest number of studies have been devoted to the activation of small molecules and to various reactions of C–C bond formation (homo- and cross-coupling, carboxylation and carbonylation, the addition to multiple bonds).

1. Electrocatalytic reduction of small molecules

A series of reviews and original papers (see, for example, the studies^{22,56–61}) have been devoted to electrocatalytic reduction of nitrogen and its oxides, carbon oxides, and molecules or ions with triple bonds (acetylene, cyanide ion). A common feature of all the above compounds is that they are electrochemically inactive and contain very strong bonds that are fairly difficult to cleave. Therefore, activation of such molecules through introducing them into the metal coordination sphere followed (or preceded) by electrochemical electron transfer is the most promising way of involving these compounds in various chemical transformations. In addition, considerable attention to electrocatalytic processes with participation of metal complexes is inspired by the idea of utilisation of the enormous reserves of N₂, CO₂ and O₂ present in the biosphere as a cheap and readily available feedstock for various chemical transformations.

Since it is impossible to cover the tremendous number of publications devoted to various processes of this type, in this review, we consider only examples of electrocatalytic binding of CO₂. These data, first, provide an idea of the main principles and features of electrocatalytic reactions and, second, they are fairly important from the practical standpoint.

Direct electroreduction of CO₂ at a metallic (for example, mercury) cathode requires a high overpotential: $E_{\text{CO}_2/\text{CO}_2^-} = -2.21 \text{ V vs. a saturated calomel electrode (SCE) in DMF}$.⁶² Other metallic cathodes, for example, copper or gold ones, are able to reduce CO₂ in an aqueous solution at somewhat less cathodic potentials (–1.3 to –1.7 V vs. SCE), but these values are also too great for practical application of this process^{63,64} because water is also reduced at these potentials with hydrogen evolution. This could be avoided by using non-aqueous solvents;^{65–71} however, such a process is unfavourable due to a high energy expenditure and undesirable reduction of components present in the solution.

A lot of data on the use of transition metal complexes for the electrocatalytic reduction of CO₂ can be found in the literature (see, for example, studies^{7,58,72,73}). As a rule, these are complexes with nitrogen-containing macrocyclic ligands such as porphyrins and their analogues, well-known as biocatalysts. Synthetic metal

complexes with nitrogen-containing macrocyclic ligands, for example, phthalocyanines (Pc) or 1,4,8,11-tetraazacyclotetradecane (cyclam) derivatives, are often not inferior to enzymes in their catalytic activity.

Metal phthalocyanines^{3,8–11,15,74–84} and metal porphyrins,^{2,12,13,19,58,73,85–87} Ni(II) complexes with cyclam derivatives,^{88–94} bis- and polypyridine complexes of Rh(II),⁹⁵ Re(I),⁹⁶ Cu(I),⁹⁷ Co(II), Fe(II) and Ni(II),^{76,84,98–101} iron and cobalt complexes with the 4,5-dihydroxybenzene-1,3-disulfonate and 2-hydroxy-1-nitrosonaphthalene-3,6-disulfonate ligands^{102,103} and other complexes can serve as catalysts for CO₂ reduction.

An important advantage of using metal complexes as catalysts for the reduction of CO₂ is the possibility of changing their reactivity by modification of the macrocyclic ligand either by introducing electron-donating or -withdrawing substituents or by replacing the central metal atom.¹⁰⁴ Indeed, a Ni(II) complex with a cyclam analogue, 3,10-dimethyl-1,3,5,8,10,12-hexaazacyclotetradecane, exhibits a much higher catalytic activity than the unsubstituted Ni(II)(cyclam) complex.¹⁰⁵ Surprisingly, the introduction of σ -acceptor substituents, for example, fluorine, into the nitrogen-containing ring also increases the catalytic activity and the selectivity of CO formation (with respect to hydrogen evolution). The Ni(II) complex with 3,3,10,10-tetrafluorocyclam proved to be the most efficient. Further increase in the number of fluorine atoms at the macrocycle leads to a lower catalytic activity.¹⁰⁶

The influence of the nature of the central metal atom on the catalytic efficiency of CO₂ electroreduction has been studied. In the case of metal complexes with *meso*-tetraphenylporphyrin, the highest current yield of CO was observed for Co, Fe and Zn complexes, while the catalytic activity of Ni, Cu, Mg and Mn compounds was fairly low.¹⁹

A wide range of monophthalocyanine complexes of various metals have been tested in the electrocatalytic reduction of CO₂ at a gas-diffusion electrode in an aqueous solution.^{3,15} The electroreduction of carbon dioxide gave CO, HCOOH and CH₄, the ratios and the current yields of which depended appreciably on the properties of the central metal atom in the phthalocyanine complex. With Group VIIIA transition metals such as Co, Ni, Fe and Pd, the reaction usually gives CO as the major product. The electrolysis of CO₂ in the presence of Sn, Pb, In and Al phthalocyanine complexes affords mainly HCOOH, and in the case of Zn phthalocyanine, approximately equal amounts of HCOOH and CO are formed. Under the action of phthalocyanine complexes of Group IIIB and IVB elements, In and Sn, formic acid is produced with the highest selectivity, and in the case of Cu, Ga and Ti, methane is formed, although in a low yield. Metal-free phthalocyanine proved to be almost inefficient in the reduction of CO₂. Thus, coordination of CO₂ to the metal atom in the complex plays an important role. The data on the use of metal phthalocyanines in reactions of CO₂ reduction (see Refs 3 and 15) are listed in Table 1.

It is of interest that the cathodic electrocatalytic activity of cobalt complexes with macrocyclic ligands increases if the Co atom is bound to the axial electron-donating ligand, for example, pyridine or imidazole.^{107–109} Thus CO₂ electroreduction in water at a glass-carbon electrode coated by Co tetraphenylporphyrin with the axial pyridine ligand occurs with a high selectivity.¹⁰⁷

Recently,¹¹⁰ investigations of diphtalocyanine complexes as catalysts for carbon dioxide electroreduction in protic media have been started. The major reaction products were CO and HCOOH (or methyl formate if electroreduction is carried out in methanol).

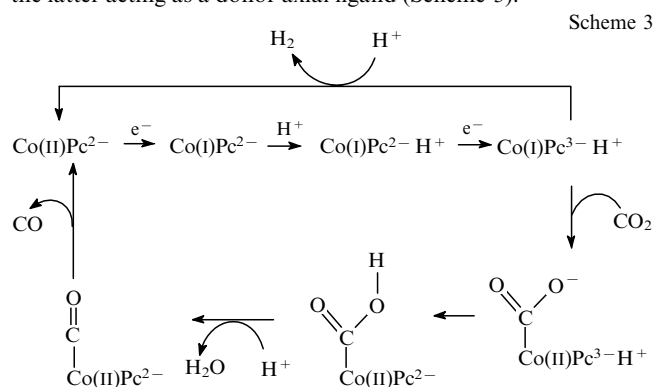
It is worthy of note that the formation of a metal–CO₂ complex is postulated as the key step in almost every study devoted to the catalytic fixing of CO₂ by transition metal complexes.^{3,9,109–114} In most cases, this is supported only by the data of IR or NMR spectroscopy because, first, the lifetime of these intermediates is short and, second, the presence of solvent molecules, also capable of coordination, hampers detailed analysis of the structure of the complex.

Table 1. Results of cathodic reduction of CO₂ in water in the presence of phthalocyanine complexes of transition metals (PcM).^{3,15}

M	<i>E</i> / V (vs. SCE)	Current efficiency (%)			
		CO	CH ₄	HCOOH	H ₂
Ti	−1.98	15.8	28.1	5.0	40.4
In	−1.96	10.0	0.8	26.8	47.7
Zn	−1.94	33.0	0	27.0	40.0
Sn	−1.93	10.0	0	71.0	20.0
Mn	−1.90	7.0	2.0	3.0	88.0
Al	−1.90	6.2	0.2	16.9	69.9
Cd	−1.84	46.0	4.2	4.8	45.5
Ni	−1.75	100.0	1.3	0.4	2.0
Mo	−1.72	0	0	2.0	98.0
Cr	−1.68	5.0	0	5.0	90.2
Pb	−1.64	5.0	0	65.0	30.0
Cu	−1.63	14.0	28.0	3.5	49.2
Pt	−1.59	4.0	0	0	95.6
Pd	−1.50	81.4	0	1.0	9.5
Co	−1.30	98.0	0	0.4	3.0
Fe	−1.21	47.0	0.3	5.0	47.3

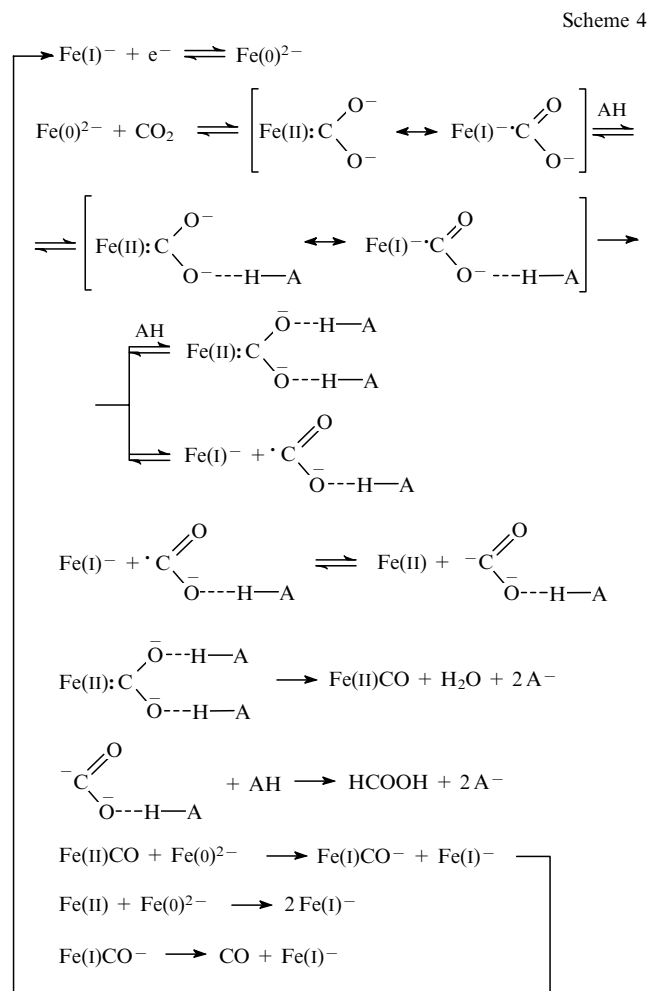
A number of calculations for ligand-free complexes MCO₂ (M is an alkali or transition metal) have been carried out (see Ref. 115 and references therein). The first systematic study into the geometry, configurational interactions and electron density distribution for a wide range of MCO₂ complexes (where M is a metal of the 3-rd period: Ca–Mn, Cu, Zn) showed the occurrence of electron transfer from the metal atom to the CO₂ group, the electron density being concentrated on the carbon atom and the M–C bond being nearly ionic. The electron transfer from the metal to CO₂ is accompanied by redistribution of electrons in the internal levels and, in particular, results in a higher electron density on the oxygen atom. Thus, coordination to the metal increased the basicity of the oxygen atoms in the CO₂ group.

Mechanisms for the electrocatalytic reduction of CO₂ have been proposed in a few publications.^{79,109} These studies deal with the reduction of CO₂ in an aqueous solution at a graphite electrode coated by PcCo bound to poly-4-vinylpyridine (PVP), the latter acting as a donor axial ligand (Scheme 3).

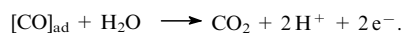


It can be seen from Scheme 3 that the catalytic process starts only in the second step of PcCo reduction because the first reduction is followed by the fast addition of H⁺ to one of the peripheral nitrogens of the phthalocyanine ring, and only the second step gives an active species capable of reducing both H⁺ and CO₂ to H₂ and CO, respectively. Nevertheless, researchers^{79,83} who studied electrocatalysis by pure PcCo adsorbed on graphite, were unable to observe directly the PcCo–CO₂ adduct.

An interesting sequence of steps taking place during CO₂ reduction catalysed by iron porphyrins has been proposed and confirmed by kinetic data.^{112,113} The key step of this process is the formation of the Fe–C bond (Scheme 4, the porphyrin ligands are omitted, AH is a Brønsted acid).



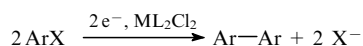
It has been shown¹¹⁶ that a rotating ring–disk electrode, in which the disk electrode is represented by graphite coated by cobalt(II) *N,N',N'',N'''*-tetramethyltetra-3,4-pyridoporphyrine and protected by a polymeric film (Nafion) and the ring electrode is represented by platinum, can be used for quantitative determination of CO₂ in aqueous solutions (the concentration range is 10^{−4}–3.2 × 10^{−2} mol litre^{−1}). The method is based on the fact that CO₂ is reduced quantitatively at the disk to give CO (at −1.15 V vs. SCE), while the latter is detected on the basis of the typical oxidation peak at the platinum ring (0.4 V vs. SCE):



2. Electroreductive coupling, addition, carboxylation and carbonylation

Electroreductive coupling reactions are extensively used in synthesis. Phosphine, tetraazamacrocyclic and polypyridyl complexes of transition metals (mainly, Ni, Pd and Pt) are used most often as catalysts. Electrochemical electron transfer can play different roles in these reactions — an electron can participate directly in the catalytic cycle, or/and labile complexes of transition metals in low oxidation states can be generated electrochemically and participate in the reaction *in situ*.

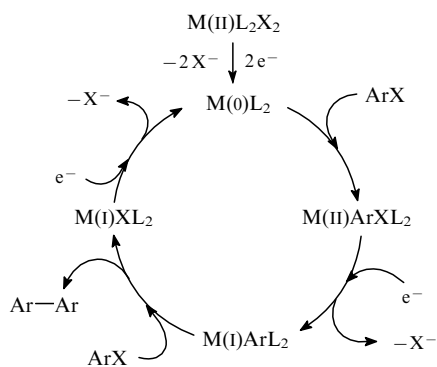
The general scheme of the electroreductive coupling can be represented in the following way:^{27,55,117,118}



X = I, Br, Cl, OTf; M = Ni, Pd;

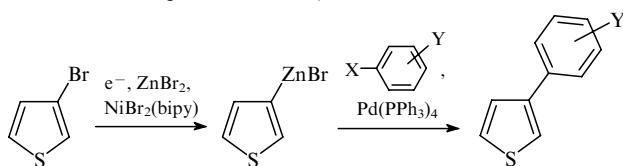
L = PPh₃, dppe, bipyridyl (bipy), *etc.*

The activity of Ni(0) and Pd(0) complexes in coupling reactions of organohalogen compounds was shown^{119, 120} to depend on a number of factors: the size of the electrochemical gap, the strength of the metal–ligand bond, and electronic and steric effects of the ligands. The first step of the catalytic cycle is the oxidative addition of an organic substrate to a zerovalent metal complex, resulting in the formation of a σ -arylnickel or σ -arylpalladium intermediate.



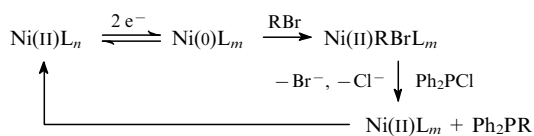
M = Ni, Pd.

Numerous reactions of this type have now been described (see the monograph²⁷ and the papers^{55, 118, 121, 122}). Among these, electrochemical synthesis of substituted 3-phenylthiophenes is noteworthy.¹²³ The reduction of a mixture of 3-bromothiophene and ZnBr₂ in the presence of the bipyridine nickel complex gives rise to 3-thienylzinc bromide, which enters into cross-coupling reactions with various aryl halides (PhI, *p*-NCC₆H₄Br, *o*-MeOC₆H₄Br, *p*-MeOC₆H₄Br).



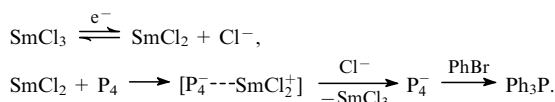
The synthesis of optically active 1,3-dienes containing chiral substituents from alkenylstannanes by electrooxidation and homocoupling with participation of CuCl₂ has been reported.¹²⁴

Phosphine and bipyridine Ni complexes serve as the catalysts of the electroreductive coupling of aryl and hetaryl halides with mono- and dichlorophosphines, which allows the synthesis of tertiary phosphines in high yields.^{125, 126}

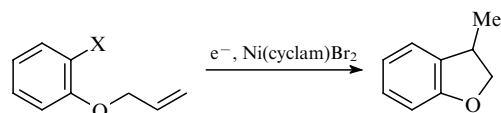


L = PPh₃.

Under the action of electrochemically generated Ni(0) or Sm(II) compounds, arylation of white phosphorus takes place.¹²⁷

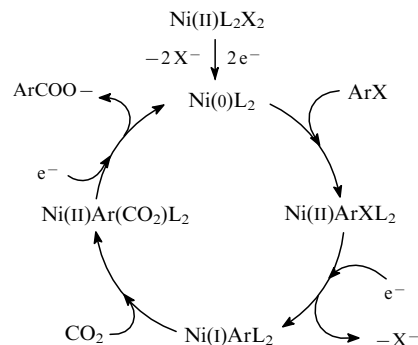


The intramolecular reductive coupling of allyl 2-halophenyl ethers catalysed by the Ni(cyclam)Br₂ complex provides the preparation of 3-methyldihydrobenzofuran in 90% yield.¹²⁸

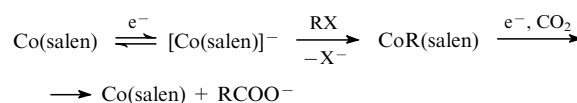


X = Cl, Br, I.

If CO₂ or CO is introduced in the reaction mixture containing an organic halide and the electrochemically generated Ni(0) complex, the reaction gives carboxylic acids or carbonyl compounds, respectively, instead of the homocoupling products.

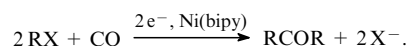


Carbon dioxide adds to Ni(I)ArL₂ approximately twice as fast as ArX; therefore, the side reaction giving biaryls scarcely takes place.^{129–133} In the presence of CO₂ and catalytic amounts of electrochemically generated Pd(0) complex, aryl and vinyl triflates are converted into aromatic and α,β -unsaturated carboxylic acids, respectively.¹³⁴ Carboxylic acids can also be prepared from allyl and benzyl halides using Co complexes as catalysts.¹³⁵

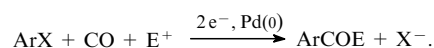


R = PhCH₂, Ph(Me)CH, MeCH = CHCH₂;
salen is bis(salicylidene)ethylenediamine.

Recently,¹³⁶ electrosynthesis of ketones from organic halides and CO catalysed by Ni(0) bipyridine complex was carried out. Study of the process mechanism showed that the reaction involves the intermediate formation of the acyl nickel complex.



The use of electrochemical electron transfer makes it possible to 'invert' the polarity of aryl halides ArCOX and introduce them into reactions with electrophiles.¹³⁷



The process includes the formation of the PdArX complex and the subsequent CO insertion, resulting in the intermediate PdArCOX complex, which is reduced more readily than the initial aryl halides; after activation by electrochemical electron transfer, this species can react with electrophiles, for example, with H⁺.

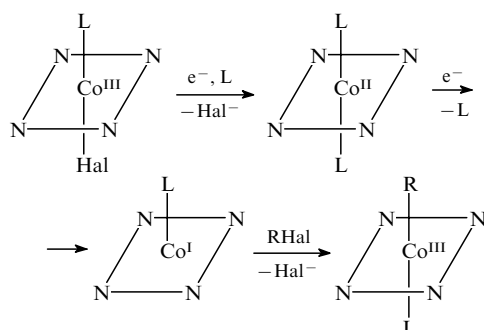
Electrocatalytic arylation of alkenes is documented. Although the process mechanism is not entirely clear, it is assumed that coordinatively unsaturated Ni(0) complexes serve as the basis for the spatial proximity of halobenzenes and alkenes; the subsequent treatment with a base yields arylalkenes.¹³⁸

IV. The formation and cleavage of carbon–metal σ -bonds

Reactions giving carbon–metal σ -bonds are very important from the theoretical and practical standpoints because they allow the synthesis of new organometallic compounds with various useful properties. We shall consider two main types of these reactions, namely, electrochemical alkylation and electrochemical arylation of metal-containing nucleophiles.

1. Electrochemical alkylation

The methods used most widely for the introduction of alkyl groups are based on S_N2 reactions of various organic compounds with metal-containing nucleophiles. The latter can be synthesised conveniently by an electrochemical procedure using reductive activation, which yields metal complexes in low oxidation states. This method was used to prepare the alkyl derivatives of Co,¹³⁹ Fe¹⁴⁰ and Rh porphyrins^{141,142} as well as complexes with other nitrogen-containing macrocyclic ligands, in particular, dimethylglyoximate¹⁴³ and phthalocyanine.¹⁴⁴



A comparative study of alkylation of electrochemically generated nucleophilic Co, Rh, Ir, Ni and Pd complexes with various nitrogen- and sulfur-containing ligands on treatment with butyl bromide was carried out.¹⁴³ Electrochemically activated reactions with transfer of the methyl group from dimethylglyoximate complexes of methylcobalt onto Au(I)¹⁴⁵ and Ni(I)¹⁴⁶ complexes and onto mercury¹⁴⁷ and germanium salts¹⁴⁸ are also known.

2. Electrochemical arylation and vinylation

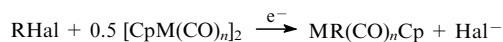
Using the approach described above, only alkyl fragments can be introduced into the metal coordination sphere. The introduction of aryl and vinyl substituents requires not only electrochemical activation of a metal-containing nucleophile but also an additional activation of the $C(sp^2)$ –Hal bond ($S_{RN}1$ reactions). Theoretical investigation into the electrochemically activated $S_{RN}1$ type reactions was started by Saveant's group.^{12,149–157} The stabilities of the radical anions formed initially, the relative rates of each step of the $S_{RN}1$ process, the most important competing reactions and the types of chain termination have been studied. A number of procedures for preparative electrosynthesis of various organic compounds underlain by $S_{RN}1$ processes have been developed.^{153,158–160}

However, until recently, the authors of only two studies^{161,162} have described examples of electrochemically activated $S_{RN}1$ reactions involving organometallic compounds, namely, the synthesis of aryl and vinyl derivatives of iron porphyrin¹⁶¹ and the reactions of the $[CpM(CO)_3]^-$ anions ($M = Mo, W$) with iodonitrobenzene.¹⁶²

Apparently, this is due to the fact that the double electrochemical activation of both reagents requires that a specified potential be strictly maintained during the reaction. This creates some difficulties for practical implementation of these processes because the reaction product can be subsequently destroyed (compounds containing a carbon–metal σ -bond are usually oxidised and reduced irreversibly with cleavage of this bond). If

the product is reduced at more cathodic potentials than the reaction begins (the activation potential of the initial reactants), the product destruction at the electrode can be avoided.¹⁶¹ Systematic investigations of electrochemically activated arylation in which the reaction product is irreversibly reduced at potentials less cathodic than the activation potential of the reactants have been started^{163–167} in relation to electrochemical arylation and vinylation of anionic iron, molybdenum and tungsten carbonyl complexes.

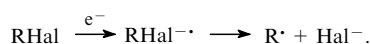
The general scheme of the reaction is as follows:



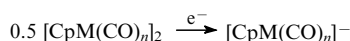
$M = Fe, Mo, W$.

Electrochemical electron transfer activates the organic halide by transforming it into a reactive radical and leads to generation of metal-containing nucleophiles as a result of cleavage of the $M-M$ bond in the dimer. The active species that arise react with each other *in situ* to give a σ -organometallic compound.

Activation of the first reactant

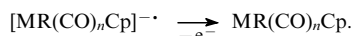
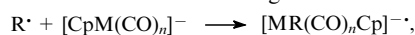


Activation of the second reactant



$M = Fe, n = 2; M = Mo, W, n = 3$.

The formation of the σ -organometallic compound



These reactions have been carried out for both aryl halides (p - XC_6H_4Hal : $X = H, Me, Cl, I, COMe, CN, NO_2$; $Hal = I, Br$; C_6F_5X : $X = H, F, Cl, Br$; C_5F_5N) and vinyl halides (Z -, E - $PhCH=CXHal$: $X = H, Ph$; $Hal = I, Br$; Z -, E - $PhCF=CFHal$, Z -, E - $Bu^tCF=CFHal$: $Hal = F, Cl, Br$).

Direct electrochemical activation of this reaction is possible only for those aryl halides that are reduced more readily than the reaction product, a cyclopentadienyldicarbonyliron derivative. This is due to the fact that electrochemical reduction of σ -organometallic compounds of this type is irreversible and is accompanied by $C-M$ bond cleavage. For any other compound, the product resulting from electrochemical activation decomposes immediately at the electrode. It can be seen from Fig. 2 that the region of

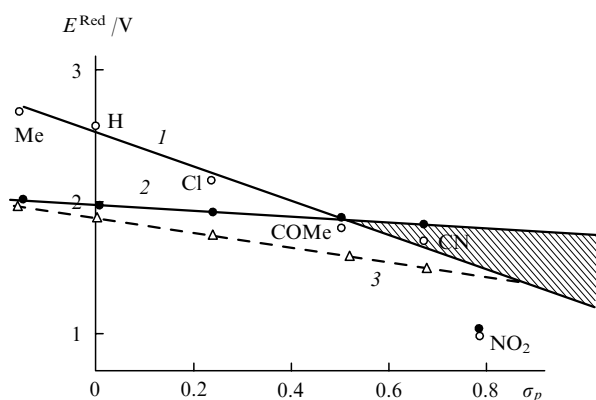


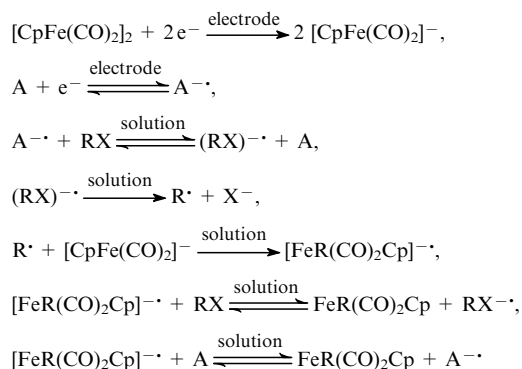
Figure 2. Reduction potentials (E^{Red}) (Pt cathode) of aryl iodides p - IC_6H_4X (1) and the products p - $CpFe(CO)_2C_6H_4X$ (2) vs. Hammett σ_p -constants of substituents. Reduction potentials of initial aryl iodides at a Hg electrode (3). The region of possible electrochemical activation of the reaction is hatched.¹⁶³

possible electrochemical activation of the reaction is rather narrow. It can be extended by decreasing the potential of the onset of the reaction, *i.e.*, the potential at which active species are generated.

Three approaches have been proposed to solve this problem. One approach includes fast potential cycling toward a less cathodic region and back; thus, at least some of the product formed at the electrode has time to diffuse into the solution.¹⁶⁴

According to the second approach,¹⁶³ the electrode material is replaced (Hg is used instead of Pt); this allows a significant decrease in the potential at which the reaction starts because this facilitates the reduction of aryl and vinyl halides (see Fig. 2, dashed line). In this case, direct electrochemical activation can be used for iodobenzene, *p*-bromobenzonitrile and other aryl halides (see Fig. 2), the reduction of which at mercury falls into the required potential range, while electrochemical activation of these compounds at platinum is impossible. For vinyl halides studied by Magdesieva *et al.*,¹⁶³ except for β -iodostyrene, the mere replacement of the electrode material does not suffice for electrochemical activation of the nucleophilic vinyl substitution because σ -vinyl derivatives of η^5 -cyclopentadienyldicarbonyliron are reduced more readily than the initial substrate even at mercury.

The third approach¹⁶⁵ implies the use of homogeneous redox catalysis in which a decrease (in magnitude) in the potential of the reaction onset is attained by adding an appropriate reversible $A/A^{\cdot-}$ redox pair, which acts as a mediator[†] by carrying an electron from the electrode to the aryl or vinyl halide.



R is aryl, vinyl.

Owing to the homogeneous redox catalysis, these reactions can be carried out for such substrates for which the replacement of electrode material alone does not result in a positive value of

$$\Delta E = E_{\text{RHal}}^{\text{Red}} - E_{\text{FeR}(\text{CO})_2\text{Cp}}^{\text{Red}}$$

(for example, *p*-iodotoluene, bromostyrenes and *Z*-bromostilbene). In addition, by using this approach, one can increase the yield of nucleophilic substitution products for substrates that formally fall into the region of possible reaction activation upon the replacement of the electrode material but still have too small ΔE values, for example, for iodobenzene (Table 2).

Thus, Magdesieva *et al.*¹⁶⁵ were the first to show experimentally that the use of homogeneous redox catalysis allows the electrochemically activated reactions of organometallic compounds to be performed under conditions where the products are redox-unstable upon direct electrochemical activation. This implies selection of a mediator whose activities with respect to the reactant and the product are appreciably different. This has markedly extended the scope of applicability of electrochemical activation, first of all, for the synthesis of σ -organometallic compounds.

Table 2. Yields of products of direct and mediator preparative electrolysis^a of aryl and vinyl halides in the presence of $[\text{CpFe}(\text{CO})_2]_2$.^{163–165}

Substrate	Potential of electrolysis /V	Product	Preparative yield (%)
<i>p</i> -MeC ₆ H ₄ I	–1.95	<i>p</i> -MeC ₆ H ₄ Fp ^b	0–1
<i>p</i> -MeC ₆ H ₄ I	cycling from –1.95 to –1.55	<i>p</i> -MeC ₆ H ₄ Fp	2–3
<i>p</i> -MeC ₆ H ₄ I in the presence of <i>o</i> -NCC ₆ H ₄ CN ^c	–1.80	<i>p</i> -MeC ₆ H ₄ Fp	43.0
PhI	–1.90	C ₆ H ₅ Fp	5.0
PhI	cycling from –1.90 to –1.55	C ₆ H ₅ Fp	15.0
PhI in the presence of <i>o</i> -NCC ₆ H ₄ CN ^c	–1.75	C ₆ H ₅ Fp	45.0
PhCH=CHI	–1.55	PhCH=CHFp	12.5
PhCH=CHI	cycling from –1.90 to –1.55	PhCH=CHFp	19.0
PhCH=CHI in the presence of <i>o</i> -NCC ₆ H ₄ CN ^c	–1.75	PhCH=CHFp	28.0

^a Electrolysis conditions: Hg, Bu₄ⁿNBF₄ (0.25 mol litre^{–1}), MeCN, Ag⁺/AgCl/KCl, 20 °C. ^b Fp = CpFe(CO)₂. ^c The phthalodinitrile concentration is 5×10^{-4} mol litre^{–1}.

This approach has permitted the preparative synthesis of about twenty aryl and vinyl derivatives of CpFe(CO)₂ containing the C(sp²)–metal σ -bond, particularly high product yields being attained when using homogeneous redox catalysis.

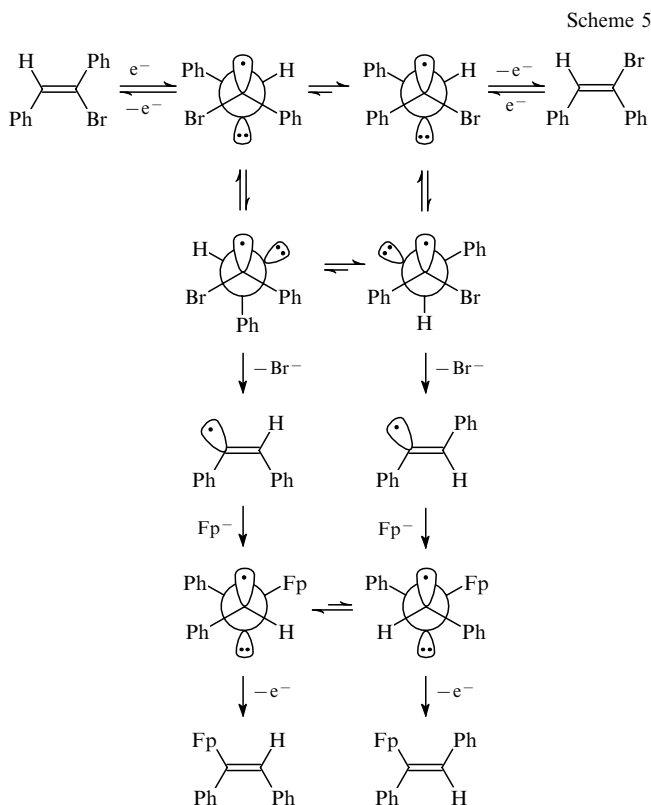
Study of the stereochemistry of the reaction products (Table 3) showed that, irrespective of the configuration of the initial vinyl halide, the product with the *trans*-arrangement of the organometallic group and the organic group always predominates. This is due to the fact that generation of the radical anion is accompanied by isomerisation to give the most stable configuration (Scheme 5).

Table 3. Results of preparative electrolysis^a of vinyl halides RCF=CFX in the presence of the $[\text{CpFe}(\text{CO})_2]_2$ binuclear complex.¹⁶⁷

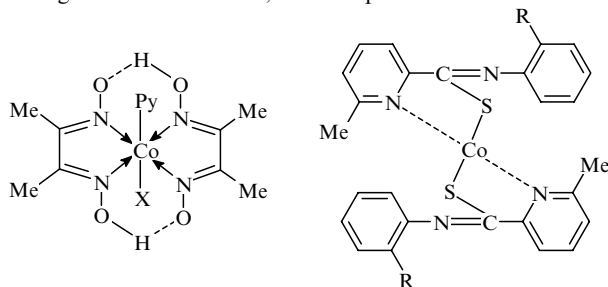
R	X	Substrate configuration	Nucleophilic substitution product	Product configuration	Preparative yield (%)
(CF ₃) ₃ C	F		(CF ₃) ₃ CCF=CFFp	<i>Z</i>	40
				<i>E</i>	traces
(CF ₃) ₃ C	Cl	<i>Z</i>	(CF ₃) ₃ CCF=CFFp	<i>Z</i>	15
				<i>E</i>	traces
(CF ₃) ₃ C	Br	<i>Z</i>	(CF ₃) ₃ CCF=CFFp	<i>Z</i>	14
				<i>E</i>	traces
Ph	F		PhCF=CFFp	<i>Z</i>	42
				<i>E</i>	5
Ph	Cl	<i>Z</i>	PhCF=CFFp	<i>Z</i>	32
				<i>E</i>	3
Ph	Cl	<i>E</i>	PhCF=CFFp	<i>Z</i>	10
				<i>E</i>	5

^a Electrolysis conditions: Hg, Bu₄ⁿNBF₄ (0.25 mol litre^{–1}), MeCN, Ag⁺/AgCl/KCl, 20 °C.

[†] Study of a wide range of conceivable mediators showed that phthalodinitrile is the compound of choice for this reaction.¹⁶⁵



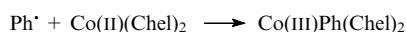
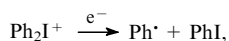
Using electrochemical activation, it is possible to arylate¹⁶⁸ Co(II) and Co(III) complexes with chelating ligands containing nitrogen and sulfur atoms, for example:



X = Py, Hal.

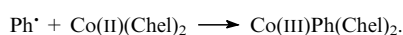
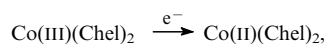
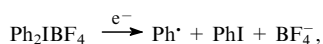
R = Me, OMe.

The essence of the 'iodonium method' proposed in one study¹⁶⁸ is to use diphenyliodonium salts including those containing various substituents in the benzene ring as arylating agents.



Chel is a chelating ligand.

Not only Co(II) complexes but also Co(III) complexes, which are normally more stable and more readily available, can be introduced in the arylation. However, in this case, electrochemical activation of both reactants is needed.

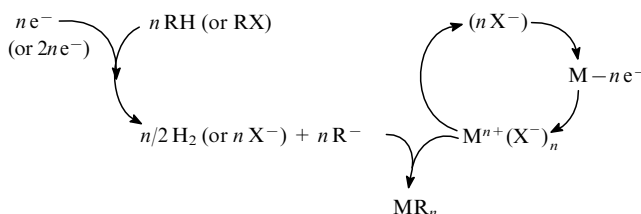


It is noteworthy that the use of diphenyliodonium salts as arylating agents has obvious advantages over halobenzenes used

traditionally in $\text{S}_{\text{RN}}1$ reactions, because the former provide generation of phenyl radicals upon electrochemical activation at much lower cathodic overpotentials.

3. Electrosynthesis with sacrificial electrodes

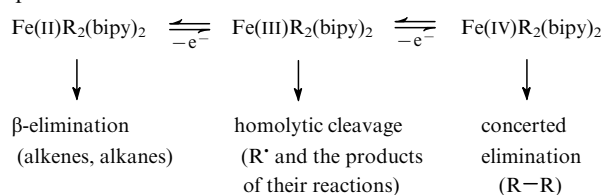
Yet another widely used electrochemical approach to the synthesis of organometallic compounds is the use of sacrificial (this is the name for soluble) anodes. In an undivided cell, metal dissolution takes place at the anode and the organic substrate is reduced at the cathode to give anions which should be stable enough to avoid side reactions with the solvent.^{28, 169–171}



Examples of syntheses with anodes made of Ti, Zr, Hf, V, Cr, Mn, Fe, Co, Ni, Cu, Al, Pb, Sn and various ligands are documented.^{172–175}

Kharisov *et al.*¹⁷⁶ have compared the traditional chemical and electrochemical methods for the synthesis of transition metal complexes with nitrogen-containing ligands. An advantage ensured by the use of sacrificial anodes is the possibility of preparing Cu, Ni, Co, Pd, Zn and Cd complexes in one step in high yields.

Electrochemical cleavage of the carbon–metal σ -bond gives in most cases organic radicals the further transformations of which are determined¹⁷⁷ by the applied potential and the solution composition.



V. Electrochemically activated reactions involving 'electron sponges'

When considering electrochemical activation of reactions involving organometallic compounds, two types of processes can be distinguished:

(1) electrochemical activation of various types of bonds (C–Hal, C–M, M–Hal, M–M, *etc.*), resulting in their cleavage to give highly reactive species (cations, anions, radicals);

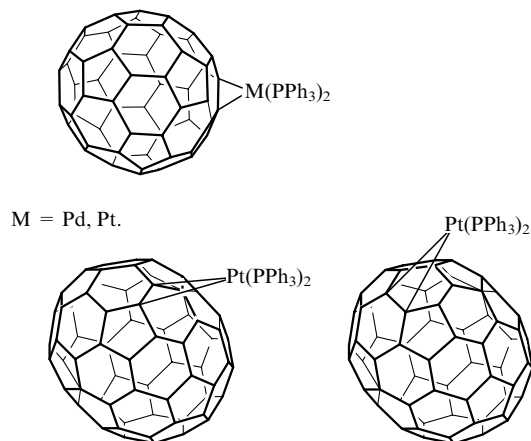
(2) activation through transfer of one or several electrons accompanied by the change in the electronic structure and, hence, properties of the molecule, but involving no bond cleavage.

In the reactions considered above, activation of the former type takes place. Now we shall give some examples of the latter type of processes.

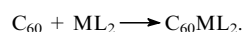
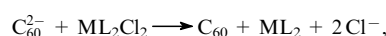
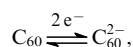
Systems capable of reversible stepwise addition or release of several (three or more) electrons are referred to as 'electron sponges'. The transfer of an electron onto such systems results in activation of the whole molecule and in the change in its properties (for example, catalytic, spectroscopic and other properties) but does not induce cleavage of any bond. A fairly large number of such systems have been reported;^{178, 179} however, here we restrict ourselves to consideration of two of them, namely, phthalocyanine complexes and fullerene derivatives, for which electrochemically activated reactions involving organometallic compounds are known.

1. Electrosynthesis of exohedral metal complexes of C_{60} and C_{70}

A unique feature of fullerenes and their derivatives is the capability of reversible stepwise addition of up to six electrons, which makes them fairly promising participants of redox processes. Recently,^{180, 181} we proposed an electrochemical method for the synthesis of exohedral complexes of C_{60} and C_{70} , namely, $C_{60}ML_2$ [$M = Pd, Pt$; $L_2 = (Ph_3P)_2$, bis(diphenylphosphino)ferrocene (dppf) or diphenylphosphinocymanthrene] and $C_{70}Pt(PPh_3)_2$ (a mixture of two isomers) from simple and stable inorganic salts (MCl_2) or complexes of platinum group metals (ML_2Cl_2).

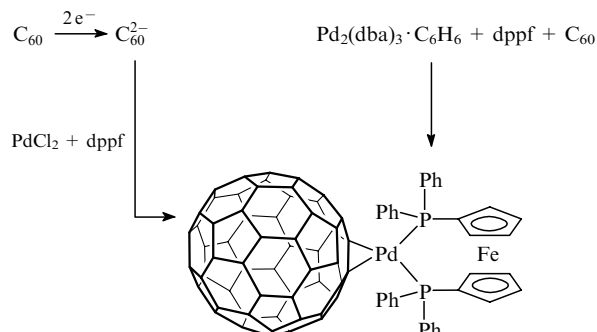


Reactive complexes of zerovalent metals sensitive to atmospheric oxygen can be generated *in situ* using electrochemically generated C_{60}^{2-} or C_{70}^{2-} dianions as reducing agents. In this case, fullerene plays a dual role acting simultaneously as an electron transporter (mediator) and as one of structure-forming reagents.

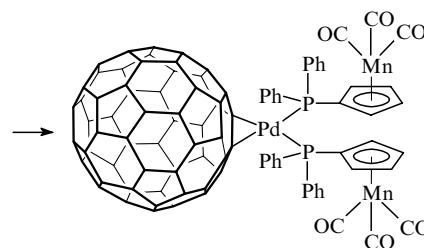
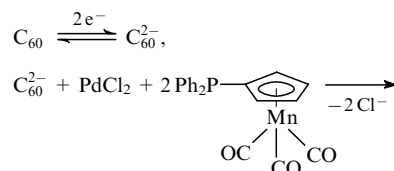


An advantage of this method is the possibility of preparing a pure monometal complex containing no polymetallated fullerenes. This is related to the fact that the electron transfer is followed by the fast reaction of C_{60} with the ML_2 compound formed *in situ*, which is formed in an exactly equimolar amount.

This approach has also been used to prepare new exohedral heteropolymetallic complexes of [60]fullerene containing Pd, Fe and Mn atoms.^{182, 183}

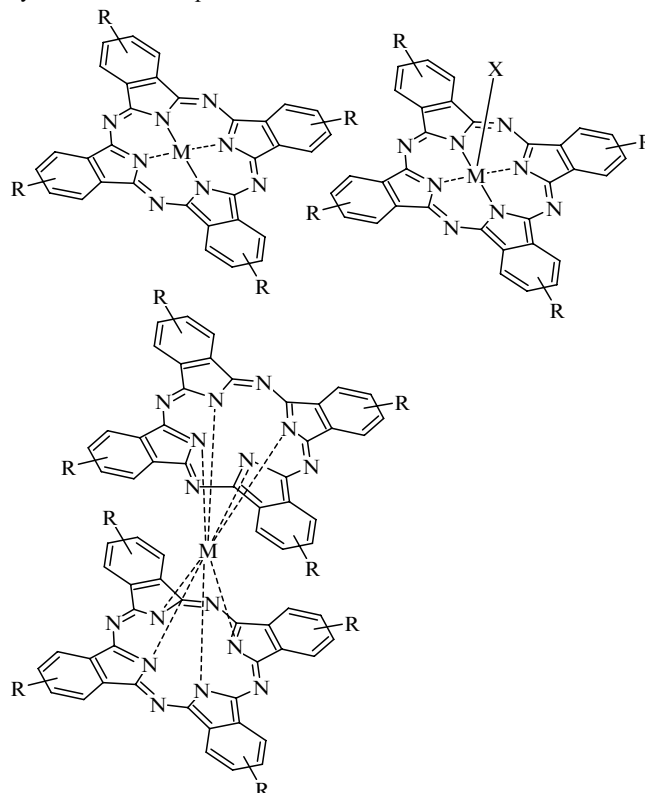


dba is dibenzylideneacetone;



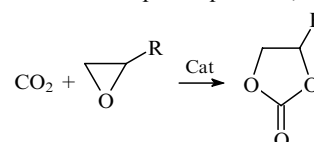
2. Electrochemically activated reactions of phthalocyanines

Typical examples of 'electron sponges' are mono- and diphthalocyanine metal complexes.



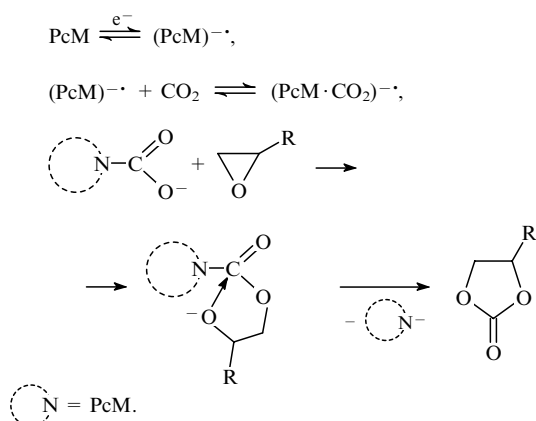
Recently, it has been found¹⁸⁴ that some diphthalocyanine complexes are able to undergo eight reversible and quasi-reversible redox transitions in the anodic and cathodic regions. Owing to this feature, they are rather promising participants of various redox processes, in particular, electrocatalytic ones. In Section III.1, we presented examples of electrocatalytic reduction of CO_2 by various complexes with macrocyclic nitrogen-containing ligands, including phthalocyanine complexes. Now we consider one more example of an electrochemically activated reaction of phthalocyanines in which the electrochemical transfer of an electron is used for catalyst activation.

The binding of CO_2 by epoxides resulting in the formation of alkylene carbonates is known¹⁸⁵ to be catalysed by metal phthalocyanines. However, this reaction proceeds under rigorous conditions, *i.e.*, in an autoclave at high pressure and temperature. With electrochemically reduced forms of metal phthalocyanines used as catalysts, this reaction was found⁷⁴ to proceed at 20 °C and under atmospheric pressure, in conformity with the scheme



$R = Me, CH_2Cl.$

The electrochemical activation of the catalyst and the subsequent nucleophilic attack occur in the following way:



Thus, electrochemically reduced forms of metal phthalocyanines exhibit much higher catalytic activities than neutral forms. Both mono- and diphtalocyanine complexes can be used as catalysts in this reaction; however, the latter offer an

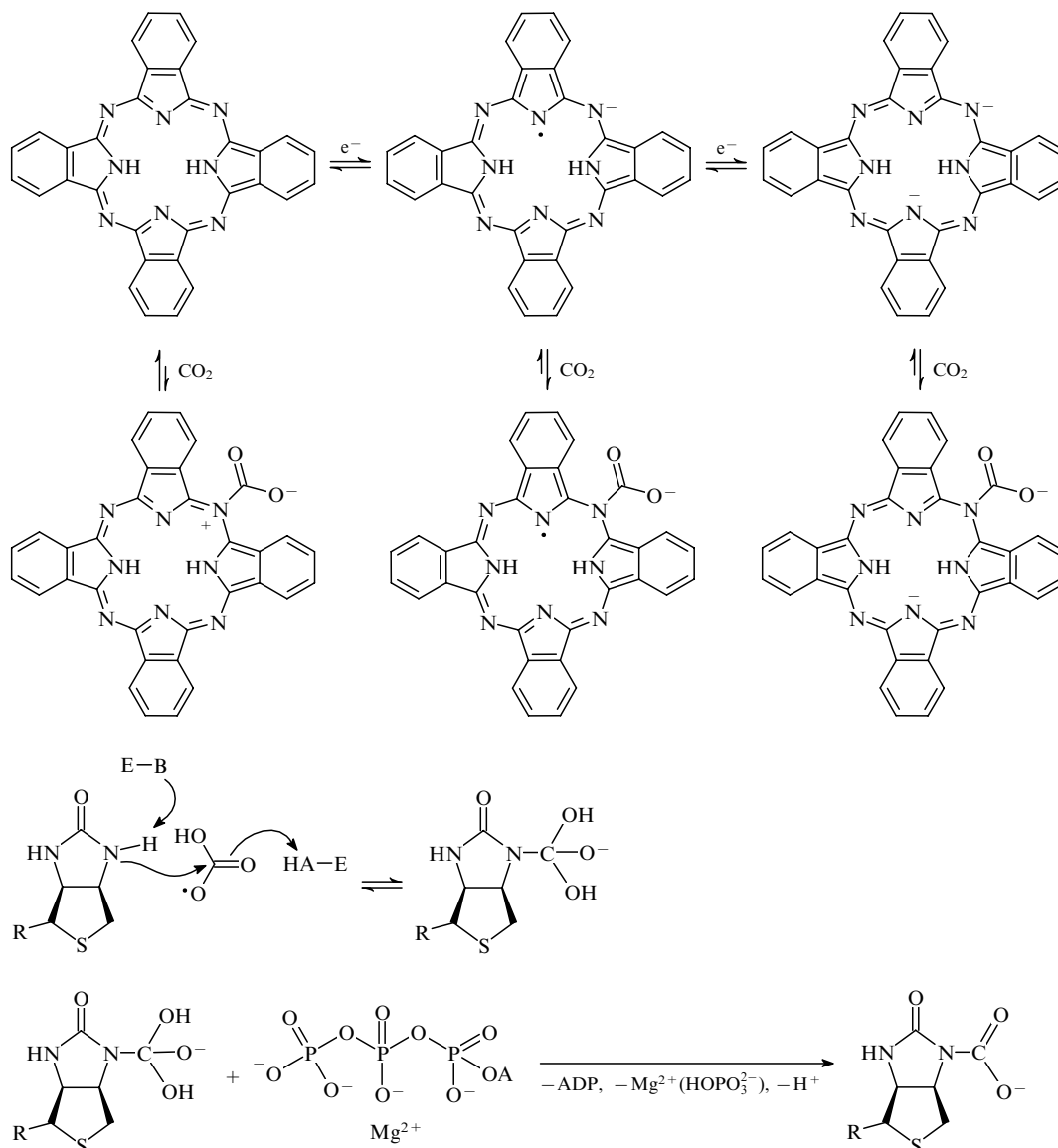
advantage, namely, in this case, the electrochemically activated binding of CO_2 can be carried out at a low cathodic polarisation (the potentials of the first redox transition of Pc_2M range from +0.01 to -0.65 V vs. Ag/AgCl/KCl).^{74, 104, 186}

A study of the influence of the catalyst immobilisation mode on the efficiency of the catalytic process showed that the highest efficiency is observed in the case of amino-substituted mono- and diphtalocyanine complexes (NH_2PcM and $\text{NH}_2\text{Pc}_2\text{M}$, respectively) electropolymerised on smooth electrodes. Turnover numbers as high as 10^4 – 10^5 have been achieved for these catalysts, which is close to the efficiency of natural enzymes.¹⁸⁷

Monomer	NH_2PcCu	NH_2PcCo	NH_2PcPd	$\text{NH}_2\text{Pc}_2\text{Lu}$	$\text{NH}_2\text{Pc}_2\text{Er}$
Catalyst turnover number in 75 min	2.65×10^5	4.7×10^3	1.05×10^3	1.4×10^4	7.0×10^3

It is of interest that carboxy-containing adducts formed under the action of phthalocyanine complexes and biotin (the co-enzyme which binds CO_2 and transports it to organic molecules *in vivo*) are structurally similar: in both cases, they contain a fragment similar to carbamic acid (Scheme 6).

Scheme 6



The above data indicate that the simulation of functioning of the active sites of enzymes operating by the proton transfer mechanism by processes occurring by a redox mechanism is possible but only at the level 'the same intermediate (in this particular case, the resonance-stabilised planar N anion) — the same product',¹⁸⁸

* * *

The information presented here demonstrates that, although numerous studies on electrochemically activated reactions involving organometallic compounds have been performed, the list of types of these reactions is quite limited. The vast majority of publications are devoted to transformations in the coordination sphere of transition metal complexes and electrocatalysis. Therefore, development of new electrochemical approaches to the synthesis of organometallic compounds and conduction of reactions involving them remains to be quite a topical task. In this review, we attempted to demonstrate the extensive potential of organic electrochemistry and thus facilitate implementation of electrochemical methods in the routine practice of chemists working with organometallic compounds.

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Modern methods for the synthesis of peptide – oligonucleotide conjugates[†]

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Abstract. The published data on the methods of chemical solution and solid-phase synthesis of peptide – oligonucleotide conjugates are reviewed. The known methods are systematised and their advantages and disadvantages are considered. The approaches to the solution synthesis of peptide – oligonucleotide conjugates are systematised according to the type of chemical bonds between the fragments, whereas those to the solid-phase synthesis are classified according to the procedure used for the preparation of conjugates, *viz.*, stepwise elongation of oligonucleotide and peptide chains on the same polymeric support or solid-phase condensation of two presynthesised fragments. The bibliography includes 141 references.

I. Introduction

Complexes of nucleic acids with proteins play an important role in the storage and transmission of genetic information. These supramolecular structures include ribosomes, chromatin, viruses and complexes of nucleic acids with enzymes and regulatory proteins. It is of note that these structures maintain their stability by virtue of protein – nucleic acid (NA) non-covalent interactions.

Protein – NA complexes the components of which are linked by covalent bonds have been known since long ago^{1–3} and became the subject for detailed investigations aimed at elucidation of their chemical structures and functions in the cell. The most convenient tools for the study of such complexes are model peptide – nucleotide conjugates.

The first peptide – oligonucleotide conjugates with phosphoramidate, phosphodiester, amide and ester bonds between the fragments were synthesised by researchers at the Department of Chemistry of M V Lomonosov Moscow State University led by M A Prokof'ev and Z A Shabarova.^{3,4} In the late 1960's – early 1970's, these scientists performed the synthesis of the first oligo-

nucleotide peptides, *viz.*, mixed biopolymers containing oligonucleotide and peptide fragments.^{5,6} However, at that time these studies were not extended further, primarily because of the lack of clearcut definitions of molecular-biological tasks which might be solved through the use of peptide – oligonucleotide conjugates.

The situation changed dramatically in the mid-1980's when it was first suggested to improve the intracellular transport of antisense oligonucleotides through their covalent attachment to various peptides able to penetrate the cell membrane. Noteworthy, the interest in peptide – oligonucleotide conjugates arose simultaneously with notable improvement of existing techniques for the formation of peptide and internucleotide bonds and the development of the solid-phase methodologies which eventually led to complete automation of oligonucleotide and peptide synthesis.

A vast number of papers on peptide – oligonucleotide conjugates published in the last 10–15 years brought forth the necessity to systematise the existing techniques of their synthesis. Previous studies on the synthesis of peptide – oligonucleotide conjugates were briefly described in the reviews^{7–10} published in the early 1990's and devoted to a broader field, *viz.*, the synthesis of oligonucleotide derivatives.

The present review includes two main sections describing the synthesis of peptide – oligonucleotide conjugates in solution and on insoluble solid supports. The methods for the preparation of oligonucleotide conjugates with amino acids and proteins fell outside the scope of the review, since each of these groups of methods is a subject for independent reviews.

In considering the methods for the synthesis of peptide – oligonucleotide conjugates in solution, the main criterion for the systematisation of the published data was the type of the chemical bond between the two components of the conjugate molecule, while the procedure for the preparation of conjugates (stepwise elongation of oligonucleotide and peptide chains on the same polymeric support or solid-phase condensation of two presynthesised fragments) was used as a criterion of choice in the analysis of solid-phase methods.

Here we do not touch upon the problems relevant to the structures of the intermediate and target compounds, for in the absolute majority of studies correct analysis has been carried out and the most advanced physicochemical approaches, particularly, standard procedures for the isolation of oligonucleotides and

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peptide–oligonucleotide conjugates have been employed. Nor did we consider the prospects of the application of peptide–oligonucleotide conjugates in antisense biotechnology, because these problems were analysed in the reviews published by Gait *et al.*¹¹ and Tung and Stein¹² in 2000. The latter publication describes the preparation of peptide–oligonucleotide conjugates, albeit in a very concise form, without going into details about the chemical reactions involved in the synthesis of hybrid molecules.

Such a limitation of the range of problems under consideration has made it possible to focus the main attention on the description of various approaches to the synthesis of peptide–oligonucleotide conjugates and the formation of covalent bonds between the oligonucleotide and peptide fragments of the conjugates and to perform a detailed analysis of the problems involved.

The principles underlying the classification and nomenclature of peptide–oligonucleotide conjugates have not been finally established yet. There exist several types of naming for the peptide–oligonucleotide conjugates. Some authors propose to consider these compounds as peptide derivatives containing an oligonucleotide substituent in the side chain. Based on this principle, it was proposed to term compounds comprising amino acid (peptide) and nucleoside (nucleotide) residues as ‘nucleo-amino acids’ and ‘nucleopeptides’.¹³ In the abbreviated form, the name of the oligonucleotide is indicated in parentheses immediately after the symbol designating the corresponding amino acid, *e.g.*, H-Ala-Ser(pATAT)-Ala-OH. This approach is often used for compilation of names of conjugates where the peptide components are linked to oligonucleotides through a phosphodiester bond formed by the OH group of the hydroxy amino acid residue and the terminal phosphate of the oligonucleotide.

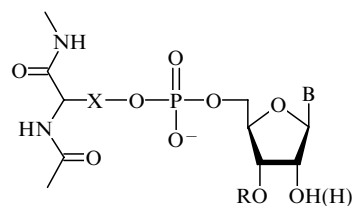
An alternative approach to the nomenclature of this class of mixed biopolymers was suggested by Z A Shabarova.⁴ All compounds containing amino acid (peptide) and nucleotide (oligonucleotide) fragments were termed as peptide–nucleotide conjugates. The name of a concrete compound is made up of two components, *viz.*, the name of a nucleotide residue and the name of an amino acid (peptide). Between these names, the designation of the type of the linkage is placed in parentheses. Thus a compound in which the phenylalanine residue is linked to uridine 5'-phosphate by a phosphoramidate bond will be termed as uridyl-(5'→N)-phenylalanine. Such nomenclature has been extensively used to describe peptide–nucleotide conjugates with a phosphodiester or a phosphoramidate bond between the fragments.

The main difficulties arise in the compilation of names for those conjugates where the oligonucleotide and peptide components are connected through a special linker possessing a complex structure. In this case, the conjugate actually consists of three components. The authors of the overwhelming majority of publications prefer to give more general names to such compounds. In foreign literature, it is the term ‘peptide–oligonucleotide conjugates’ (‘hybrids’) that has become especially popular.

II. Synthesis of peptide–oligonucleotide conjugates in solutions

1. Conjugates with phosphodiester bonds between the fragments

Studies of covalent complexes isolated from adenoviruses, polyoviruses and certain bacteriophages^{2,3} have demonstrated that the protein component of these compounds is linked to the nucleic acid through a phosphodiester bond formed by the OH group of the hydroxy amino acid and the 5'-terminal phosphate group of the polynucleotide.



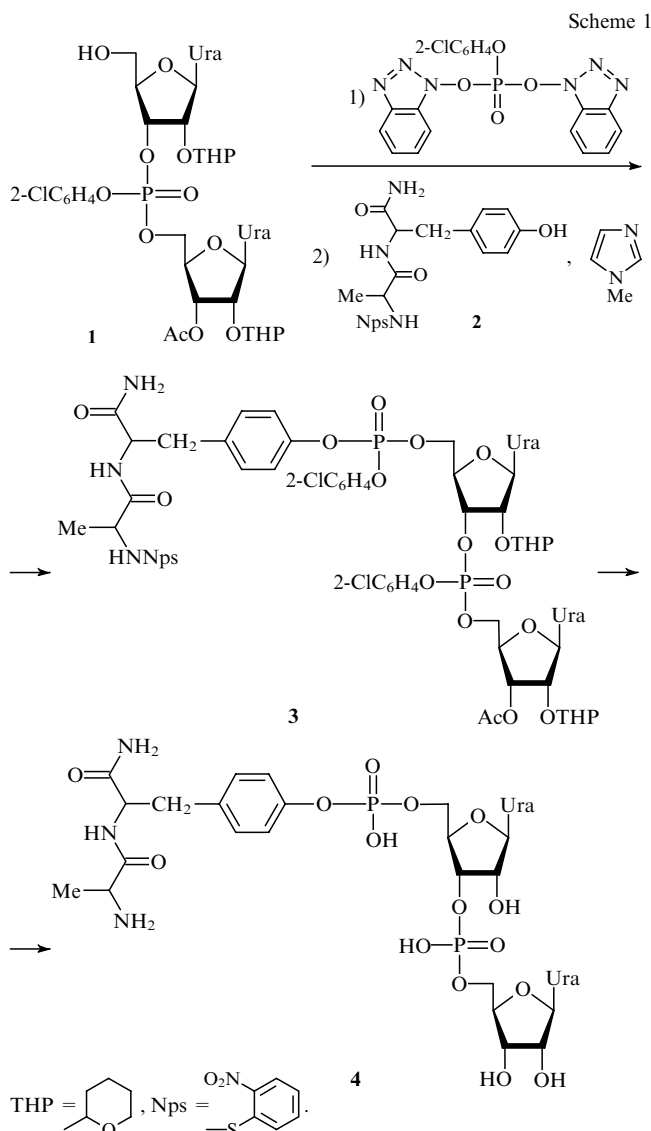
X = $-\text{CH}_2-$, $-\text{CH}_2\text{CH}_2-$, $-\text{CH}(\text{CH}_3)-$, $-\text{CH}_2\text{C}_6\text{H}_4-$;

R, a polynucleotide chain;

B, hereinafter, a heterocyclic base.

It has been found that topoisomerase I-induced transformations of DNA involve the formation of a DNA–protein structure in which the protein is covalently bound to the cleavage site of a double helix chain through a tyrosine residue.¹⁴

In order to simplify the analysis of complex NA–protein structures, it seems expedient to use model compounds, *e.g.*, peptide–oligonucleotide conjugates of the phosphodiester type. In this context, the main attention is given to the development of efficient procedures for the synthesis of these compounds. Thus van Boom *et al.*¹⁵ have proposed to this end phosphorylation of the hydroxy group of a peptide by the 5'-phosphate group of an oligonucleotide. Partially protected dinucleoside phosphate **1** and the N-blocked dipeptide amide, Nps-Ala-Tyr-NH₂ (**2**) (Scheme 1), were used as the key compounds.¹⁵ An alternative



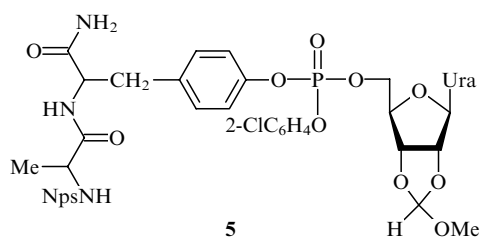
approach to the synthesis of peptide–oligonucleotide conjugates of the phosphodiester type is based on the reaction of an *O*-phosphorylated peptide and an oligonucleotide with a free 5'-hydroxy group.

In both cases, the investigators had to solve at least two problems, *viz.*, to choose an optimum method for the activation of the phosphate residue and to search for adequate procedures for the protection of all functional groups of the peptide and the oligonucleotide which are not to be phosphorylated or involved in the condensation. It is of note that the removal of the protective group should be carried out under mild conditions to prevent side reactions.

2-Chlorophenyl bis(benzotriazolido) phosphate in pyridine was used for the phosphorylation and simultaneous activation of dinucleoside phosphate **1**. The dipeptide **2** was added to the activated derivative formed in the presence of *N*-methylimidazole to give a fully protected peptide–oligonucleotide conjugate **3** in 80% yield. The latter was isolated by column chromatography on silica gel. Of extreme importance is the fact that the condensation of the oligonucleotide and peptide components leads to the formation of a phosphotriester bond between them. In an alternative procedure for the synthesis of compound **3**, the hydroxy group of the tyrosine constituent of the peptide is phosphorylated by the bifunctional phosphorylating reagent after which dinucleoside phosphate **1** is added to the reaction mixture. The yield of the peptide–oligonucleotide conjugate **3** prepared by this method was 78%.

Deprotection of the functional groups in compound **3** giving the targeted product **4** was carried out using the following reaction sequence.¹⁵ First, both 2-chlorophenyl phosphate-protective groups were removed by treatment with the oximate ion. The main difficulty in this deprotection is connected with the presence of an additional aryloxy group in one of the phosphotriesters formed through the tyrosine side chain. Since in this case the pK_a values of the leaving groups are close to that of the remaining aryloxy group, the possibility of selective scission of the 2-chlorophenyl group under the action of *syn*-4-nitrobenzaloxime and N^1,N^1,N^3,N^3 -tetramethylguanidine was problematic.

In order to examine the possibility of selective removal of the 2-chlorophenyl protective group, the authors performed the synthesis of a model compound **5**.



The reaction products formed upon its deprotection did not contain dipeptide **2**. The structure of H-Ala-Tyr(pU)NH₂ was confirmed by ³¹P NMR spectroscopy. Thus, it was concluded that the 2-chlorophenyl phosphate-protective group could be selectively removed with *syn*-4-nitrobenzaloxime and N^1,N^1,N^3,N^3 -tetramethylguanidine.¹⁵

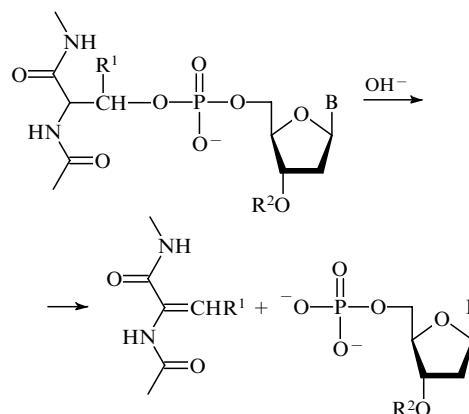
The removal of the 3'-*O*-acetyl group from compound **3** was effected by treatment with triethylamine in aqueous methanol. The 2-nitrophenylsulfenyl (Nps) and the 2'-*O*-tetrahydropyranyl (THP) groups were cleaved at room temperature by treatment with hydrogen chloride in methanol for 3 h and with aqueous HCl (pH 2) for 14 h.

The study by the same group of Dutch investigators¹⁶ is considered to be a logical continuation of their previous work.¹⁵ An attempt was undertaken to develop a reliable procedure for the preparation of peptide–oligonucleotide conjugates of the phosphodiester type with the DNA fragment linked to the peptide through a serine or a threonine residue. As a matter of fact, the problem in the synthesis of such peptide–oligonucleotide con-

jugates is associated with the high lability of the phosphodiester bond. This circumstance significantly complicates the deprotection and restricts the range of the reagents used.

The analysis of published data^{3,4} prompts a conclusion that the stabilities of the phosphodiester bonds in oligonucleotidyl-(5'→O)–peptides depend on the nature of the hydroxy amino acid due to the difference in the mechanisms of cleavage of the phosphodiester bonds. If the tyrosine residue is involved, the bond is stable in moderately acidic and alkaline media, but is cleaved under strongly alkaline conditions in exactly the same way as in ordinary phosphoric acid diesters. If the phosphodiester bond involves a serine or a threonine residue, this undergoes β-elimination in alkaline media with the liberation of a phosphomonoester group, *i.e.*, of an oligonucleotide containing 5'-terminal phosphate. In the case of serine, the peptide fragment formed as a result of this reaction contains a dehydroalanine residue (Scheme 2).

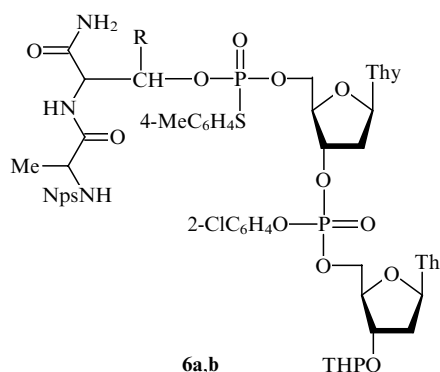
Scheme 2



$R^1 = \text{H, Me; } R^2, \text{ polynucleotide chain.}$

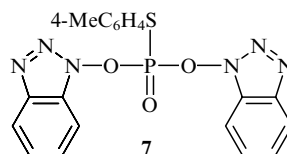
The hydrolytic stabilities of serine and threonine derivatives are different,³ the latter being more resistant to alkaline treatment.

The conjugates **6a,b**



$R = \text{H (a), Me (b)}$

were prepared¹⁶ using a procedure similar to that described above. *S*-*p*-Tolyl bis(benzotriazolido) phosphothioate (**7**) was used as a phosphorylating reagent, since the *p*-tolylsulfenyl group (Mps) is split off under mild conditions.¹⁶



The yield of compound **6a** was 80%. Compound **6b** was prepared in a relatively low yield (50%), which can be attributed to low solubility of the dipeptide Nps-Ala-Thr-NH₂ in a dioxane–pyridine mixture.

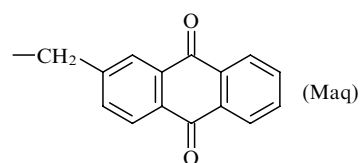
Removal of the Mps group from the completely protected peptide–oligonucleotide conjugate **6a** was performed by treatment with an excess of silver acetate in aqueous pyridine. The splitting of the Mps group was completed in 48 h at room temperature. However, the deprotection of the internucleotide phosphate by the oximate ion led to the cleavage of the phosphodiester bond between the components of the hybrid molecule **6a** by the β -elimination mechanism (^{31}P NMR spectroscopic data). It is of note that the removal of the phosphate-protective groups in compound **6b** using the same reagents did not affect the phosphodiester bond. Tetrabutylammonium fluoride has proved to be a milder reagent for the splitting of the 2-chlorophenyl protective group. The removal of Nps and THP groups was performed with 0.01 M HCl (pH 2) (0–5 °C, 16 h).

The stabilities of the peptide–oligonucleotide conjugates H-Ala-Ser(pTT)-NH₂ and H-Ala-Thr(pTT)-NH₂ in alkaline media have been studied.¹⁶ Studies by ^{31}P NMR spectroscopy have demonstrated that H-Ala-Ser(pTT)-NH₂ was completely hydrolysed by 0.15 M NaOH (20 °C, 25 min) to form the dinucleotide pTT, whereas no complete hydrolysis of H-AlaThr(pTT)-NH₂ occurred after 9 h treatment with alkali under identical conditions.

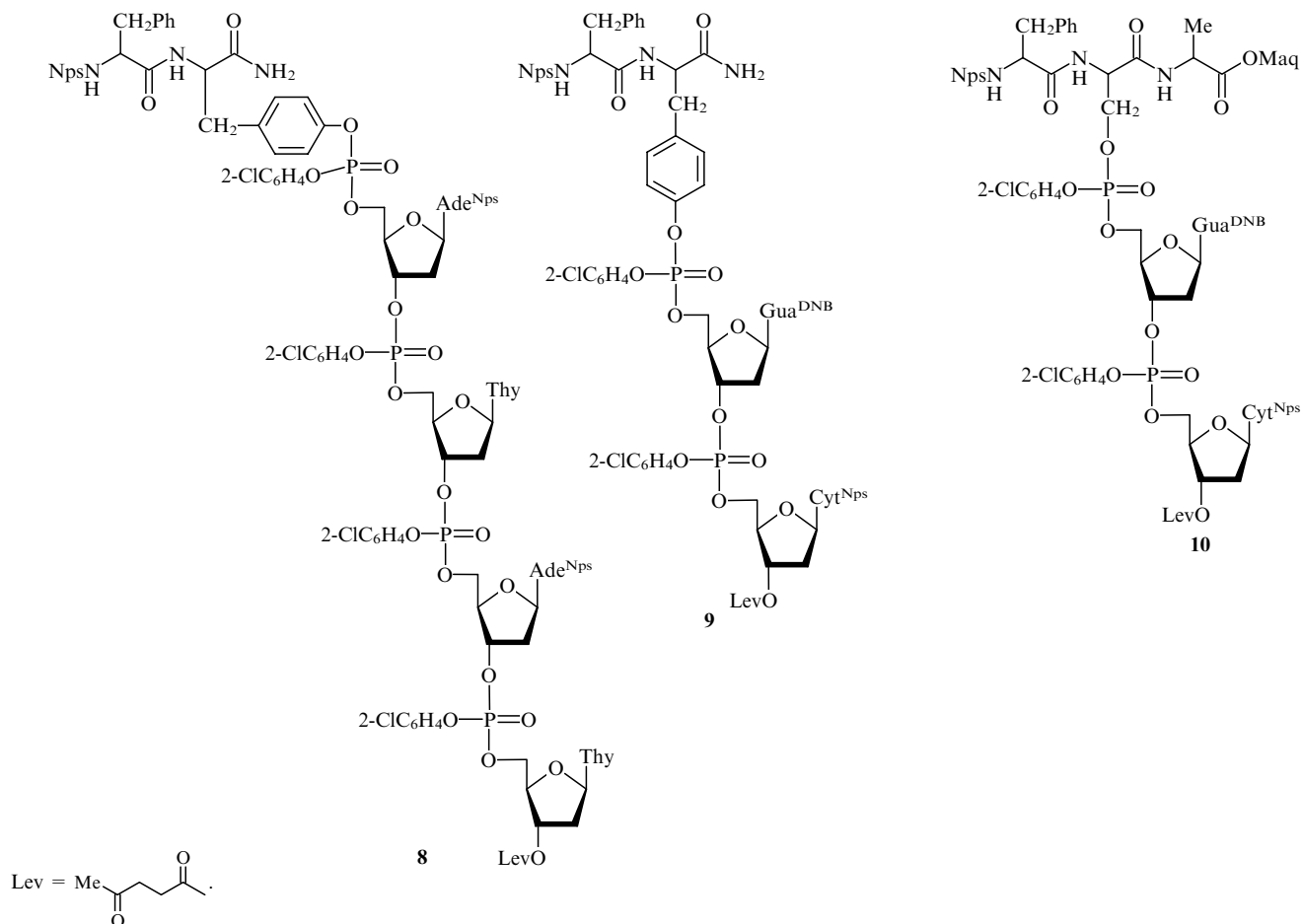
In further studies, the same group of investigators used this approach to obtain conjugates with a heterooligonucleotide component.^{17, 18} The problem arising in such a synthesis relates to the necessity of protection of exocyclic amino groups of the heterocyclic bases. The authors had to abandon the use of acyl protective groups employed in routine oligonucleotide syntheses, because their removal by treatment with concentrated ammonia leads to the cleavage of the phosphodiester bond between the oligonucleotide and the peptide formed with the involvement of the hydroxy group of serine or threonine. This could result in the base-catalysed racemisation of amino acid residues. Therefore,

the recourse to the protective groups commonly employed in peptide synthesis was made in the synthesis of peptide–oligonucleotide conjugates.

Van Boom *et al.*¹⁵ have protected the NH₂ groups of adenine and cytosine with the Nps group. The latter is relatively easily introduced, is stable under conditions of phosphorylation and increases the stability of N-glycosidic bond of purine nucleosides in acid media. However, an attempt to synthesise *N*²-nitrophenylsulfenyldeoxyguanosine failed.¹⁸ Therefore, advantage was taken of *N,N*-di-*n*-butylformamidine protection (N=CHNBu₂, DNB) of the exocyclic NH₂ group of guanine, which withstands column chromatography on silica gel and can be removed by mild treatment with hydrazine. It should be noted that it was exclusively amides of *N*-protected peptides that have been used as starting components for the synthesis of peptide–oligonucleotide conjugates in early studies,^{15, 16} while later Dutch investigators used peptides with terminal carboxy groups protected as allyl (All)¹⁷ or anthraquinon-2-ylmethyl (Maa) esters.¹⁸

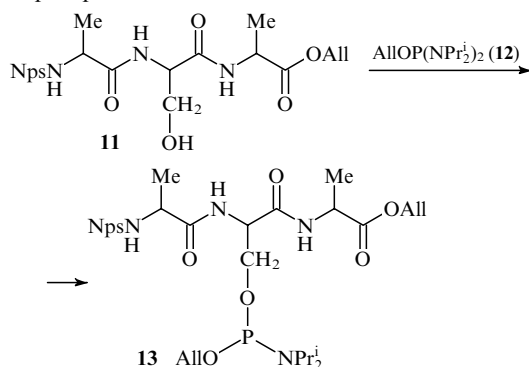


The approaches to the synthesis of the peptide–oligonucleotide conjugates H-Phe-Tyr(pATAT)-NH₂, H-Phe-Tyr(pGC)-NH₂ and H-Phe-Ser(pGC)-Ala-OH (see Refs 17, 18) are, on the whole, similar to those proposed in earlier studies,^{15, 16} but the procedures used for the deprotection of the intermediate fully protected peptide–oligonucleotide conjugates **8**–**10** have been modified: Nps-protection was cleaved with 2-mercapto-pyridine, while 3'-levulinoyl (Lev) and DNB protections were removed by hydrazine hydrate.

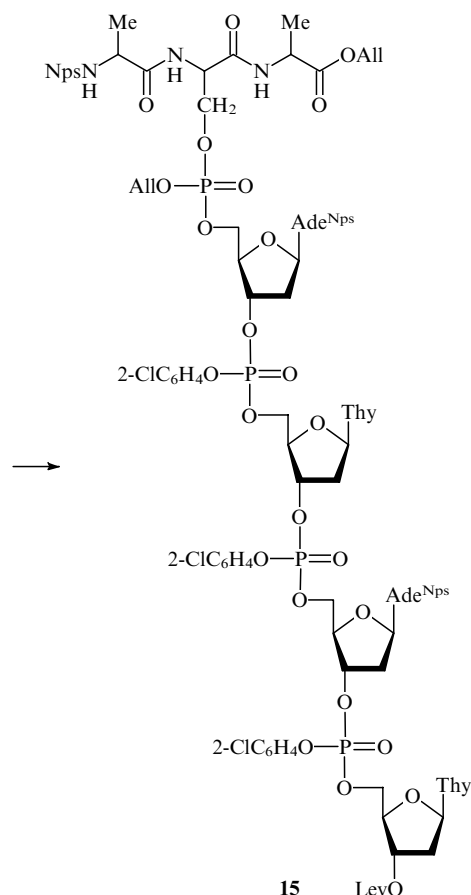
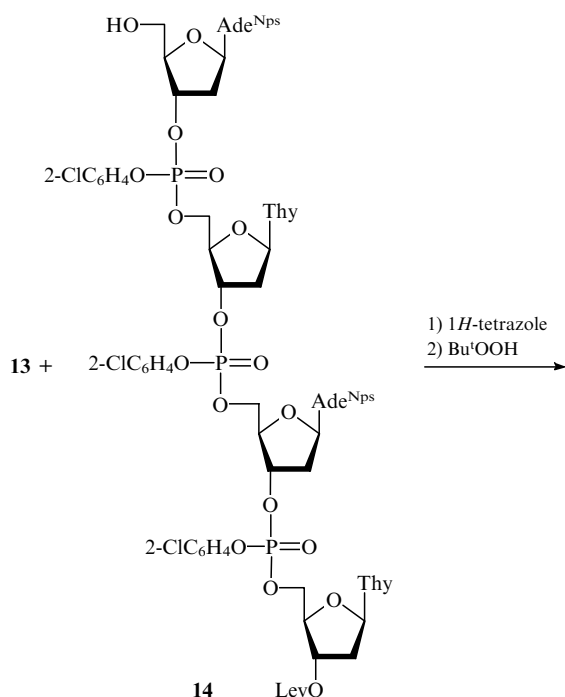


The phosphotriester method has initially been used to prepare H-Ala-Ser(pATAT)-Ala-OAll.¹⁷ The yield of the fully blocked peptide–oligonucleotide conjugate was 64%. The removal of protective groups was carried out by the same method as that used for compound **8**. An alternative approach consisting of phosphorylation of the tripeptide Nps-Ala-Ser-Ala-OAll by 2-chlorophenyl bis(benzotriazolido) phosphate and subsequent reaction of the activated tripeptide derivative with the partially protected tetramer ATAT was inefficient. The phosphorylation of the hydroxy group of serine led to the formation of the undesired symmetrical product.

These difficulties were successfully overcome through the use of the phosphoramidite method.¹⁷



The tripeptide **11** was first treated with equimolar amounts of 1*H*-tetrazole and the phosphitylating reagent **12** in acetonitrile after which equimolar amounts of the tetramer **14** and 1*H*-tetrazole were added to the phosphite **13** formed. The duration of the reaction was 18 h. The phosphite unit in the resulting conjugate was oxidised to the phosphate by treatment with *tert*-butyl hydroperoxide.



The notable advantage of this method is the use of the allyl protective group in the phosphotriester bridge between the tripeptide and the oligonucleotide in the completely protected peptide–oligonucleotide conjugate **15**, which is easily removed with aqueous pyridine. The only disadvantage of the phosphotriester and phosphite versions of H-Ala-Ser(pATAT)-Ala-OAll synthesis is that the carboxy group of the C-terminal amino acid could not be recovered by transition metal complexes.

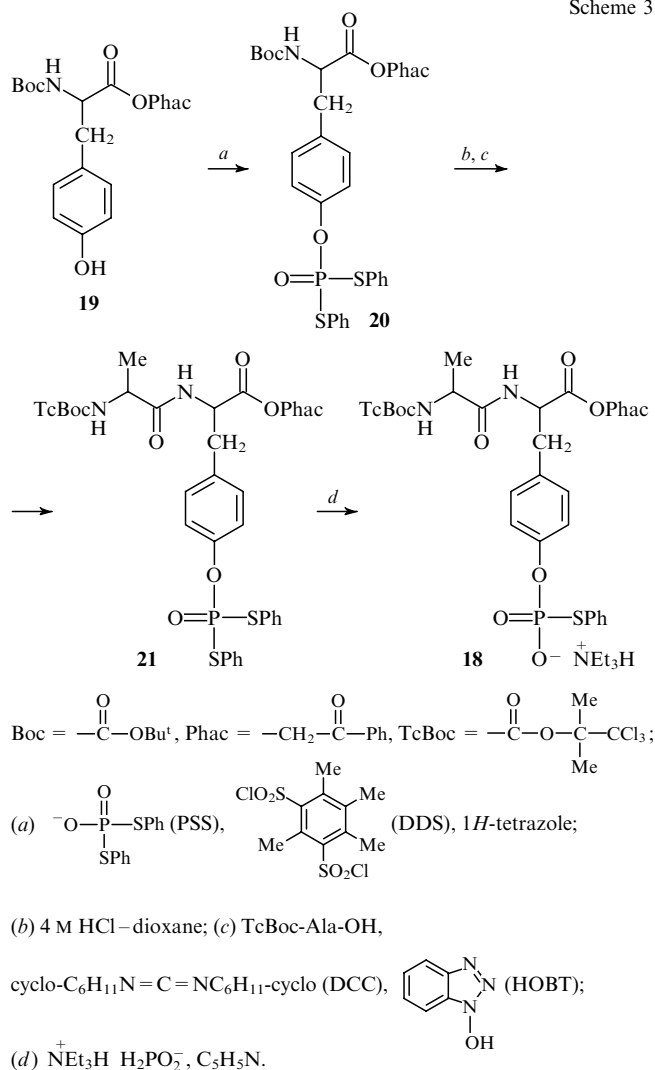
Of special interest are the studies by Japanese investigators^{19,20} who have developed an original procedure for the preparation of peptide–oligonucleotide conjugates of the phosphodiester type, *viz.*, H-Ala-Tyr(pUU)-OH (**16**) and H-Ala-Ser(pTT)-Phe-OH (**17**) based on the chemistry of phosphothioates.

Synthesis of the phosphorylated dipeptide component **18** was carried out using the Boc-strategy (Scheme 3).¹⁹

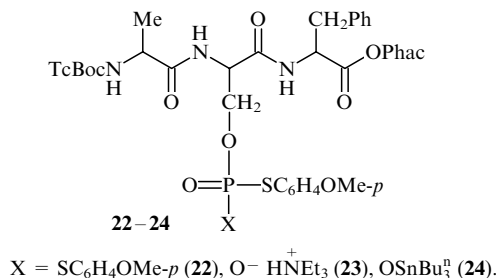
In the first step, the partially protected tyrosine derivative **19** was phosphorylated by *S,S*-diphenyl phosphodithioate (PSS) in the presence of isoduroldisulfonyl chloride (DDS). *N*-protected alanine was added to the phosphorylated tyrosine derivative **20** after deprotection of the amino group. *N,N'*-Dicyclohexylcarbodiimide and 1-hydroxybenzotriazole were used as the condensation reagent in the formation of the peptide bond. Selective splitting of one phenylthio group in the derivative **21** was achieved by treatment with triethylammonium hypophosphate in pyridine.¹⁹

The phosphorylated tripeptide **22** was prepared in a similar way.²⁰ In this case, the hydroxy group of serine was phosphorylated by *S,S*-bis(*p*-methoxyphenyl) phosphodithioate (MPSS).

Scheme 3



However, treatment of compound **22** with a solution of triethylammonium hypophosphate in pyridine yielded MPSS rather than compound **23**.²⁰ Presumably, this was due to β -elimination of phosphodithioate. Therefore, selective removal of one *p*-methoxyphenylthio group was achieved by milder treatment with bis(tributyltin) oxide which afforded compound **24**.

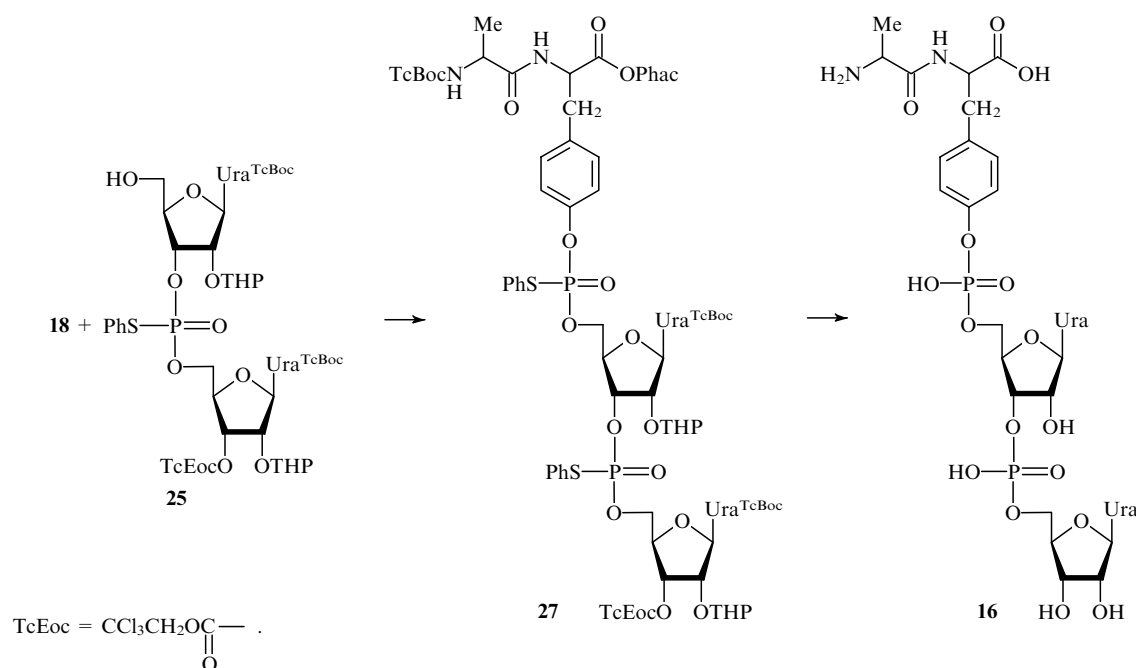


The syntheses of partly protected dinucleotide components **25** and **26** (Schemes 4 and 5) made use of PSS and DDS as bifunctional condensation reagents. The uracil and thymine N^3 -TcBoc protective group can be removed by reduction with zinc in acetylacetone under neutral conditions.

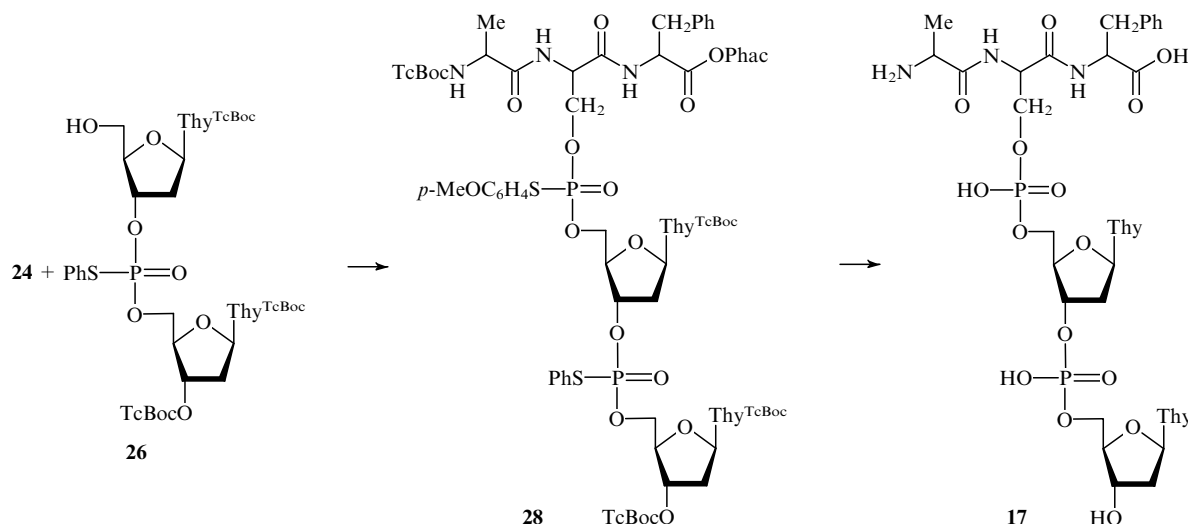
In the synthesis of the target peptide–oligonucleotide conjugate **16**, compounds **18** and **25** were introduced into the reaction with DDS and 3-nitro-1,2,4-triazole (Scheme 4). The fully protected peptide–oligonucleotide conjugate **27** was obtained in 73% yield.¹⁹

The use of the same reagents in the synthesis of the peptide–oligonucleotide conjugate **17** (Scheme 5) results in the formation of both the target compound **17** and the tripeptide containing a dehydroalanine residue. Therefore, the reaction was carried out in the presence of *N*-methylimidazole and an excess of triisopropylbenzenesulfonyl chloride (TPSCI).²⁰ Successive deprotection of compounds **27** and **28** afforded the conjugates **16** and **17**, respectively. The phosphate groups were deprotected with an excess of $(\text{Bu}_3\text{Sn})_2\text{O}$. The TcBoc, Phac and TcEoc groups were cleaved by reduction with zinc in acetylacetone. The 2'-*O*-tetrahydropyranyl groups were removed from compound **27** using a standard procedure (0.01 M HCl, pH 2).

Scheme 4



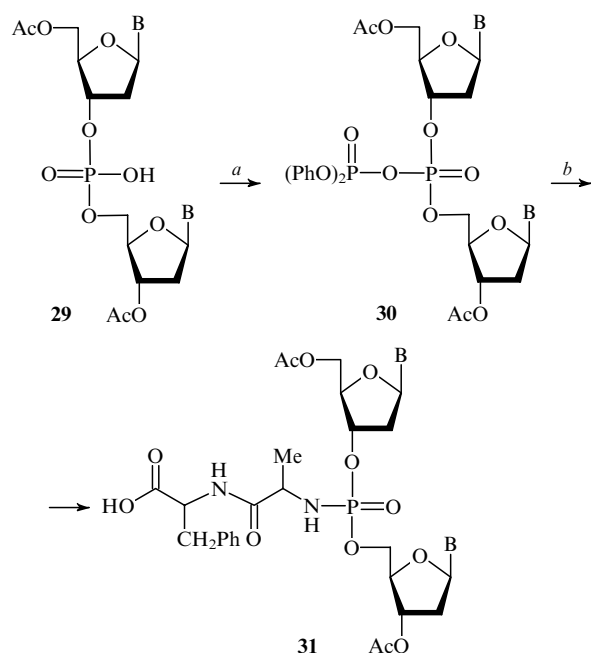
Scheme 5



2. Conjugates with phosphoramidate bonds between the fragments

From the historical point of view, mixed biopolymers with the phosphoramidate bonds between the oligonucleotide and the peptide fragments were the first to be synthesised. The possibility of modification of the internucleotide phosphate group was demonstrated by Prokof'ev, Shabarova *et al.*^{5,21} in the example of dinucleoside phosphates (Scheme 6).

Scheme 6



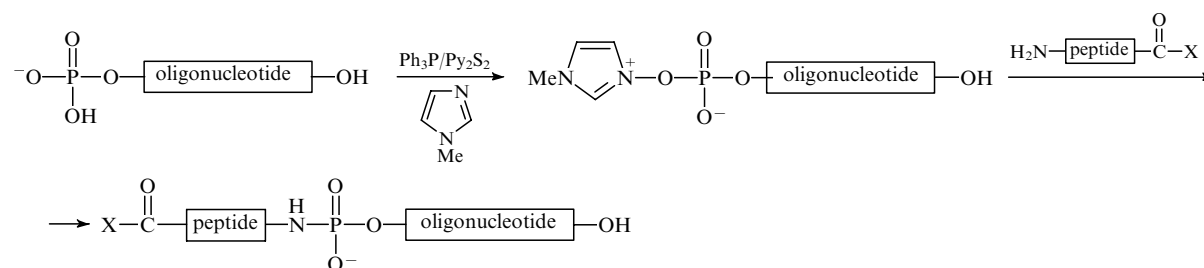
(a) $(\text{PhO})_2\text{P}(\text{O})\text{Cl}$; (b) H-Ala-Phe-OH .

Treatment of dinucleoside phosphate **29** containing protected hydroxy groups with diphenylphosphochloridate yielded the corresponding non-symmetrical pyrophosphate **30**. The latter represented an active phosphorylating reagent. Reaction of pyrophosphate **30** with the dipeptide H-Ala-Phe-OH is accompanied by nucleophilic substitution at the internucleotide phosphorus atom; the role of the leaving group is played by the diphenyl phosphate anion. The advantages of this method are as follows: (i) the synthesis of pyrophosphate does not affect heterocyclic base residues; (ii) pyrophosphate can be introduced into a reaction with the nucleophile without preliminary isolation. The yield of the target product **31** was 75%. However, this method⁵ gave satisfactory results only in the case of deoxyribo derivatives; in the presence of a protected 2'-hydroxy group, the degree of conversion was only 10%.

An alternative approach to the synthesis of peptide–oligonucleotide conjugates of the phosphoramidate type was developed by a group of Novosibirsk investigators.^{22–25} The α -amino group of the peptide reacts with preactivated 3'- or 5'-terminal phosphate of the oligonucleotide. The advantage of this approach is the possibility to use non-protected fragments of nucleic acids. This, in turn, is due to the fact that the phosphate residue is selectively activated with a mixture of triphenylphosphine and 2,2'-dipyridyl disulfide in the presence of the nucleophilic catalyst *N*-methylimidazole (Scheme 7). Under these conditions, the internucleotide phosphate groups and the reactive centres of heterocyclic bases are not involved. The mechanism of this activation of phosphoric acid monoesters is considered in detail in the review by Zarytova.²⁶

In the study,^{22,23} the 5'-terminal phosphate group was activated in a mixture of dimethylformamide and dimethyl sulfoxide. The oligonucleotides were solubilised in organic solvents as cetyltrimethylammonium (cetavlon) salts. The activation of the phosphate residues of the oligonucleotide gives rise to *N*-methylimidazolide which reacts with the amines with $\text{p}K_a$ values in a very

Scheme 7

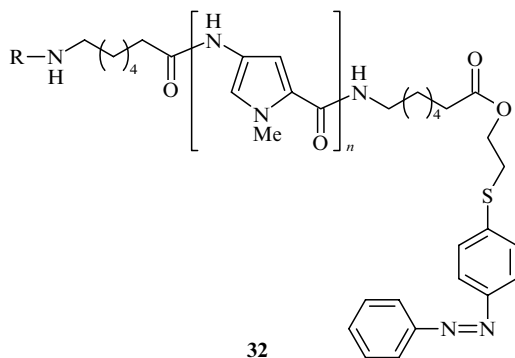


$\text{X} = \text{OMe}, \text{NH}_2$.

broad range; with an increase in pK_a , the rate of the phosphoramidate bond formation increases. The guanidine group of arginine in the peptides H-Pro-Arg-Val-OMe and H-(Leu-Arg) $_n$ -Gly-NH $_2$ ($n = 2-4$) is basic. In order to prevent the reaction of the latter with the activated phosphate group of the oligonucleotide, the peptides were introduced into the reaction in the form of trifluoroacetate salts. Under these conditions, the guanidine group remains protonated throughout the reaction and the role of the main nucleophilic centre after selective deprotonation by triethylamine is played by the α -amino group of the peptide.

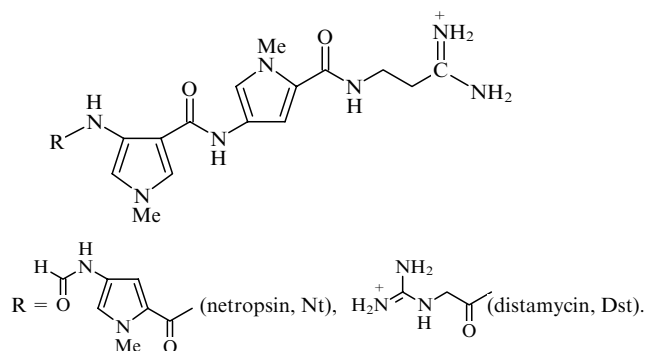
The presence of a P–N bond in the peptide–oligonucleotide conjugates formed was confirmed by ^{31}P NMR spectroscopy and acid hydrolysis under conditions of cleavage of the phosphoramidate bond (0.1 M HCl, 18 h). The target peptide–oligonucleotide conjugates were isolated by reversed-phase HPLC in 70%–85% yields. It was noted²³ that the addition of the peptide to the oligonucleotide increases the hydrophobicity of the latter. In the reversed-phase HPLC, the retention time of the reaction product increases in comparison with that of the original oligonucleotide.

The method described above was used for the conjugation of a synthetic analogue of the peptide antibiotic netropsin with oligothymidylic and oligodeoxyadenylic acids.²⁴ In this case, the peptide was attached to the 3'-end of the oligonucleotide. The yields of the conjugates **32** were 30%–50%.

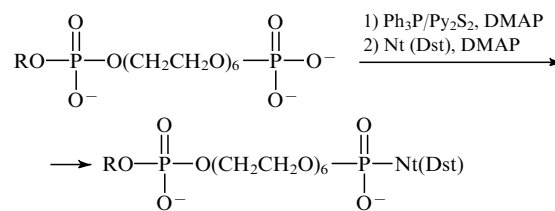


32 $n = 2-5$; R, fragment of the oligonucleotide chain.

A somewhat different approach was proposed for the synthesis of covalent complexes of non-modified oligonucleotides and their thiophosphate analogues with netropsin (Nt) or yet another peptide antibiotic, *viz.*, distamycin (Dst).²⁵

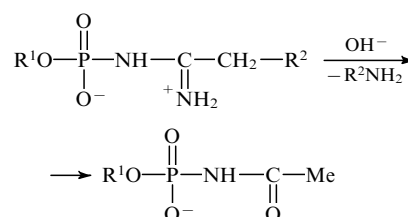


Automated phosphoramidite oligodeoxyribonucleotide synthesis was used to prepare oligonucleotides bearing, at their 3'- or 5'-ends, hexaethylene glycol linkers with phosphate groups. This was followed by the activation of the terminal phosphate groups by redox reagents of the types Ph_3P and Py_2S_2 in the presence of 4-dimethylaminopyridine (DMAP), after which a peptide antibiotic (Nt or Dst) was added to the activated oligonucleotide together with an excess of DMAP. The latter is thought²⁵ to be necessary for neutralisation of the positive charges of the amidine and guanidine groups.



R, fragment of the oligonucleotide chain.

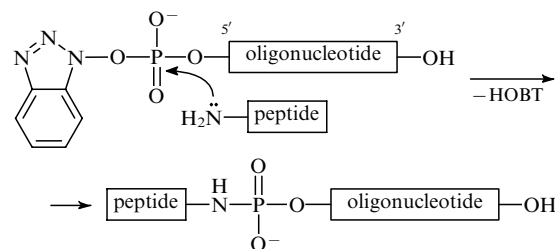
Presumably,²⁵ a covalent P–N bond formed between the antibiotic and the NA fragment involves the amidine group of the antibiotic. Indirect evidence can be derived from the fact that the rates of hydrolysis of oligonucleotide netropsin and acetamidine derivatives under the action of concentrated aqueous ammonia are identical. Apparently, the hydrolysis is accompanied by deamination:



R¹, fragment of the oligonucleotide chain, R², residue of the antibiotic.

A group of investigators representing the Moscow research team led by Z A Shabarova²⁷ have developed a method for the carbodiimide-induced activation of terminal phosphate groups of oligonucleotides by *N*-hydroxybenzotriazole (HOBT). HOBT esters are rather stable in aqueous media and can effectively phosphorylate nucleophilic reagents with the formation of covalent bonds (Scheme 8). Amino acids and peptides can be used as nucleophilic reagents.

Scheme 8



This was applied to the synthesis of the Gly-Gly-(5'→N)-(pTCTAG) conjugate²⁸ and to the synthesis of oligodeoxyribonucleotides with the antibiotic polymyxin B1, which represents a polycationic peptide attached to the 5'-terminal phosphate group.²⁹ The yields of the product reached 80%. An undecanucleotide conjugate has been designed and successfully prepared with 3'-terminal phosphate attached to the antibiotic daunomycin and the 5'-terminal phosphate attached to polymyxin B1, the latter serving to facilitate the penetration of the oligonucleotide through the cell membrane. This conjugate was isolated by polyacrylamide gel electrophoresis (PAGE); its total yield was 20%.

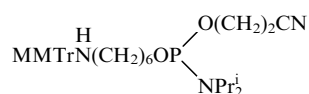
The extension of these methods²⁷⁻²⁹ to RNA derivatives was a logical continuation of the studies.³⁰ Conditions for effective synthesis of HOBT esters of 5'-oligoribonucleotides were selected. The formation of a specific complex of this duplex with the peptide Tat was demonstrated in the example of a synthetic RNA complex possessing a binding site for the protein Tat HIV-1. The covalent coupling of the activated RNA duplex to the peptide proceeded with 20%–30% efficiency and did not require any additional activation. Thus, the peptide Tat–TAR RNA complex is an example of effective covalent coupling of a protein to RNA within a specific complex.

Synthesis of a conjugate of a triplex-forming oligonucleotide with a functionally important peptide has recently been described. Such a conjugate is a convenient tool for the study of modulation of gene expression.^{31, 32}

3. Conjugates with amide bonds between the fragments

The studies^{33–40} are devoted to the synthesis of peptide–oligonucleotide conjugates with the amide bond between the fragments formed as a result of the reaction of the activated α -carboxy group of the peptide with the aliphatic NH_2 group incorporated into the oligonucleotide.

The aliphatic amino group is usually attached to the 5'- or the 3'-end of the oligonucleotide through a polymethylene spacer in the course of automated phosphoramidite synthesis. Commercially available 6-aminoethyl 2-cyanoethyl *N,N*-diisopropylphosphoramidite, the amino group of which is protected by the 4-monomethoxytrityl (MMTr) group, a convenient reagent for the preparation of DNA fragments with 5'-terminal NH_2 groups.



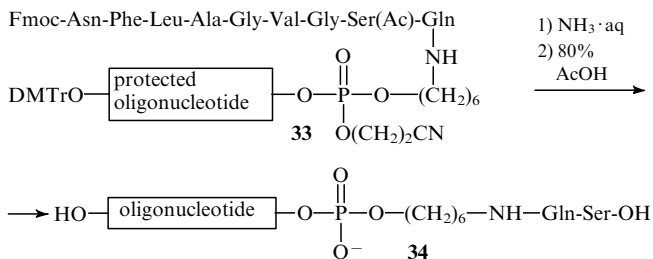
The synthesis of oligonucleotides containing a 3'-aminoalkyl group is carried out with the use of a special UV-cleavable polymeric support with a photolabile anchor containing a terminal aminohexanol group (Scheme 9). The attachment of the first nucleotide is performed in an automated DNA synthesiser, whereas the splitting of the oligonucleotide with the 3'-terminal amino group incorporated is effected by UV irradiation.⁴¹ The main advantage of this method is that the presence of a photolabile anchor group facilitates the synthesis of protected oligonucleotides with only the aliphatic amino group free.

Such a partially protected oligonucleotide was introduced into a condensation with one of the two *N*-blocked tripeptides, viz., Fmoc-Gly-Gly-Gly-OH (Fmoc is 9-fluorenylmethoxycarbonyl), or Fmoc-Gly-Gly-His-OH (see Scheme 9). The activation of the carboxy groups in the tripeptides was carried out by a $\text{Ph}_3\text{P}-\text{Py}_2\text{S}_2$ system in the presence of DMAP. The reaction was carried out in dimethylformamide at room temperature because of the possibility of cleavage of the Fmoc group and concomitant oligomerisation of the tripeptide under more drastic conditions. The yield of the peptide–oligonucleotide conjugates after deprotection and isolation by ion-exchange HPLC or PAAG electrophoresis was 89%–99%.

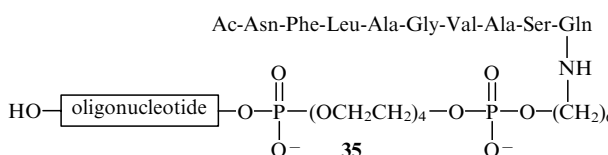
The condensation of short peptides and oligonucleotides using redox reagents was shown⁴² to be accompanied by epimerisation of the C-terminal amino acid residue. Model experiments showed

that the degree of epimerisation reached 30% under these conditions (^1H NMR spectroscopic data).

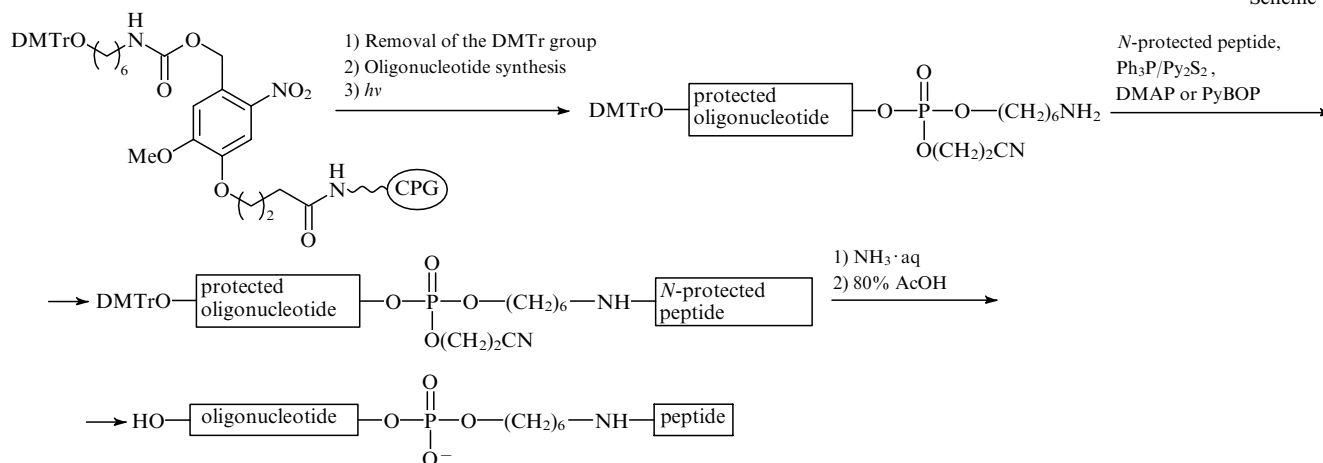
An attempt has been made³⁴ to prepare peptide–oligonucleotide conjugates with long peptide chains. In order to activate the terminal carboxy group of the peptide, the authors used (benzotriazol-1-yloxy)tripyrrolidinophosphonium hexafluorophosphate (PyBOP).³⁴ However, mass spectrometric analysis performed after deprotection of the peptide–oligonucleotide **33** formed and isolation of the target product revealed that its peptide component contains only two amino acid residues (compound **34**).



It is suggested³⁴ that the cleavage of the peptide component at the amide bond between the serine and glycine residues was due to $\text{N} \rightarrow \text{O}$ acyl migration. Apparently, the free OH group of serine liberated upon treatment with ammonia attacks the amide bond between the serine and glycine residues, which is followed by the scission of the peptide chain due to hydrolysis of the ester bonds. The use of milder procedures for the removal of protective groups (0.4 M NaOH in methanol, 17 h) did not give any positive results either. This problem could be overcome by replacing the glycine residue by the alanine residue in order to create steric hindrances in the site of possible nucleophilic attack. Some other changes necessary for further formation of a stable helical complex between the peptide–oligonucleotide conjugate and the complementary NA target were also effected, viz., the α -amino group of the peptide was protected by the acetyl group and an additional tetraethylene glycol bridge was introduced between the 3'-terminal nucleotide and the alkylamine in order to separate the peptide fragment from the DNA chain. In this case, the yield of the conjugate **35** was 72%.



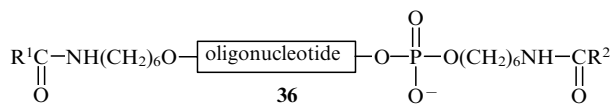
Scheme 9



GPG, controlled pore glass;

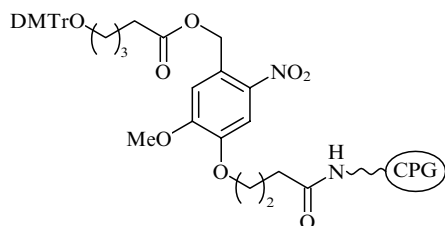
DMTr, 4,4'-dimethoxytrityl protective group; PyBOP, (benzotriazol-1-yloxy)tripyrrolidinophosphonium hexafluorophosphate.

The peptide–oligonucleotide 3',5'-bisconjugates **36** were successfully obtained using the polymeric support mentioned above in the first step. The peptide–oligonucleotide 3'-conjugates were synthesised according to Scheme 9 after which the 5'-terminal HO group was made to react with commercially available 6-aminoethyl 2-cyanoethyl *N,N'*-diisopropylphosphoramidite to which another peptide was then attached.³⁵



R¹, R², peptide residues.

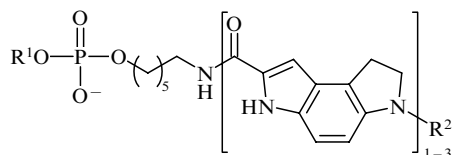
The use of protected oligonucleotides with 3'-terminal carboxy groups for the synthesis of peptide–oligonucleotide conjugates was a natural continuation of these studies.³⁶ A UV-cleavable polymeric support was also employed.



The covalent bond between the 3'-end of the oligonucleotide and the N-end of the peptide is easily formed even in the case of spatial hindrance created by the N-terminal amino acid. Excellent results were obtained in the coupling of tetrapeptides; the conjugates were obtained in 89%–95% yields.

Special mention should also be made of a synthesis of a series of peptide conjugates by coupling them to non-protected oligonucleotides T₆ and T₁₀ containing 5'-terminal NH₂ groups using PyBOP as the condensation reagent.³⁷

Synthesis of covalent oligonucleotide complexes with a synthetic analogue of the peptide antibiotic CC-1065 has been described.³⁸

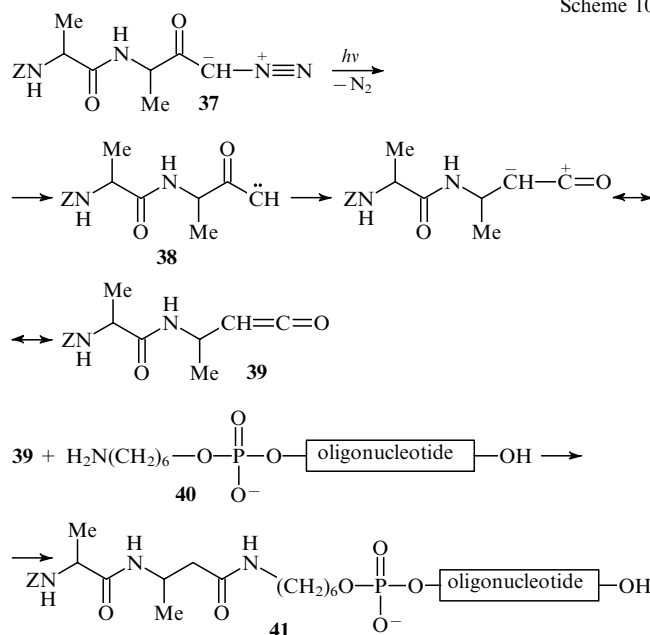


R¹, oligonucleotide chain, R² = CONH₂, Boc.

This method includes condensation of 2,3,5,6-tetrafluorophenyl ester of a peptide and a deprotected oligonucleotide bearing a 5'- or 3'-terminal amino group. The reaction is carried out in dimethyl sulfoxide. No detailed description of the synthesis of the DNA fragments containing a 5'- or 3'-terminal aminohexyl residue is provided. The oligonucleotides were introduced into the reaction as cetavlon salts. The yields of the condensation products were 60%–90% (HPLC data). It is noted that precipitation of the reaction products by the addition of a 2% solution of LiClO₄ in acetone and their further isolation by reversed-phase HPLC decreases the total yield to 15%–50%.

An interesting approach to the synthesis of peptide–oligonucleotide conjugates containing an amide bond was proposed by Swiss investigators.³⁹ Their method is based on the Wolff rearrangement. Diazo ketone **37** was used as a peptide component, and an oligothymidylate, as an oligonucleotide. The reaction was carried out in dimethylformamide. The diazo ketone **37** is decomposed upon UV irradiation with abstraction of the nitrogen molecule to give carbene **38** which undergoes the Wolff rearrangement to be further converted into ketene **39** (Scheme 10). The latter reacts with oligothymidylate **40** containing a 5'-terminal amino group. The yield of the peptide–oligonucleotide conjugate

Scheme 10

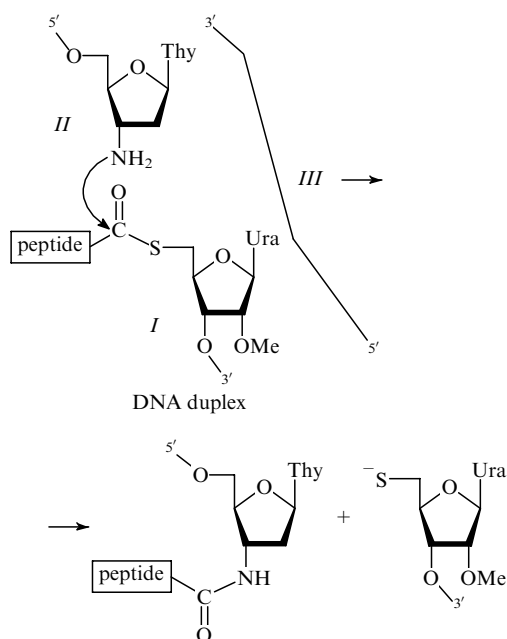


Z = PhCH₂OCO.

41 is 35%. The attempts to introduce diazo ketone **37** into the reaction with heteropolymeric DNA molecules were unsuccessful. The authors attribute this phenomenon to the poor solubilities of the heteropolymers in dimethylformamide. The presence in the reaction mixture of water molecules competing with oligonucleotides for the reaction with ketenes is an alternative explanation for the low yields.

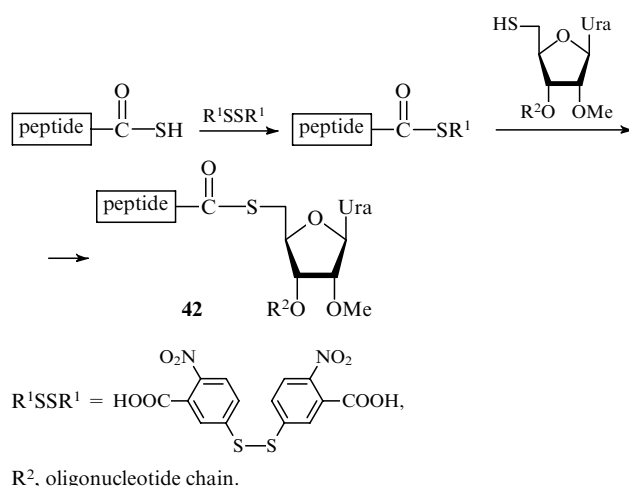
The approaches discussed above to the synthesis of oligonucleotide peptides largely entail the use of reactions occurring in organic solvents. An original procedure for the formation of covalent bonds between peptides and oligonucleotides in aqueous solutions based on the chemical ligation method has been developed.⁴⁰ This consists in approaching the reacting groups in the terminal fragments of the oligonucleotides *I* and *II* as a result of complementary interactions of these oligonucleotides with the complementary adjacent sites of the oligonucleotide *III* (Scheme 11).

Scheme 11



The peptides used in the study⁴⁰ were prepared in the form of carboxythionic acids by solid-phase synthesis on a polymeric support. Treatment of these peptides with Ellman's reagent [5,5'-dithiobis(2-nitrobenzoic acid)] gave the carboxythionic acid *S*-ester. The latter reacted with an oligonucleotide containing a 2'-*O*-methyl-5'-deoxy-5'-thiouridine to give the oligonucleotide peptide **42** with the thioester bond (Scheme 12). The reaction was carried out for 30 min at 25 °C in a buffer solution (pH 8.0) in the presence of spermidine. The product formed **42** is stable at room temperature for 24 h, but is easily hydrolysed at 37 °C over the same period.⁴⁰

Scheme 12



The condensation of the peptide linked to a single-stranded fragment of the oligonucleotide *I* with the oligonucleotide *II* containing 3'-terminal 3'-amino-3'-deoxythymidine within the DNA duplex is the key step in the synthesis of peptide–oligonucleotide conjugates possessing amide bonds (see Scheme 11). A DNA duplex represents a highly ordered system; in its cleavage site, the terminal 3'-amino group of one oligonucleotide and the thioester group of the other peptide are located in close proximity to one another and are spatially oriented in a definite manner owing to the interactions stabilising the double helix. As a consequence, the chemical reaction is characterised by high selectivity and high rate, which are unattainable for this type of conversion occurring outside the helical complex. Under optimum conditions (2–4 mmol of spermidine, pH 8, 37 °C), the condensation was completed in 15–30 h; the peptide–oligonucleotide conjugates were obtained in good yields (60%–85%). Owing to the weakly alkaline medium, the 3'-amino group remained non-protonated, while the presence of spermidine in the reaction mixture favoured additional stabilisation of the DNA duplex.

This approach allows simultaneous synthesis of several peptide–oligonucleotide conjugates possessing different structures. This is possible when an oligonucleotide with a 3'-amino group is involved in the simultaneous formation of two different DNA duplexes as has been demonstrated in the study under discussion.

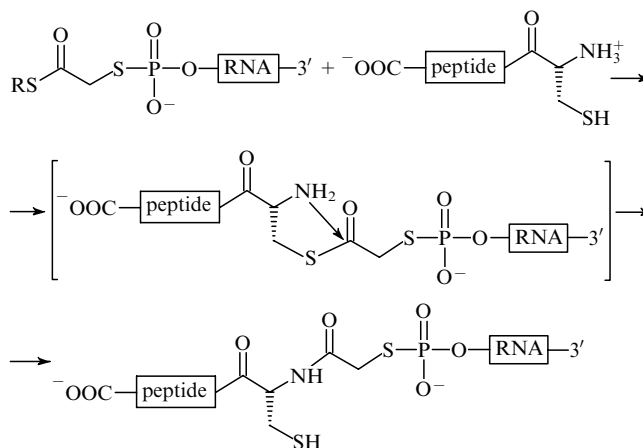
Peptides of various lengths underwent condensation with oligonucleotides. However, reactions with short peptides encountered serious difficulties because of possible formation of cyclic structures. This is due to the fact that the α -amino group of the peptide, along with the 3'-amino group of the DNA fragment, can attack the carbonyl carbon atom resulting in the formation of a cyclic peptide. Moreover, yet another prerequisite for efficient condensation is that the C-terminal amino acid residue of the peptide did not contain a branched side chain, *i.e.*, its C-end should be devoid of isoleucine or threonine residues.

The use of a non-modified oligonucleotide with a 3'-terminal hydroxy group in the condensation is also noteworthy.⁴⁰ Here, the formation of an ester bond between the peptide and the DNA fragment occurs; the yields of peptide–oligonucleotide conjugates with ester bonds are lower than those with amide bonds. In

contrast to the amide bond, the ester bond is easily hydrolysed in alkaline media (0.01 M NaOH) at 25 °C for 1 h.

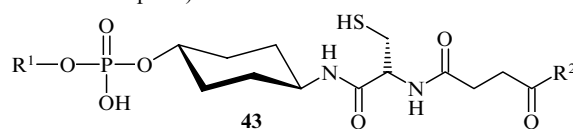
A more recent report⁴³ describes selective non-matrix chemical ligation of modified RNA containing the 5'-*S*-thioester group and polypeptides with N-terminal cysteine residues which affords peptide–5'-RNA conjugates (Scheme 13).

Scheme 13



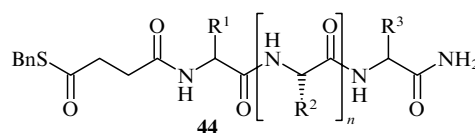
This reaction included transthioesterification and subsequent spontaneous intramolecular rearrangement resulting in the formation of a peptide bond. The authors observed high selectivity of ligation (50% yield of the conjugate of 102-membered RNA with a 13-membered peptide) at low (micromolar) concentrations of the reactants. This reaction proceeds under non-denaturing conditions favouring the preparation of NA–protein conjugates with simultaneous preservation of the native structure of the protein. The synthesis of peptides carrying N-terminal cysteine residues does not present a problem. The 5'-terminal phosphothioate residue can be easily introduced into a ribo- or deoxyribonucleic acid either chemically or enzymatically.

The term 'native ligation' (by analogy with condensation of two unprotected peptide fragments, one of which contains a C-terminal *S*-carboxythioate group and the other one contains an N-terminal cysteine, which is routinely used in peptide chemistry⁴⁴) was used^{45,46} to describe a new procedure for the preparation of peptide–oligonucleotide conjugates **43** (in the absence of a template).

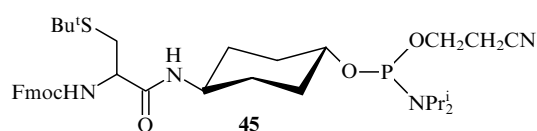


R^1 , fragment of an oligonucleotide chain,
 R^2 , fragment of a peptide chain.

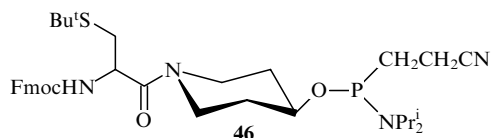
This method is based on the reaction of the peptide **44** modified by the introduction of the *S*-thioester group in its N-end with an oligonucleotide containing a 5'-terminal cysteine residue which is introduced using compound **45**.



R^1, R^2, R^3 , side chains of amino acids.



S-Benzyl thiosuccinate **44** was obtained in the last step of a standard automated peptide synthesis (Fmoc strategy). The *O*-*trans*-4-(*N*^α-Fmoc-*S*-*tert*-butyl-L-cysteiny)aminocyclohexanol phosphoramidite **45** was attached to the 5'-end of the oligonucleotide in the course of a standard solid-phase phosphoramidite synthesis. The preparation of the phosphoramidite synthon **46** based on 4-hydroxypiperidine has also been described.⁴⁶

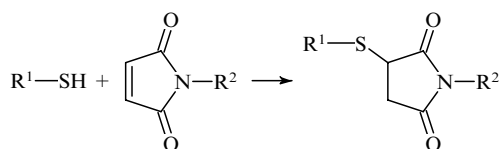


The peptide **44** and the oligonucleotide modified by compound **45** (or **46**) after deprotection and detachment from the resin were condensed without additional purification in water–organic solvents to which tris(2-carboxyethyl)phosphine (in order to remove the *S*-*tert*-butyl group *in situ*) and thiophenol (in order to increase the efficiency of thiol exchange) were added.

Some reactions between peptides and oligonucleotides of various sequences and lengths have been described and the ways to increase the efficiency of their synthesis have been considered.⁴⁵ The peptide–oligonucleotide conjugate **43** was the main product in all cases; sometimes, its yield reached 75%. The side reaction, *i.e.*, intramolecular cyclisation involving the succinyl fragment of the peptide, took place only with glycine at the N-end. No doubt, further experiments are necessary in order to optimise the composition of the solvent, reaction conditions (particularly, for long-chain peptides with a secondary structure). However, even now it is quite clear that the method in question⁴⁵ can be used for the preparation of oligonucleotide conjugates with a very broad range of peptides with small restrictions for amino acid sequences. This approach has obvious advantages over the method considered above for the synthesis of peptide–RNA conjugates,⁴³ since it allows the use of peptides with thioesters at their C- and N-ends and a 5'-cysteinyl-substituted oligonucleotide prepared by a standard phosphoramidite procedure. The method⁴³ allows the use of exclusively N-terminal cysteine-containing peptides and RNA modified with 5'-phosphothioate.

4. Conjugates with sulfide bonds between the fragments

The optimum variant of peptide–oligonucleotide synthesis seems to be the one in which the reactive group of the oligonucleotide reacts selectively with the reactive group of the peptide, whereas other functional groups of both macromolecules are not involved. For example, the conjugation can be effected by the addition of thiols to maleimides.



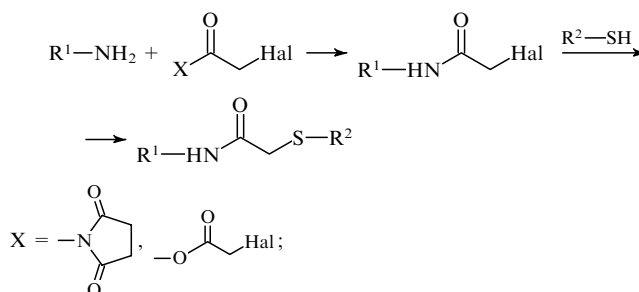
R^1, R^2 , an oligonucleotide or a peptide chain fragments.

The sulfhydryl or the maleimide active groups are first introduced into the oligonucleotide or the peptide using various reagents. It should be noted, however, that the role of a reaction centre can be played by the HS group of the cysteine residue initially present in the peptide. It is preferable, as a rule, that the sulfhydryl group is localised in the oligonucleotide, whereas the maleimide group, in the peptide.^{47–58} An alternative variant^{59–63} is that the HS group of the N- or C-terminal cysteine residue reacts with the maleimide group incorporated into the oligonucleotide chain.

In both cases, the reaction is carried out in aqueous or water–organic media (pH 6.0–7.2) at room temperature. The peptide is almost always taken in an excess (from 4 to 15 equiv.); in only one study, the ratio between the two components of the reaction mixture was 1 : 1.⁴⁸ The reaction time varies from 1 to

20 h. The yields of the conjugates vary within a sufficiently broad range, *viz.*, from 30% to 90%.

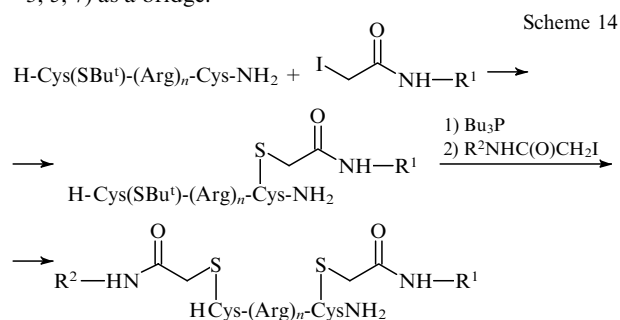
The formation of a thioether bond between the oligonucleotide and the peptide can also take place as a result of a nucleophilic attack of the HS group at the carbon atom of the halogenoacetyl derivative. For this purpose, the halogenoacetic acid residue is incorporated into oligonucleotides or peptides.^{64–72}



R^1, R^2 , an oligonucleotide or a peptide chain fragments.

As a rule, the oligonucleotide containing an iodoacetyl group reacts with an excess of the cysteine-containing peptide in neutral media at room temperature.^{64–67} The reaction time is 12–20 h. The yields of the conjugates usually vary from 55% to 98%. Reed *et al.*⁶⁸ performed the synthesis in a weakly alkaline medium (pH 8.3). The authors cite interesting results concerning the dependence of the reaction rate on the net charge of the peptide. Thus the reaction of a modified oligonucleotide with a peptide containing one arginine residue and four lysine residues (the net charge is +5) is complete within a few minutes. In the case of the other two peptides with the net charges of +1 and zero, the reaction time is 3 and 20 h, respectively. The authors presume that the increase in the condensation rate is caused by electrostatic interactions of the negatively charged phosphates in the DNA molecule with the positively charged side groups of lysine and arginine of peptides.

The synthesis of peptide–oligonucleotide conjugates in which two DNA fragments are linked through a peptide bridge has been described (Scheme 14)⁶⁴ with H-Cys(SBu^t)-(Arg)_n-Cys-NH₂ ($n = 3, 5, 7$) as a bridge.



R^1, R^2 , fragments of oligonucleotide chains; $n = 3, 5, 7$.

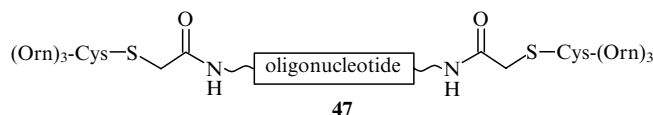
Initially, the free HS-group of the C-terminal cysteine residue reacted with the iodoacetyl group localised at the 5'-end of one oligonucleotide. In order to prevent the removal of the *S*-*tert*-butyl group, it was necessary to carry out the reaction in a neutral medium. After termination and chromatographic isolation of the peptide–oligonucleotide conjugate, the second thiol group was deprotected by treatment with a large excess of tributylphosphine at room temperature for 4 h. Taking into consideration low solubility of tributylphosphine in water, the removal of the protective group was carried out in a biphasic water–dichloromethane system.

The authors presume that tributylphosphine has a salient advantage over dithiothreitol which is widely used for the reductive cleavage of the S–S bond. On termination of the reaction, the excess of dithiothreitol should be removed, whereas in reactions with tertiary phosphine the separation of the organic phase from

the aqueous phase is sometimes sufficient. It was found that complete cleavage of the *S*-*tert*-butyl group should be carried out first, and only after this has been done, another oligonucleotide containing an iodoacetyl group at its 3'-end is to be added to the reaction mixture. Otherwise, the removal of the *S*-protective group occurs at a slow rate, since iodoacetic acid and its amide can form quaternary phosphonium salts with Bu₃P.

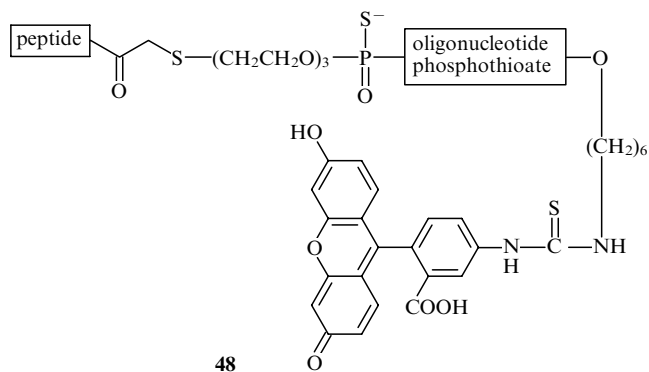
The reaction of the HS group of the N-terminal cysteine residue of the peptide–oligonucleotide conjugate with the electrophilic centre of the second oligonucleotide proceeded in a weakly alkaline medium, which made it possible to increase the yield of the target product. It should be noted also that all the reactions were carried out in a lithium chloride solution.⁶⁴ The reason lies in poor solubility of the peptide–oligonucleotide conjugate in water due to the interactions of the phosphate groups of DNA with positively charged guanidine groups of arginine, which are attenuated by the presence of lithium chloride. At the same time, the oligonucleotide pairs containing a peptide bridge are readily soluble in water because they contain an excessive (with respect to the guanidine groups) amount of negatively charged phosphates.

This approach was also used to prepare the conjugate **47** the two peptide fragments in which were attached to the 3'- and 5'-ends of the oligonucleotide.



In the studies,^{69–72} the bromoacetic acid residue was introduced into the peptide fragment prior to the condensation with an oligonucleotide containing an HS group. The bromoacetyl derivative of the peptide was taken in excess (from 5 to 25 equiv.). The reaction was carried out at room temperature for 5–20 h. The yield of the target product was 70%–100%. The effect of the medium acidity (pH 7.0, 7.5, 7.9 and 8.5) on the completeness of the reaction and the dependence of the reaction rate on temperature have been studied.⁶⁹ It was found that the peptide–oligonucleotide conjugate was formed in quantitative yield in less than 3 h at 40 °C and pH 7.0 and 7.5.

The publication⁷² devoted to the synthesis of the complex fluorescently labelled peptide–oligonucleotide conjugate **48** provides an illustrative example of a successful application of the above-described procedure to the synthesis of peptide–oligonucleotide conjugates. This was preceded by the synthesis of 19–25-membered oligodeoxyribonucleotide phosphothioates containing a 5'-terminal protected thiol group and an amino group at the end of the linker attached to its 3'-end. This bisfunctionalised oligonucleotide was introduced into the reaction with a fluorescein isothiocyanate (FITC) fluorescent label at the 3'-amino group; the thio group was then deprotected and reacted with the *N*-bromoacetyl derivative of the peptide.

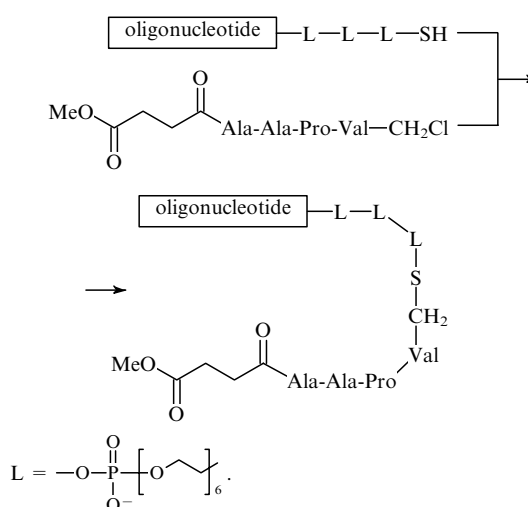


Special emphasis is laid on the possibility of performing large-scale synthesis of the conjugate **48**. The success of this synthesis depended on the development of a new procedure for deprotection

of oligonucleotides in which the oligomers were treated with a mixture of dipyridyl disulfide and concentrated ammonia in the presence of phenol and methanol. This deprotecting mixture enables splitting of the oligonucleotide from the polymeric support, liberation of the 3'-terminal amino group, deprotection of the phosphate and amino groups of heterocyclic bases and the conversion of the 5'-terminal thioacetyl protective group into the pyridyl disulfide group. The presence of phenol in the deprotecting mixture makes it possible to avoid the side reaction associated with a large-scale synthesis. Usually, the deprotection of internucleotide phosphates affords an electrophile, *viz.*, acrylonitrile (CH₂=CHCN), which reacts with the nucleophilic sulfur of the (oligonucleotide–linker–SH) system to give the undesirable product oligonucleotide–linker–SCH₂CH₂CN.

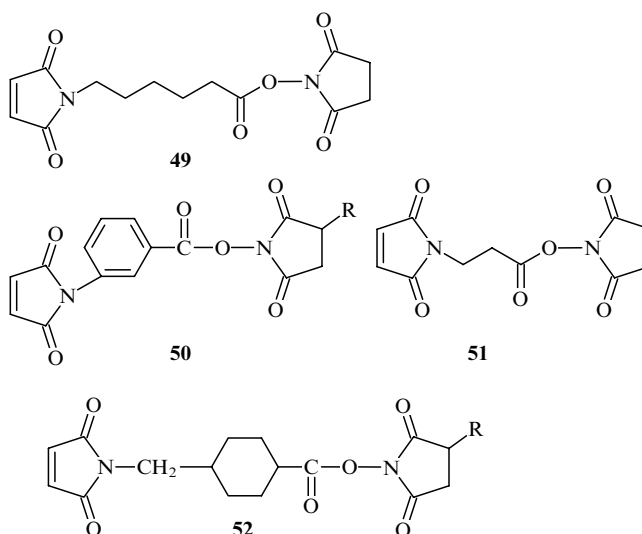
The synthesis of peptide–oligonucleotide conjugates based on the reaction of peptidyl chloromethyl ketone with an oligonucleotide containing a 3'-terminal thio group has been described (Scheme 15).⁷³

Scheme 15



The conjugation of the oligonucleotide with the peptide was carried out in a water–organic solution (pH 7.5) at room temperature for 12–16 h. The yield of the target product was 60%.

Activated esters of ϵ -maleimidohexanoic (**49**),^{47, 48} 3-maleimidobenzoic (**50**),^{51, 53, 54, 59, 60} β -maleimidopropionic (**51**)^{55, 56} and 4-maleimidomethylcyclohexanecarboxylic (**52**)^{57, 61–63} acids were used as heterobifunctional reagents for the incorporation of the maleimide group into peptides and oligonucleotides.



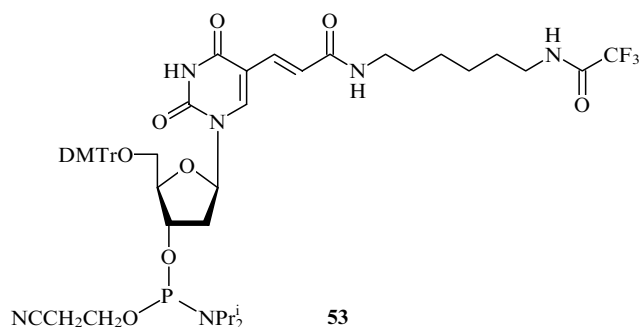
R = H, SO₃Na.

In the study,⁴⁸ the α -amino group of the peptide was acylated by the reagent **49** in water at pH 7.0 for the incorporation of the maleimide group into the peptide. This reaction was also carried out in methanol in the presence of triethylamine.⁴⁷ In the majority of cases, the peptide was prepared by solid-phase synthesis; after deprotection, the free α -amino group was acylated by one of the above-mentioned bifunctional reagents in the presence of 1-hydroxybenzotriazole.^{51, 53–56}

Low storage stability of maleimide peptide derivatives containing lysine residues in aqueous media was noted.⁵¹ A complex mixture of reaction products is formed after a period of 3–4 days as a result of the reaction of the ϵ -amino groups of lysine residues with the maleimide group. To prevent side reactions, it is proposed to introduce the modified peptide into the reaction immediately after its detachment from the polymeric support.

It was recommended to incorporate the bromoacetic acid residue into peptides by performing the acylation of the peptide ϵ -group by bromoacetic acid anhydride in the course of the solid-phase synthesis.^{69–71}

The synthesis of maleimide derivatives of oligonucleotides includes two steps, *viz.*, the automated oligonucleotide synthesis followed by modification of the oligomeric chain formed by 6-(4-monomethoxytrityl)aminoethyl 2-cyanoethyl *N,N*-diisopropylphosphoramidite.^{59–62} The aliphatic amino group was introduced into the predetermined position of the DNA fragment using a commercially available 3'-phosphoramidite derivative of the modified nucleoside **53**.⁶³



After splitting of the oligonucleotide from the polymeric support and removal of protective groups, the aliphatic amino group reacted with one of the heterobifunctional reagents **49–52** containing a maleimide group (pH 7–8). The average yields of the oligonucleotide maleimide derivatives are 60%–70%.

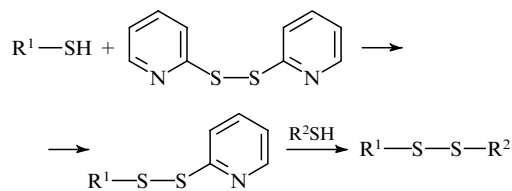
The methods for the preparation of oligonucleotides containing iodoacetic acid are similar. The amino group attached to the 3'- or 5'-end of the oligonucleotide through a hexamethylene bridge is acylated by *N*-hydroxysuccinimide ester^{64–66} or iodoacetic anhydride in a water–organic mixture.⁶⁸

5. Conjugates with disulfide bonds between the fragments

To this point, we have dealt with various procedures for the synthesis of conjugates, the oligonucleotide and peptide components of which were linked by stable covalent bonds. However, the development of techniques for the synthesis of peptide–oligonucleotide conjugates with easily cleavable bonds between the fragments is a no less important task. Such a bond can be represented by an S–S bond, which can be formed and cleaved under conditions acceptable for various biological processes.

The synthesis of conjugates with disulfide bonds between their peptide and oligonucleotide fragments can be carried out using three main approaches. First, this is in the oxidation of the HS groups of the oligonucleotide and the peptide with atmospheric oxygen with the formation of a disulfide bridge. In this case, the peptide is taken in an excess, the yield of the conjugate is 60%.⁶¹ However, according to Azhayev *et al.*⁷⁴ the yields of peptide–oligonucleotide conjugates prepared by this method are extremely low (0.4%–23%).

The other two approaches consist of the activation of the HS group of the oligonucleotide or the peptide with 2,2'-dipyridyl disulfide.^{61, 74–81}

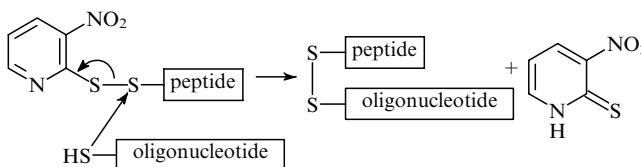


R^1, R^2 , oligonucleotide or peptide chain fragments.

The reaction is carried out under mild conditions at room temperature.

Unprotected peptides and oligonucleotides can form non-covalent complexes due to electrostatic interactions of the negatively charged phosphates of DNA with positively charged side groups of the peptides. Such complexes are precipitated from solutions. Having regard to this circumstance, potassium chloride and acetonitrile, which neutralise molecular charges and facilitate their dissolution, are added deliberately to the reaction mixture.⁷⁶ It is also recommended to carry out the synthesis of the conjugates in 90% formamide.⁷⁴

The introduction of the *S*-(3-nitro-2-pyridylsulfenyl)cysteine residue (Cys^{Npys}), which is Boc-protected at the α -amino group, is a distinctive feature of a conjugation method.^{51, 69} It is noteworthy that the Npys-protective group is resistant to acid treatment. After cleavage from the polymeric support and removal of protective groups (with the exception of the Npys group), the peptide formed in the solid-phase synthesis is introduced into the reaction with a DNA fragment containing an HS-group under mild conditions. The reaction of the HS group of the oligonucleotide with the Npys-protected thiol group of the cysteine of the polypeptide yields a conjugate with the S–S bond between the peptide and the oligonucleotide fragments.



It should be noted that the HS group can be introduced into oligonucleotides in several ways. First, it can be attached to the 3'- (see Refs 54 and 56) or 5'-end (see Refs 51, 53, 55) of the DNA fragment using linkers of various lengths. Second, the synthesis of a protected nucleoside 3'-phosphoramidite containing a thiol group can be followed by its introduction into any predetermined position of the oligomeric chain by the automated oligonucleotide synthesis.

Earlier it was mentioned that it is cysteine-containing peptides that are usually coupled to oligonucleotides. However, some methods permit the introduction of HS groups into peptides devoid of the cysteine residues. Thus β -mercaptopropionic acid was attached to the N-terminal amino acid residue in the course of solid-phase peptide synthesis.⁷⁴

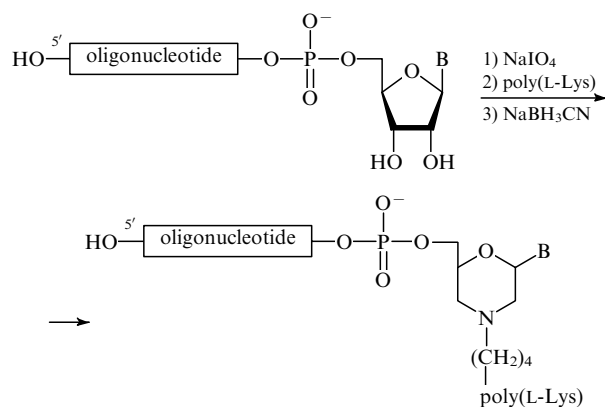
6. Synthesis of conjugates using a carbonyl derivative of one of the fragments

Syntheses of conjugates considered below are based on the reaction of carbonyl compounds with nucleophiles. The indisputable advantage of the carbonyl groups is that they do not require additional activation and their reactions proceed with high selectivities.

Dialdehyde derivatives of nucleic acids were extensively used in previous studies, *e.g.*, in the structural elucidation of the monomeric components of RNA and DNA. The methods for the introduction of aldehyde groups into carbohydrate fragments

of nucleic acids and the properties of the thus modified derivatives have recently been reviewed.^{82, 83}

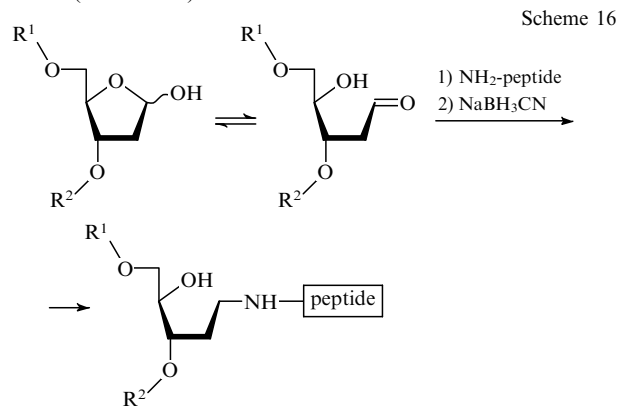
Lebleu *et al.*^{84–89} have performed a successful synthesis of peptide–oligonucleotide conjugates based on dialdehyde oligonucleotide derivatives. After periodate oxidation, the oligonucleotide with a 3'-terminal ribo fragment was subjected to condensation with poly(L-lysine) followed by reduction by sodium cyanoborohydride. The linkage between the peptide and the oligonucleotide fragments was effected through the morpholine ring formed.



A (2'→5')(A)_n-polyribonucleotide prepared by enzymatic synthesis was used as an oligonucleotide with a 3'-terminal ribo fragment;⁸⁴ in the case of oligodeoxyribonucleotide, this was introduced with the help of T4 RNA ligase;⁸⁵ the ribo fragment was the first to be attached to a polymeric support and the oligonucleotide was prepared by the automated synthesis.⁸⁷

The early works of Lebleu *et al.*^{84–87} reported the antisense properties of conjugates of dialdehyde oligonucleotide derivatives with peptides and their possible applications in the study of various biological systems. The results of testing of the complexes for the ability to inhibit replication of HIV-1 were published later (the oligonucleotide fragment of the complex was found to be complementary to the translation initiation centre of the Tat-protein).^{88, 89} Some sequence-specific antiviral effects of these compounds were observed.

In the study,⁹⁰ the electrophilic centres of oligonucleotides were generated enzymatically: the uracil residues were cut off from the oligonucleotide chain using uracil–DNA glycosylase to obtain the apurine/apyrimidine fragments. This was followed by modification of the aldehyde-containing oligonucleotides by various ligands carrying an amino group. In particular, the attachment of tripeptides to such oligonucleotides has been described (Scheme 16).



R¹, R², oligonucleotide chain fragments.

A highly efficient selective procedure for oligonucleotide synthesis involving the formation of oximes and thiazolidines has recently been proposed.⁹¹ In their search for an 'ideal' conjugation

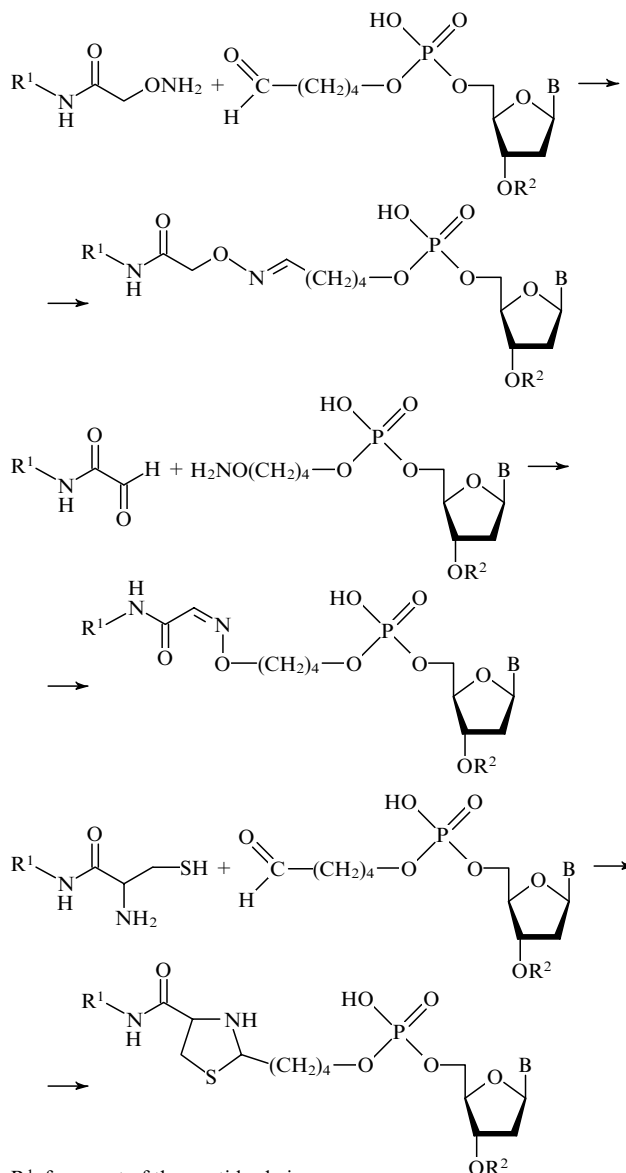
procedure, *i.e.*, the simplest one-step reaction between a free peptide and an oligonucleotide under physiological conditions, the authors made their choice in favour of two novel types of binding groups, *viz.*, the oxime and the thiazolidine groups.

The synthesis of conjugates involving the formation of an oxime (reaction of an aldehyde with an aminooxy derivative) and thiazolidine (reaction of the aldehyde with 1,2-aminothiol) is shown in Scheme 17.

The aldehyde or the aminooxy group were incorporated into the oligonucleotide fragment at the 5'-end, while the peptide contained the corresponding complementary group, *viz.*, the aminooxy- or the 1,2-aminothiol groups for the reaction with the aldehyde-containing oligonucleotide or the α-N-glyoxyloyl group for the reaction with the aminooxy oligonucleotide derivative.

5'-Modified oligonucleotides were prepared by the standard automated synthesis using the corresponding modified 3'-phosphoramidite derivatives in the final step.⁹¹ In turn, the N-terminal position or the side chain of lysine in the peptides was functionalised by introducing the aldehyde or the aminooxy groups by means of oxidative cleavage of the serine residue or using *N*-Boc-*O*-(carboxymethyl)hydroxylamine, respectively. The thiazolidine ring between the peptide and the oligonucleotide is formed in

Scheme 17



R¹, fragment of the peptide chain,
R², fragment of the oligonucleotide chain.

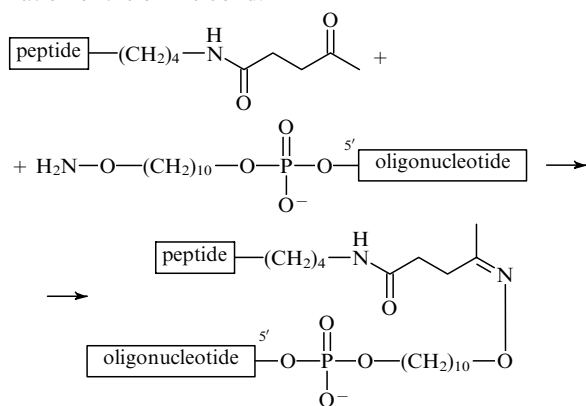
those cases where the original peptide is modified by attachment of cysteine at the N-end or at the side chain of lysine.

Oxime can also be formed in the DNA duplex. In this case, the 5'-aldehyde-containing oligonucleotide is hybridised with the complementary DNA chain and the DNA duplex formed is introduced into the reaction with a peptide carrying the aminoxy group. This strategy opens up fresh opportunities for post-synthetic modifications of single- and double-stranded DNA.

The formation of an oxime bond between the oligonucleotide and the peptide fragments occurs at a high rate and with high selectivity. However, oligonucleotides possessing aminoxy groups are seldom introduced into reactions with peptides carrying aldehyde groups, since such oligonucleotides easily react with any carbonyl groups and are therefore not very convenient. Those peptide-oligonucleotides in which the oligonucleotide and the peptide fragments are linked through the thiazolidine ring are less stable than those containing an oxime bond.

Later, the same authors⁹² reported the synthesis of conjugates using oligonucleotides with 3'-terminal carbonyl groups. The 3'-terminal aldehyde group was generated by mild periodate oxidation of a 1,2-aminoalcohol attached to the 3'-end of the oligonucleotide in the automated synthesis on a standard commercially available polymer. The oligonucleotide thus prepared reacted with a peptide containing an aminoxy group similarly to the 5'-aldehyde-containing oligonucleotide.⁹¹

Simultaneously, another group of investigators⁹³ published a paper devoted to the synthesis of peptide-oligonucleotide conjugates from oligonucleotides containing 5'-terminal aminoxy groups and peptides containing N-terminal lysine groups with the side chains modified by the reaction with levulinic anhydride, *i.e.*, peptides with N-terminal keto groups. In this case, the binding of the oligonucleotide and the peptide fragments occurred due to formation of the oxime bond.



The preparation of conjugates involving the formation of oximes has been described by Dey and Sheppard.⁹⁴ The keto group was introduced into the C(5)-position of the oligonucleotide uracil through a spacer.

III. Solid-phase synthesis of peptide-oligonucleotide conjugates

The performance of chemical reactions on insoluble polymeric supports is one of the main techniques in modern organic synthesis. The idea underlying this method is virtually versatile and applicable to a wide variety of biopolymers and their analogues. In the past few decades, the solid-phase method has become a routine procedure in the synthesis of peptides and oligonucleotides; therefore, investigators give considerable attention to the development of strategies and tactics of chemical synthesis of peptide-oligonucleotide conjugates which is partly or completely performed on a solid phase.

This strategy is based on the construction of amino acid and nucleotide sequences which includes either stepwise elongation of peptide and oligonucleotide chains on the same solid support or

condensation of the two preformed fragments. The second route implies the attachment of a preformed peptide to an oligonucleotide synthesised on a solid phase and immobilised on a polymeric support.

In development of the strategy of chemical synthesis of peptide-oligonucleotide conjugates, special emphasis is laid on the choice of optimum methods for the formation of amide and phosphodiester bonds and a search for the most adequate combinations of protective groups designed for peptides and nucleic acid fragments and conditions for the deprotection (the latter should be selected with due regard to the stability of the target peptide-oligonucleotide conjugates). The choice of method for the formation of a bond between the peptide and the oligonucleotide fragments is also of great importance.

1. Stepwise synthesis of peptide and nucleotide fragments on a single solid support

The synthesis of oligonucleotides and peptides includes a series of repeated operations involving structurally similar monomeric components. The sequential synthesis of the oligonucleotide and the peptide fragments of the hybrid molecule on a single solid support can raise serious problems connected with the impossibility, in principle, of combining some standard procedures inherent in the solid-phase oligonucleotide and peptide syntheses. Therefore, meticulous selection of methods and optimisation of experimental protocols are necessary in order to ensure acceptable yields of target products and to avoid the formation of by-products.

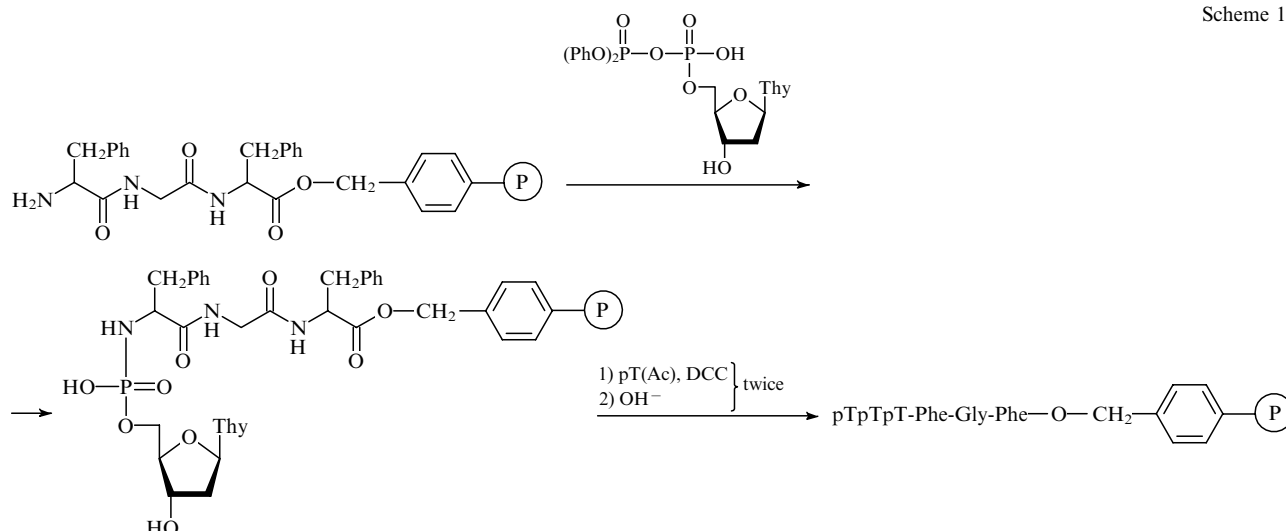
In 1972, M A Prokof'ev, Z A Shabarova *et al.* published a paper of fundamental importance⁶ in which they gave the first description of a solid-phase synthesis of peptide-oligonucleotide conjugates (Scheme 18).

The authors used a classical Merrifield support, which represents a chloromethylated styrene-divinylbenzene (2%) copolymer. The synthesis of the peptide fragment was carried out using Boc-protected amino acids and *N,N'*-dicyclohexylcarbodiimide (DCC) as a condensation reagent. The choice of amino acids was determined so as to avoid complications resulting from the splitting of the target product off the polymer. The first nucleotide was attached to the peptidyl polymer by the so-called pyrophosphate method, which consists in the activation of the phosphate group of the nucleotide owing to the formation of mixed anhydride with diphenyl phosphate. This reaction was carried out in dry DMF in the presence of a tenfold excess of thymidine 5'-phosphate-diphenyl phosphate mixed anhydride (20 °C, 100 h). The elongation of the oligonucleotide chain was carried out by the phosphodiester method. The condensation was performed in dry pyridine in the presence of a five- or a tenfold excess of 3'-*O*-acetylthymidine 5'-phosphate and a fivefold excess of dicyclohexylcarbodiimide with respect to thymidyl-(5'→N)-Phe-Gly-Phe. The deprotection of the 3'-hydroxy group of the nucleotide was carried out in alkaline aqueous dioxane (pH 9). Such a treatment ensured a practically complete removal of acetyl protection without splitting of the dinucleotidyl-(5'→N)-peptide off the polymer.

The final step included hydrolysis of the ester bond between the polymer and the trinucleotidyl-(5'→N)-peptide. The authors encountered serious difficulties because of both steric hindrances and the impossibility of using strong acids, which might result in cleavage of the phosphoramidate bond. The maximum extent of cleavage of the ester bond (10%) is achieved by treating the oligonucleotidyl-(5'→N)-peptide with NaOH in aqueous dioxane.

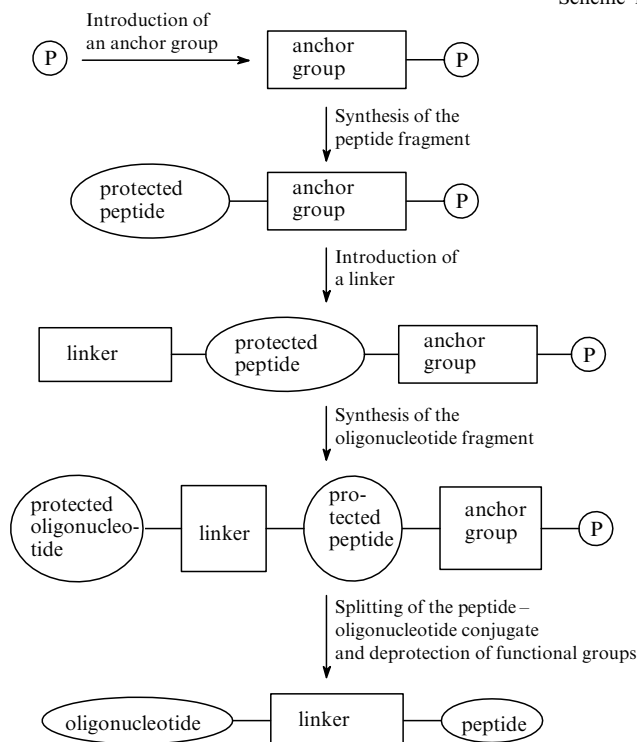
In its modern modification, this approach combines stepwise synthesis of the peptide from the C-end and subsequent elongation of the oligonucleotide chain on the peptidyl polymer by the phosphoroamidite method (Scheme 19). If the peptide is devoid of hydroxyamino acid residues, the synthesis of the DNA fragment should be preceded by incorporation of a hydroxy group into the peptidyl polymer. For this purpose, the α -amino group is acylated by a bifunctional reagent which contains an activated

Scheme 18



carboxy and a protected hydroxy group. This promotes the insertion of a linker between the N-end of the peptide and the oligonucleotide.

Scheme 19



a. Solid support

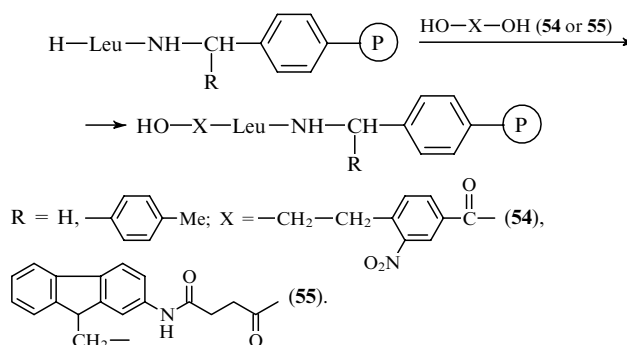
The success of a solid-phase synthesis largely depends on the correct choice of solid support. The most popular support is controlled pore glass (CPG).^{95–102} It is common practice to use CPG with a pore diameter of 500 Å. The synthesis of peptide–oligonucleotide conjugates on silica gel (Fractosil) has also been described.¹⁰⁰ However, in a more recent publication¹⁰² the same authors had to admit that the use of CPG was preferable, since this solid support allows the synthesis of the target product in higher yields even at lower specific loading with the first monomeric unit. At the same time, some investigators (see, *e.g.*, Refs 103–105) call into question the expediency of CPG application, since the synthesis of the peptide fragment on this support affords products with shorter chains in addition to the target oligomer. In the authors' opinion,^{53, 103} the formation of short peptide chains can

be avoided through the use of a copolymer of polyethylene glycol with polystyrene (PEG-PS). In a series of publications by Spanish investigators,^{104–113} the use of a copolymer of styrene with 1% divinylbenzene has proved to be especially efficient in peptide synthesis.

b. Introduction of an anchor group

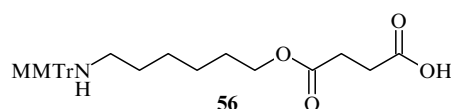
The first amino acid, which is to become a C-terminal residue in the peptide fragment to be synthesised, is attached to the support through the ester bond. In order to effect the esterification reaction between the amino acid and the solid support, the latter should contain reactive groups. Special methods for chemical modification of the support are being developed.

The use of polystyrene modified by aminomethyl^{106–109} or *p*-methylbenzhydrylamine^{109, 110} groups as a polymeric support is reported. In the first step, the NH₂ group of the support was acylated by *N*-protected leucine used as an internal standard. After removal of the amino protective group, the leucyl polymer was treated with a bifunctional reagent, *viz.*, 3-nitro-4-(2-hydroxyethyl)benzoic acid (**54**)^{106–110, 113} or *N*-(9-hydroxymethylfluoren-2-yl) succinamide (**55**).¹⁰⁹



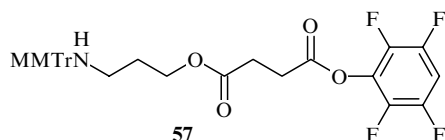
The presence of a bridge between the support and the C-terminal amino acid residue allows splitting of the target product from the solid phase under very mild conditions under the action of base. The linkers can be attached directly to the support, *e.g.*, to PEG-PS containing an amino group.^{53, 103}

The use of *N*-protected 6-aminohexyl succinate **56** as a linker has been described.⁵³



Commercially available CPG containing 3-aminopropyl groups was used^{95–97, 100–102} for the synthesis of peptide–oligo-

nucleotide conjugates. In this case, chemical modification of the solid support was reduced to the acylation of 3-aminopropyl groups by activated esters of 4-hydroxybutyric^{95–97} or 10-hydroxydecanoic acid^{100–102} with the hydroxy groups protected as acid-labile dimethoxytrityl and pixyl (9-phenyl)xanthen-9-yl derivatives. Two additional ϵ -aminocaproic acid molecules were introduced between the 4-hydroxybutyric acid residue and the aminopropyl support.⁹⁷ Lukhtanov *et al.*⁹⁹ used porous glass modified by an extended linker containing a terminal NH_2 group. The latter was acylated with the activated ester **57**.



It is of note that the addition of the first amino acid to the support and the formation of the amide bond in the course of solid-phase synthesis of peptide fragments are usually carried out by the methods involving carbodiimide, activated esters or symmetrical anhydrides.

c. Protective groups

Temporary protection of α -amino groups of amino acids is mainly accomplished using Boc^{53, 99, 101–103, 106–110} or Fmoc^{95–98, 100} groups. Sequential solid-phase synthesis of peptide and oligonucleotide fragments demands protection of reactive side groups of certain amino acid residues. Protective groups are selected in order to ensure selective removal of other groups. The Fmoc^{53, 101, 103, 104} or the Boc group^{95, 96} are most commonly used for the protection of ϵ -amino groups of lysine; trifluoroacetyl (Tfa)¹⁰⁴ and 1-(4,4-dimethyl-2,6-dioxocyclohexylidene)ethyl (Dde)¹⁰⁰ protective groups are used less frequently. The latter withstands splitting of the N^α -Fmoc group by treatment with 20% piperidine in DMF. The β -carboxy group of aspartic acid is protected by conversion into 9-fluorenylmethyl ester.^{53, 103, 106, 108} The possibilities for the protection of the indole (in) ring of tryptophan are rather limited. N^in -Formyl protection is one of them. It is stressed¹⁰⁴ that the use of this protection in the synthesis of peptide–oligonucleotide conjugates prevents the formation of side product. Marchan *et al.*¹⁰⁴ have succeeded in obtaining Boc-Arg(Fmoc)₂-OH which can be used in the solid-phase synthesis of the peptide fragment of the conjugate.

It is known¹¹¹ that unprotected amide groups of asparagine or glutamine residues in the peptide fragments of conjugates can undergo phosphorylation during subsequent elongation of the oligonucleotide chain. However, this side reaction proceeds at a very low rate which excludes the necessity of blocking side groups of asparagine and glutamine.^{53, 104}

Grandas *et al.*^{109, 110, 112} protected the hydroxy group of homoserine by the dimethoxytrityl group leaving the HO groups of serine, threonine and tyrosine unprotected.^{106–110} Other authors¹⁰¹ recommend protecting the hydroxy groups of serine as allyl carbonates. Assuming that the use of the Fmoc-strategy of solid-phase peptide synthesis may result in partial cleavage of this protective group, the authors gave preference to the Boc-strategy.

Despite the vast variety of techniques for the protection of the imidazole (im) ring of histidine, no ideal protective group has been

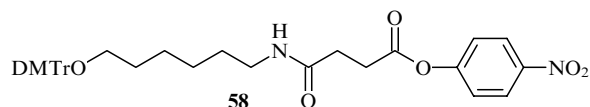
found for this compound. In the synthesis of peptides containing this amino acid, N^im -benzyloxymethyl protection was used and deprotection was effected by catalytic hydrogenolysis over palladium black in the presence of cyclohexa-1,4-diene. According to Truffert *et al.*,¹⁰² such a treatment should not have any negative effect on the stability of the oligonucleotide fragment of the conjugate. However, this method can hardly be considered satisfactory, since the authors failed to completely remove the peptide–oligonucleotide conjugate formed from the catalyst's surface.

The use of the Boc or the Fmoc groups for the protection of the imidazole ring of histidine cannot be recognised as very convenient either. The reason is that treatment of the peptide–oligonucleotide conjugate with trifluoroacetic acid to remove the N^im -Boc group can result in hydrolysis of the N-glycosidic bonds in purine nucleotides, whereas the N^im -Fmoc group is rather labile under conditions of the solid-phase synthesis. In the authors' opinion,¹⁰² the tosyl (Tos) group is especially convenient for the protection of the imidazole ring of histidine. This group is removed under the action of 1-hydroxybenzotriazole commonly added to the reaction mixture in order to inhibit racemisation in the formation of the peptide bond promoted by DCC. Two procedures for the protection of the imidazole ring of histidine by the tosyl and 2,4-dinitrophenyl groups have been developed by Beltrán *et al.*¹¹⁰ These authors share the opinion that 1-hydroxybenzotriazole can be replaced by tetrazole which has proved to be an efficient reagent when combined with DCC. The analysis of reversed-phase HPLC data led the authors to conclude that the use of Boc-His(Tos)-OH and deprotection of the imidazole ring immediately prior to the elongation of the oligonucleotide chain is the most efficient approach to the solid-phase synthesis of the peptide fragment.

d. Introduction of the linker

After termination of solid-phase synthesis of the peptide component of the conjugate containing a hydroxy amino acid residue,[‡] deprotection of the α -amino group is followed by its repeated selective protection by introducing the phenylacetyl (Pac)^{106–108, 113} or the acetyl (Ac) group^{109, 110} after which the oligonucleotide synthesis is performed (Scheme 20).

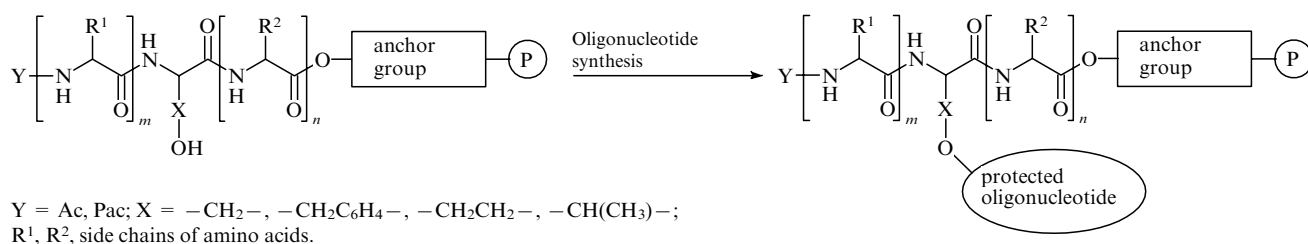
If the peptide fragment of the conjugate is devoid of hydroxy amino acids, deprotection is followed by acylation of the free α -amino group by a compound containing an activated carboxy group and a protected hydroxy group.^{53, 95–103} *p*-Nitrophenyl *O*-pixyl-4-hydroxybutyrate,^{97, 99} *p*-nitrophenyl^{100, 101} and pentafluorophenyl¹⁰² *O*-dimethoxytrityl-10-hydroxydecanoates and compound **58**^{53, 95, 96, 103} are used as acylating reagents.



The incorporation of the aliphatic OH group into the peptide and its further selective deprotection make the synthesis of the DNA fragment possible.

[‡] For incorporation of homoserine into the peptide chain, N^α -Pac-*O*-DMTr-Hse is introduced into the condensation reaction in the form of the triethylammonium salt.^{109, 110}

Scheme 20



e. Synthesis of the oligonucleotide fragment

In the studies^{95–102} where CPG was used as a solid support, automated solid-phase phosphoramidite synthesis of an oligonucleotide component of a conjugate was carried out according to a standard protocol. If a copolymer of styrene with ethylene glycol^{53, 103} or a copolymer of styrene with 1% divinylbenzene^{106–113} are used as polymeric supports, the standard procedures had to be modified in order to increase the yields in each step of the oligonucleotide synthesis. These modifications include a severalfold increase in the time required for implementation of all the main steps of internucleotide bond formation, the use of 5-(2-nitrophenyl)tetrazole instead of tetrazole and a significant increase in the concentration of the nucleotide solution in dichloromethane.

In the overwhelming majority of studies, the elongation of the oligomeric chain was carried out in the direction 3'→5' except for the cases where 5'-phosphoramidites of protected deoxynucleosides were used as monomeric components.^{106–108} Labile protective groups^{106, 108, 109, 113} were used together with acyl ones for the protection of exocyclic amino groups of heterocyclic bases. For instance, the *N,N*-dimethylformamidine and *tert*-butylphenoxyacetyl groups were used for the protection of the NH₂ groups of adenine and guanine, while the isobutyryl and the *tert*-butylphenoxyacetyl groups were used for cytosine.

f. Cleavage of conjugates from the solid support and deprotection of functional groups

The problem which has to be solved for the successful solid-phase synthesis of peptide–oligonucleotide conjugates by stepwise elongation of peptide and oligonucleotide chains is to find optimal conditions for the deprotection of functional groups and cleavage of the bonds between the conjugate and the support. Thus it is not recommended to liberate the conjugate from the support by treatment with strong acids or by using acid-labile protective groups because of the risk of partial apurinisation of DNA. For this reason, in the majority of studies post-synthetic treatments were carried out under mild basic conditions. The apprehensions that alkaline treatment might lead to racemisation of the amino acid residues at the α -carbon atom were not confirmed.⁵³ It was noted also that alkaline treatment of conjugates in which the peptide is linked to the oligonucleotide through a serine residue favours the cleavage of the phosphodiester bond between the two fragments.^{3, 4} This reaction includes cleavage of the C–O bond and occurs as base-catalysed β -elimination (see Scheme 2). However, a detailed analysis of this problem showed¹⁰⁸ that treatment of conjugates with a concentrated aqueous ammonia–dioxane mixture (1 : 1) at room temperature for 15–24 h did not cause the cleavage of the bond between the oligonucleotide fragment and the serine residue.

A convenient procedure was developed^{106–109} for the liberation of peptide–oligonucleotide conjugates from the solid phase by treatment with 0.05 M tetrabutylammonium fluoride in tetrahydrofuran at room temperature for 30–60 min. Such treatment ensures simultaneous removal of β -cyanoethyl protective groups from internucleotide phosphates and splitting of the 9-fluorenylmethyl ester of aspartic acid. This is followed by deprotection of exocyclic amino groups of heterocyclic bases under the action of a mixture of concentrated aqueous ammonia and dioxane (1 : 1) at room temperature for 15–18 h. The latter procedure was also carried out at 55 °C (see Ref. 110). Apparently, more drastic conditions were required for the removal of the isobutyryl protective group from the exocyclic amino group of the guanine base in the DNA fragment. The same procedure was used for the removal of some other protective groups, *e.g.*, the tosyl and the 2,4-dinitrophenyl groups (from histidine).

However, an attempt of de la Torre *et al.*⁵³ to liberate a peptide–oligonucleotide conjugate from the polymeric support (PEG-PS) using tetrabutylammonium fluoride failed. It was assumed that polyethylene glycol, which is a constitutive element of the support, prevents β -elimination catalysed by the fluoride

ion. The use of tetrabutylammonium fluoride is also unacceptable for the liberation of those peptide–oligonucleotide conjugates in which the components of the conjugate are linked through the hydroxy group of tyrosine. In this case, the two parts of the hybrid molecule are linked through a phosphotriester bond. It is therefore quite probable that the nucleophilic attack of the fluoride ion at the phosphorus atom will be accompanied by the cleavage of the P–O bond with the formation of a stable phenoxide ion. Therefore, Robles *et al.*¹⁰⁹ proposed to use a mixture of concentrated aqueous ammonia and dioxane (1 : 1) at 55 °C for 18 h for the liberation of the peptide–oligonucleotide conjugate from the solid support. It should be noted that the carboxy group of the C-terminal amino acid is converted into the amide group under these conditions.

The use of concentrated aqueous ammonia for the cleavage of peptide–oligonucleotide conjugates from the solid support and concomitant removal of protective groups yielded a mixture of products.^{53, 96} This can be explained by the fact that the cleavage of the ester bond under the action of concentrated ammonia is accompanied by the formation of both an amide and an ammonium salt. Prior to ammonolysis, the oligonucleotide–peptidyl polymer was treated with a solution of 0.5 M 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in acetonitrile.⁵³ This made it possible to remove the *N*⁶-Fmoc and β -cyanoethyl groups and to cleave the 9-fluorenylmethyl ester of aspartic acid. In the authors' opinion, this reaction order should exclude the conversion of the ester into the amide.

In order to liberate the protected peptide–oligonucleotide conjugate from the support, Truffert *et al.*¹⁰⁰ used a 50% solution of ethanolamine in absolute ethanol (60 °C, 30 h). The final product was obtained in the form of monoethanolamide in a very low yield. To increase the yield, Truffert *et al.*^{101, 102} used 0.1 M NaOH instead of ethanolamine. Under these conditions, hydrolysis of the ester bond between the peptide–oligonucleotide conjugate and the support is completed in 2 h at room temperature and is accompanied by a simultaneous removal of other protective groups, *e.g.*, the β -cyanoethyl groups from internucleotide phosphates, the tosyl group from histidine, the allyloxycarbonyl group from serine and the Fmoc or Dde groups from lysine. The authors note that deprotection of exocyclic amino groups of adenine, cytosine and guanine requires no less than 24 h.

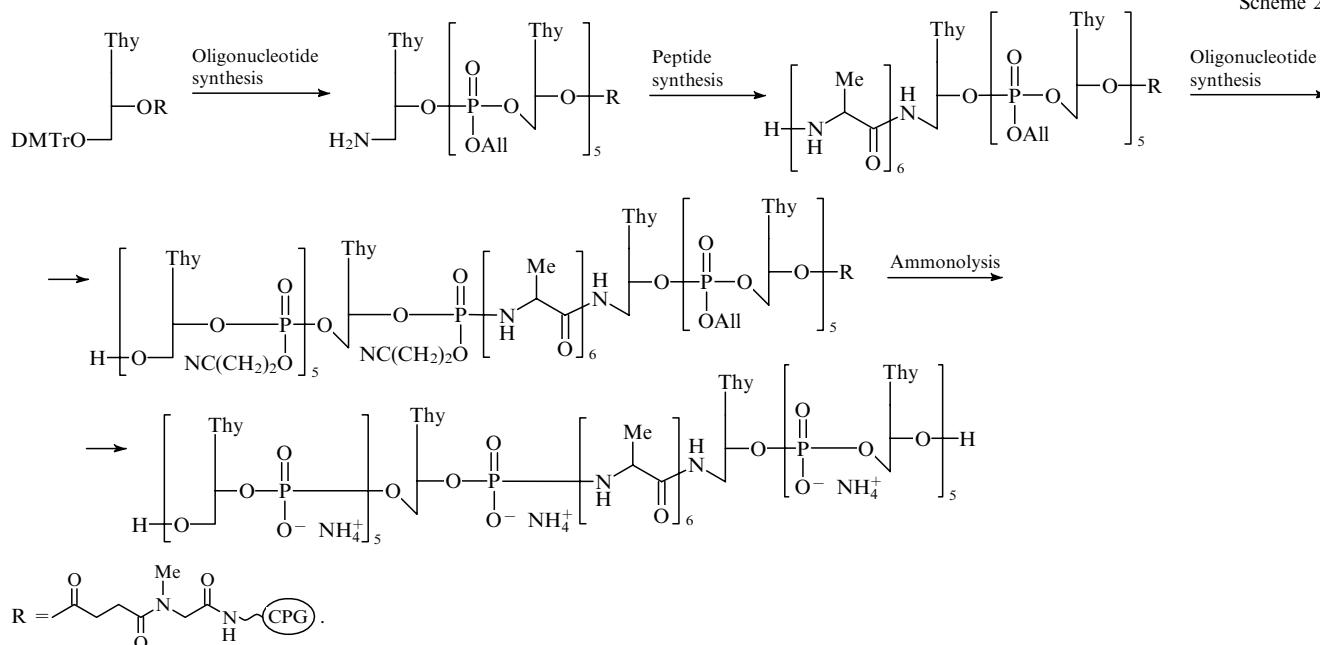
The use of the Boc-protection for the side amino group of lysine is undesirable, since its removal proceeds under rather drastic conditions [treatment with trifluoroacetic acid and 1,2-ethanedithiol (9 : 1) for 5 min^{95, 96}] which may lead to hydrolysis of *N*-glycosidic bonds in the oligonucleotide fragment and subsequent destruction of the target product.

2. Sequential synthesis of oligonucleotide and peptide fragments on the same solid support

In the studies considered above, peptide–oligonucleotide conjugates were prepared by stepwise synthesis, *viz.*, the peptide fragment of the hybrid molecule was first synthesised on a solid phase after which it was possible to proceed to the synthesis of the oligonucleotide chain. In an alternative approach, the DNA fragment is synthesised first. The main limitation of this method is the impossibility of using the Boc-strategy for the peptide synthesis.

The solid-phase synthesis of oligonucleotides with a 5'-terminal reactive NH₂ group has been described.^{114–117} To this end, the 5'-amino-5'-deoxythymidine residue was incorporated into the oligomeric chain in the final step of automated phosphoramidite synthesis. The nucleoside thus modified plays the role of a linker between the oligonucleotide and the peptide fragments of the conjugate. The Fmoc-strategy was used for the elongation of the peptide chain by Bergmann and Bannwarth¹¹⁴ (Scheme 21); the activation of the carboxy group was carried out *in situ* using *O*-(benzotriazol-1-yl)-*N,N,N'*-tetramethyluronium hexafluorophosphate (HBTU). The allylic group was selected as the phosphate-protective group instead of the β -cyanoethyl group

Scheme 21



commonly used for this purpose, because in this study the Fmoc-group was removed by a strong base (DBU) instead of piperidine. For the same reason, the solid-phase synthesis was carried out on modified CPG. To ensure the stability of the bond between the oligonucleotide and the support during DBU treatment, a sarcosine residue was incorporated into the anchor group.

After termination of the synthesis of the peptide fragment, synthesis of another oligonucleotide chain was begun with the use of 2-cyanoethyl *N,N*-diisopropylphosphoramidites of 2'-deoxynucleosides. This procedure afforded conjugates in which two DNA fragments were linked through a peptide fragment. These were liberated from the solid support by consecutive treatment with $\text{Pd}[\text{PPh}_3]_4$ and morpholine in a $\text{DMSO}-\text{THF}-\text{dioxane}-0.5\text{ M HCl}$ mixture (2:2:2:1) at 60°C for 3 h and then with 30% aqueous ammonia at room temperature for 2 h. It should be noted that the bond between the peptide and the second oligonucleotide is of a phosphoramidate type, which is not cleaved in the post-synthetic deprotection of the peptide-oligonucleotide conjugate and its liberation from the solid support.

An analogous synthetic scheme was developed for the preparation of conjugates in which the oligonucleotide fragment is a heteropolymer.^{115, 116}

Special mention should be made of one of the most recent studies carried out by Bleczinski and Richter¹¹⁷ which describe a procedure for the preparation of cyclic peptide-oligonucleotide conjugates. Fmoc-protected amino acids and All-protected nucleoside phosphoramidites were used as the starting compounds. This approach was used to obtain the cyclic hybrid Glu-Leu-T**T*-DP-Lys (**59**) (T* is 5'-amino-5'-deoxythymidine, DP is 3-hydroxy-2,2-dimethylpropionic acid). The amide bond of the 'head-to-tail' type was formed by the ϵ -amino group of lysine and the γ -carboxy group of glutamic acid. The structure of compound **59** was confirmed by ^1H NMR spectroscopy and MALDI-TOF mass spectrometry. The cyclic conjugate appeared to be resistant to exo- and endonucleases. By varying the peptide fragment, it was possible to obtain an analogous 39-membered ring.

3. Synthesis of peptide-oligonucleotide conjugates on solid supports with a bifunctional branched anchor group

An approach to the synthesis of peptide-oligonucleotide conjugates proposed in the early 1990's¹¹⁸⁻¹²¹ and further successfully developed in the studies carried out in the past three years¹²²⁻¹²⁵ is of considerable interest. The oligonucleotide

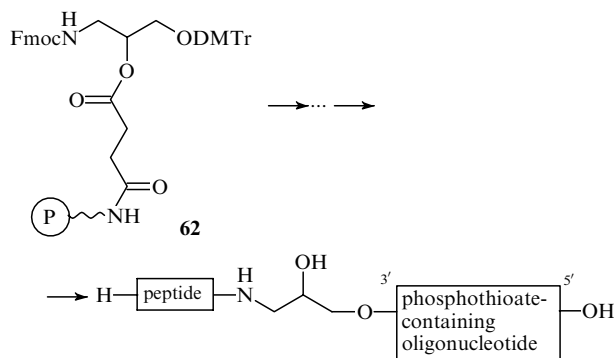
syntheses were performed on solid supports with branched anchor groups containing HO and NH_2 groups. The presence of this group allows sequential attachment of monomeric units, first, of one type and then, of another type, on the same support. Post-synthetic treatments result in a hybrid molecule in which the oligonucleotide and the peptide fragments are connected through a linker. The distinctive feature of this method is that the bifunctional[§] linker is attached directly to the solid phase rather than to one of the fragments of the synthetic conjugate. 3-Aminopropane-1,2-diol¹¹⁸ and 6-amino-2-hydroxymethylhexan-1-ol¹¹⁹ can be used as linkers. The hydroxy and amino functions are protected by the DMTr and Fmoc groups commonly used for this purpose.

In these studies,^{118, 119} the peptide fragment was synthesised first. In the peptide synthesis, the ϵ -amino group of lysine was protected by the Boc group; the hydroxy group of serine and the thiol group of cysteine were protected by the *tert*-butyldimethylsilyl (TBDMS) and trityl (Tr) groups, respectively, whereas the amino groups of adenine and guanine were protected by the 2-(acetyloxymethyl)benzoyl group, while those of cytosine were protected by the acetyl group.

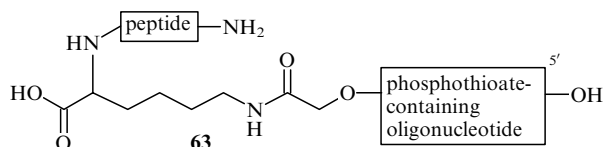
The main difference in the approaches proposed by Canadian¹¹⁸ and American¹¹⁹ investigators consists in the choice of an insoluble support and the method for its chemical modification.

The polymer employed by the Canadian investigators Juby *et al.*¹¹⁸ was commercially available Teflon to which 5'-*O*-dimethoxytrityl-2',3'-di-*O*-acetyladenosine was attached through an extended linker. The first step was the selective removal of the DMTr protective group from the 5'-hydroxy group followed by the introduction of a protected 3-aminopropane-1,2-diol residue using the amidite strategy to yield derivative **60** (Scheme 22). This was employed for the peptide and then for the oligonucleotide synthesis. After completion of the peptide and oligonucleotide syntheses, the functional groups were deprotected under mild conditions by treatment with ethylenediamine in absolute ethanol (1:1) at 55°C for 1 h. (This procedure for the removal of protective groups was specially developed in the synthesis of oligonucleotide methylphosphonate derivatives.) The cleavage of the target product from the solid phase was carried out in two steps. At first, the *cis*-glycol group of the 2',3'-di-*O*-acetyl

[§]It would be more correct to speak about a tri- rather than about a bifunctional linker, since it contains one more reactive group involved in the formation of a covalent bond with a solid support.



Later, the same authors¹²⁵ performed the synthesis of the peptide–oligonucleotide conjugate **63** using a polymeric support with a branched linker.



4. Synthesis of oligonucleotide peptides by fragment condensation

The essence of this method is in the formation of a covalent bond between the presynthesised peptide and the oligonucleotide after completion of the automated oligonucleotide synthesis but prior to the cleavage of the nucleic acid fragment from the solid support. The main advantage of this approach is that one component of the conjugate is not exposed to the effect of chemical reagents used for the synthesis of the other component as is the case with sequential solid-phase synthesis of peptide–oligonucleotide conjugates.

Very often, peptide–oligonucleotide conjugates are prepared by the reaction of an oligonucleotide containing free 5'-hydroxy groups and immobilised on an insoluble support with a peptide phosphoramidite derivative in the presence of tetra-zole.^{108, 111, 126–133} The peptide phosphoramidite derivatives can be prepared in good yields by the reaction of the hydroxy group of serine or tyrosine with a standard phosphitylating reagent.^{108, 126–132} It was also proposed to phosphitylate the C-terminal amide group of the peptide.^{111, 133}

As in the case of other methods for the synthesis of peptide–oligonucleotide conjugates, the main efforts of investigators were directed at a search for the mildest conditions for post-synthetic treatment. This is especially important in those cases where the formation of the phosphodiester bond between the oligonucleotide and the peptide fragments of the conjugate involves the serine residue. Such compounds destroy under alkaline conditions. In contrast, those molecules, which contain phosphoramidate bonds, are unstable in strongly acidic media.

van Boom *et al.*¹²⁸ protected the α -amino group of the peptide by the *p*-nitrobenzyloxycarbonyl group and the ω -carboxy groups of aspartic and glutamic acids were converted into *p*-nitrobenzyl esters. These protective groups are removed simultaneously with a sodium dithionite–sodium hydrogencarbonate mixture. The exo-

cyclic amino groups of the heterocycles were protected by the 2-(*tert*-butyldiphenylsilyloxymethyl)benzoyl group. Oxalic acid served as a linker between the first nucleoside and the polymer.¹²⁸ Liberation of the target product from the solid phase with simultaneous deprotection of heterocyclic bases and internucleotide phosphates was carried out using tetrabutylammonium fluoride in aqueous pyridine.

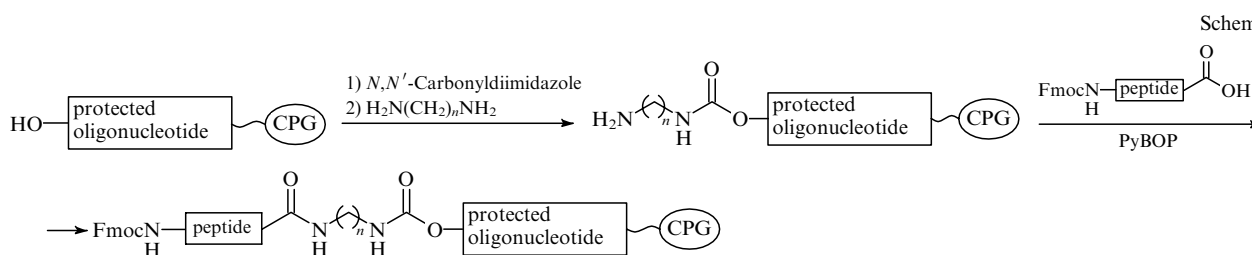
It is known that allyloxycarbonyl and allyl protective groups are split off under mild conditions. These groups were used^{129–131} for the protection of the functional groups of the oligonucleotide (exocyclic amino groups of heterocyclic bases, internucleotide phosphates) and the peptide (terminal NH₂ and COOH groups) fragments. These protective groups are easily removed by a palladium complex in the presence of diethylammonium formate.

The synthesis of peptide–oligonucleotide conjugates containing nucleotidyl-(5'→O)-serine fragments was performed using protection of the lateral carboxy group of aspartic acid by any of the three esters, *viz.*, 9-fluorenylmethyl, benzyl or 2-(2-nitro-4-acetylphenyl)ethyl esters.¹⁰⁸ The exocyclic amino groups of adenine residues were protected by benzoyl or *N,N*-dimethylformamidino group. The cleavage of the peptide–oligonucleotide conjugate from the solid support and removal of protective groups were carried out using three different methods, *viz.*, by treatment with concentrated aqueous ammonia, potassium carbonate or lithium hydroxide in a methanol–dioxane mixture. It is of note that the authors¹⁰⁸ failed to correctly characterise the target product and to confirm its structure by mass spectrometry and amino acid analysis data.

The methods for the synthesis of conjugates containing an amide bond between the oligonucleotide and the peptide fragments were considered in the section devoted to the solution synthesis of peptide–oligonucleotide conjugates (see Section II.3). The difficulties reported in the publications^{38, 39} could be largely overcome by performing the solid-phase condensation of the oligonucleotide and the peptide components, which significantly increased the yield of the target product. The decomposition of diazoketone **37** (see Scheme 10) was carried out in the presence of silver benzoate rather than under UV irradiation in the apprehension that in the latter case the reaction rate would decrease due to partial absorption of energy by the solid support (polystyrene or CPG).³⁹

The condensation of the pentapeptide Ac-Ala-Tyr-Gln-Val-Phe with tri- and tetranucleotides containing 5'-terminal 5'-amino-5'-deoxythymidine residues and immobilised on a solid phase was reported by Tetzlaff *et al.*¹¹⁵ However, these authors drew attention to the low efficiency of this reaction, which they attributed to the low solubility of the peptide in dimethylformamide.

The recently published data deserve special mentioning. Thus, Gait *et al.*^{134, 135} used the following approach for the incorporation of an aliphatic amino group into the DNA fragment: the 5'-hydroxy group of the CPG-linked oligonucleotide following removal of the terminal DMTr protective group was activated by *N,N*-carbonyldiimidazole and introduced into the reaction with a diamine (Scheme 25). When PyBOP was used as a condensation reagent in the presence of 1-hydroxybenzotriazole, the degree of racemisation at the α -carbon atom of the C-terminal amino acid was very small. Nevertheless, peptides containing C-terminal



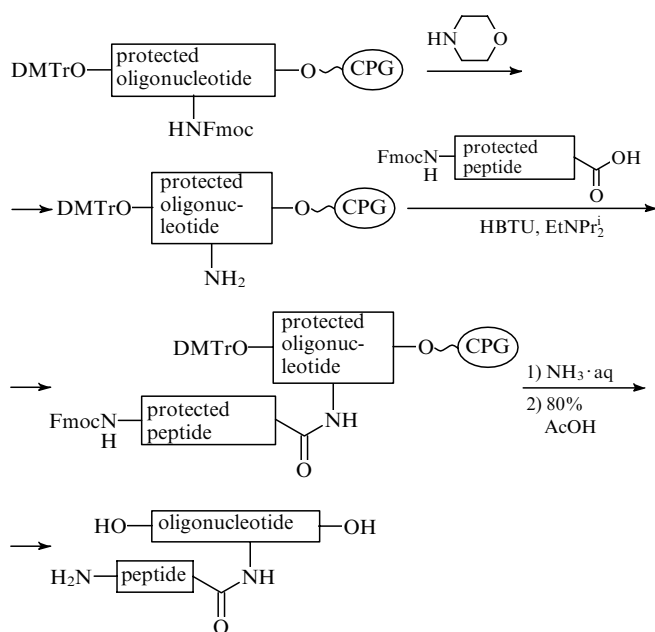
$n = 3, 6, 12$.

glycine were selected for conjugation to oligonucleotides, since in this case the α -carboxy group of the peptides could be activated without any risk of racemisation. A tetrapeptide containing non-polar amino acid residues and an octapeptide built up of polar amino acids were used as peptide fragments, while various homo- (e.g., T₁₂) and heterooligonucleotides were used as oligonucleotides. The conjugation of both peptides to T₁₂ proceeded with high efficiency.^{134, 135} However, the yields of peptide–oligonucleotide conjugates prepared by condensation with heterooligonucleotides were very low. The authors failed to explain the reason for this phenomenon. Neither did the changes in experimental conditions, *i.e.*, the use of PEG-PS instead of CPG, a larger peptide excess (10 instead of 5 equiv.) and higher temperature (40 °C), give any positive result.

It was suggested that the main problem is related to poor solubility of protected heterooligonucleotides in dimethylformamide due to their high hydrophobicity. This problem was overcome by selective removal of β -cyanoethyl protective groups by triethylamine in acetonitrile which caused some increase in the yields of the target products. In the majority of cases, the elongation of the linker containing the amino group also had a beneficial effect on the conjugate yields.

A modification of this reaction was employed¹³⁶ in the condensation of a presynthesised peptide with a blocked oligonucleotide immobilised on a solid phase and containing a linker attached to the C(2')-atom of the carbohydrate fragment (Scheme 26). Oligodeoxyribonucleotides employed contained either three modified nucleosides, *viz.*, 2'-(3-aminopropionyl)-amino-2'-deoxy-*arabino*-adenosine, 2'-(3-aminopropionyl)amino-2'-deoxyuridine or 2'-amino-2'-deoxy-*arabino*-adenosine.

Scheme 26



First, the Fmoc-protected amino group attached to the C(2')-atom of the carbohydrate fragment of one of nucleotide residues either directly or through a linker was selectively deprotected with 50% morpholine in dimethylformamide for 1 h. Then the oligonucleotide with the free NH₂ group reacted with a protected peptide fragment.

Two short peptides, *viz.*, *N*^α-Fmoc-Leu-Gly and *N*^α-Fmoc-Tyr-D-Ala-Phe-Gly, were selected as peptide fragments. In both cases, the C-terminal amino acid residue was represented by a glycine residue. The latter circumstance is very important, since in this case the activation of the carboxy group of the peptides was not accompanied by racemisation due to the absence of a chiral carbon atom in the glycine molecule.

The reaction of the *N*^α-blocked peptide with the oligodeoxyribonucleotide immobilised on CPG-500 was carried out in anhydrous dimethylformamide in the presence of HBTU and ethyldiisopropylamine. The reaction was complete within 1–2 h and gave high yields (80%–90%). In the final step, the conjugate was cleaved from the solid support and the functional groups of the oligonucleotide and the peptide components were deprotected.

The use of the solid-phase method requires large excesses of the peptides and the condensation reagent. This increases the efficiency of formation of the amide bond; the excesses of dimethylformamide-soluble reagents are easily removed by thorough washing of the support.

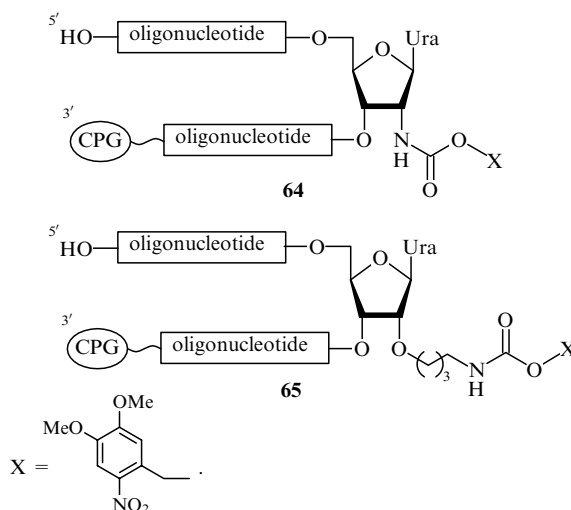
The main advantage of Fmoc protection of amino groups is that this can be removed in two ways. The first approach entails post-synthetic treatment of the oligonucleotide with saturated aqueous ammonia. The second approach consists of the removal of the Fmoc group with morpholine in an anhydrous medium, which allows selective deprotection of the aliphatic amino group of the oligonucleotide. Under these conditions, the oligonucleotide is not split from the support, and its other functional groups remain protected.

An approach proposed by Zubin *et al.*¹³⁶ allows simultaneous attachment of several peptide fragments to the oligonucleotide, since the modified nucleoside fragment containing an aliphatic amino group can be inserted into any predetermined position of the oligomeric chain and the number of inserts is not limited in principle. Another salient advantage of this approach is that the 5'- and 3'-ends of the oligonucleotide fragment of the conjugate remain free, which allows the attachment of various reporter groups, *e.g.*, radioactive or fluorescent labels.

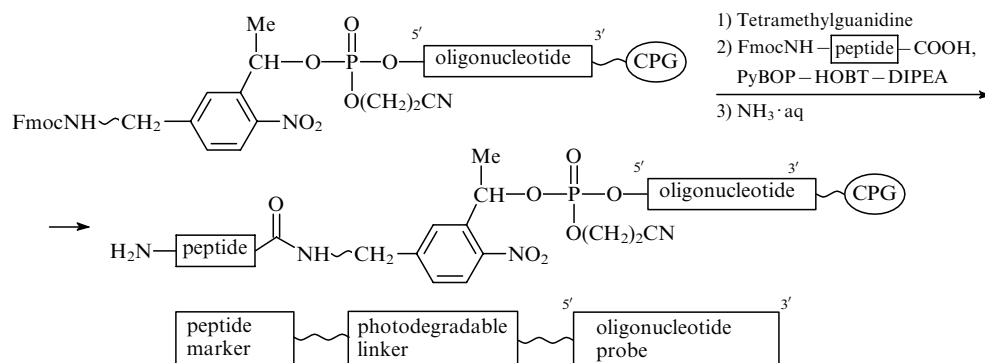
Certain difficulties arise when this method is used for the synthesis of oligonucleotide conjugates with larger peptides. The problem is associated with the activation of carboxy groups. Moreover, this method demands the use of large excesses of peptides, which is hardly justified from the economical point of view.

The approach based on successive attachment of small peptide fragments to oligonucleotides is an alternative. After attachment of the first fragment, the *N*^α-Fmoc group has to be removed, after which the next fragment is introduced into the reaction. *N*^α-Fmoc-Leu-Gly and *N*^α-Fmoc-Tyr-D-Ala-Phe-Gly were used for the synthesis of oligodeoxyribonucleotide conjugates with peptides containing four and eight amino acid residues.

A similar ideology is shared by Hwang and Greenberg^{137, 138} who have succeeded in incorporating 2'-modified phosphoramidite synthons into different positions of the oligonucleotide chain in the course of automated synthesis. The amino group at the C(2') atom of the synthon was protected by the photolabile protective group (X).

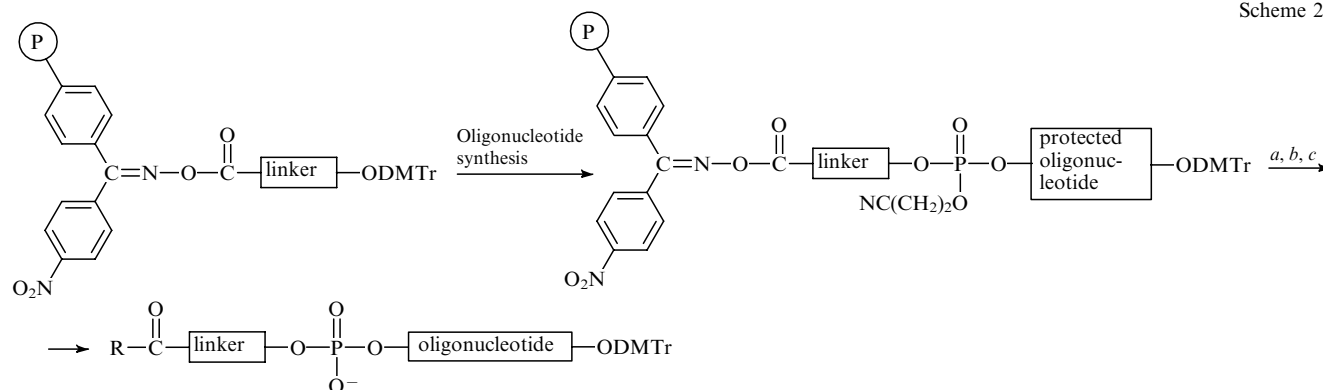


Scheme 27



DIPEA is diisopropylethylamine.

Scheme 28



Linker is $-(CH_2)_6-$, $-Gly-NHCO(CH_2)_6-$, $-Gly-Gly-Gly-NHCO(CH_2)_6-$;

(a) EtNPr₂ⁱ; (b) RH (RH is H-Gly-Gly-Gly-NEt₂ or H-Leu-Ala-Lys(Tfa)-Leu-NEt₂); (c) NH₃·aq.

The attachment of tripeptides to the modified oligonucleotides **64** and **65** afforded the corresponding conjugates with satisfactory (70%–80%) yields.

The synthesis of photodegradable peptide-oligonucleotide conjugates designed for detection of target NA sequences by the MALDI mass spectrometry methods has been described (Scheme 27).¹³⁹

The photodegradable conjugate contains an oligonucleotide probe for target DNA or RNA sequences and a peptide mass marker easily detectable by mass spectrometry after hybridisation and subsequent photodegradation of the conjugate.

A special polymer with ketoxime functional groups was proposed for oligonucleotide synthesis (Scheme 28).^{140,141} The anchor group (linker) was attached to the support through an ester bond. The use of such supports facilitates the cleavage of the target product under the action of nucleophiles, the role of a nucleophile can be played by the peptide fragment.

IV. Conclusion

The analysis of published data suggests that no versatile method for the synthesis of peptide-oligonucleotide conjugates of any structure exists. This is due to the fact that several factors play crucial roles in the synthesis of peptide-oligonucleotide conjugates, viz., the type of modified nucleic acid fragment, the amino acid sequence, the size of the peptide, the conjugation procedure and the type of bond connecting the two parts of the hybrid molecule. The possibility of varying these parameters within a sufficiently broad range and of using their different combinations have given a strong impetus to the appearance of numerous publications devoted to novel methods for the synthesis of peptide-oligonucleotide conjugates. However, because of serious limitations of each of these methods, very few of them have found

wide acceptance in the preparative synthesis of peptide-oligonucleotide conjugates. In this connection, a search for optimal approaches to the synthesis of peptide-oligonucleotide conjugates still remains a very urgent task.

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Theoretical studies of transition metal complexes with nitriles and isocyanides

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Abstract. Theoretical studies of transition metal complexes with nitriles and isocyanides are reviewed. The electronic structures and the nature of coordination bonds in these complexes are discussed. The correlation between the electronic structures of transition metal complexes with nitriles and isocyanides and their structural properties, spectroscopic characteristics, and reactivities are considered. The bibliography includes 121 references.

I. Introduction

It is known that free nitriles ($N \equiv CR$) and isocyanides ($C \equiv NR$) containing no strong acceptor substituents R are poorly reactive or even inert in a number of processes, for example, in nucleophilic addition. If these molecules are involved as ligands in transition metal complexes, the situation reverses because complex formation leads to activation of nitrile and isocyanide ligands. Reactions, which proceed under drastic conditions, if at all, with free nitriles and isocyanides, every so often occur under relatively mild conditions with coordinated ligands. In some reactions with coordinated ligands, the rate is increased by a factor of 10^{18} as compared to that in the reaction with the corresponding free ligand.^{1–4} Nitriles and isocyanides thus activated can be used in the synthesis of new compounds with the $C-O$, $C-N$, $C-C$, $C-S$ and $C-P$ bonds, which cannot be prepared without resorting to transition metals. Cycloaddition of the corresponding reagents to the inner-sphere nitrile and isocyanide ligands affords tetrazoles and oxadiazolines, respectively, which are widely used in pharmacology.

The design of new antitumour drugs is yet another field of application of nitrile complexes. Thus the imino-ether compounds *trans*-[PtCl₂{NH=C(OMe)Me}₂] prepared by the nucleophilic addition of methanol to the [PtCl₂(NCMe)₂] complex exhibited high antitumour activity.^{5,6} This result was unexpected because *cis* isomers of platinum complexes with N-donor ligands generally show higher antitumour activity as compared to the corresponding *trans* isomers.

Coordinated nitriles also find application in catalysis. For example, large-scale production of acrylamide and nicotinamide is based on catalytic (including, catalysis by metal ions^{4,7–9}) hydrolysis of nitriles. Metal-promoted hydrolysis of nitriles and isocyanides can be used for detoxication of industrial wastes containing these compounds. Finally, some nitrile complexes of transition metals possess nonlinear-optical properties.^{10,11}

Interesting properties of transition metal complexes with nitriles and isocyanides and their wide industrial applications have given impetus to a substantial increase in the number of publications devoted to these compounds. The results of experimental studies of their reactivities have been surveyed in reviews.^{1,4,12–17} However, the data from theoretical investigations of nitrile and isocyanide coordination compounds were not systematised. At the same time, transition metal complexes with other ligands have been extensively studied by quantum-chemical methods[†] in the last decade. These investigations were motivated primarily by the necessity of interpreting and systematising the ever-growing body of experimental information. Besides, theoretical methods are sometimes the only tool in studying unstable compounds and intermediates formed in the course of many chemical reactions.

In this review, the results of theoretical investigations of transition metal complexes with nitriles and isoelectronic isocyanides are generalised. The electronic structures and the nature of coordination bonds in these compounds are discussed. The correlations between the electronic structures of these complexes and their structural characteristics, spectroscopic properties, and reactivities are considered. Studies concerned with analysis of interactions between ligands and some transition metals are partially included for comparison.

II. Electronic structures of complexes and the nature of coordination bonds

Two models, *viz.*, the ligand field theory and the Dewar–Chatt–Duncanson (DCD) model, are most commonly used for the qualitative description of the nature of coordination bonds in transition metal complexes. The latter model is applied to complexes containing ligands with multiple bonds. These theories are based on the molecular orbital method and treat the formation of coordination bonds as a result of interactions between the valence

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[†] The results of theoretical studies of transition metal complexes (primarily, carbonyl, carbene, carbyne and π -complexes) are surveyed in reviews.^{18–24}

orbitals of the ligand and the metal atom. Of particular interest is the elucidation of the character of the highest occupied (HOMO) and lowest unoccupied (LUMO) molecular orbitals because they are primarily responsible for the chemical reactions and determine the spectroscopic and other physical properties of compounds.

Systematic studies of nitrile and isocyanide complexes by quantum-chemical methods were started only recently and most of the publications date back to 1990s.[‡] The DCD model^{25,26} is commonly used for the description of these complexes. According to this model, the metal–ligand coordination bond involves the σ -component, which originates from the transfer (donation) of the electron density from the occupied σ -orbitals of the ligand to the unoccupied d -orbitals of the metal atom, and the π -component resulting from π -back donation. By π -back donation is meant the electron density transfer from the highest occupied d -orbitals of the metal atom to the free valence antibonding π^* -orbitals of the ligand resulting in two-electron stabilisation of the frontier MOs of the complex. In addition, the π -component of the coordination bond often includes the contributions of the highest occupied π -orbitals of the ligand whose interactions with the occupied d -orbitals of the metal atom lead to destabilisation of the HOMOs (Fig. 1).

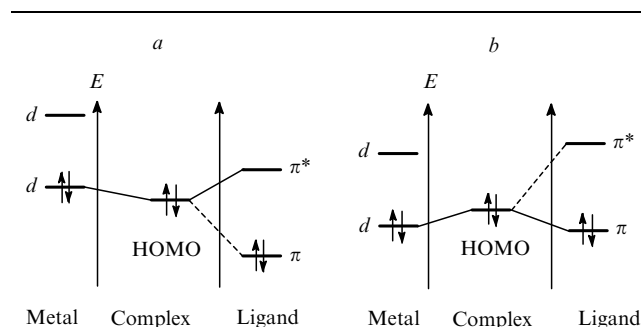


Figure 1. Scheme of formation of the HOMO of complexes containing ligands with multiple bonds.

(a) Ligands possessing strong π -acceptor properties, (b) ligands possessing weak π -acceptor properties.

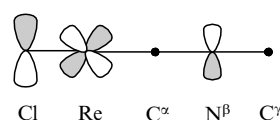
Apparently, the contributions of the π - and π^* -MOs of the ligand to the HOMO of the complex are determined by the relative energies of the valence orbitals of the metal atom and the ligand. The $d(\text{M})-\pi^*$ -MO(ligand) interaction prevails in the HOMOs of the complexes with ligands possessing strong π -acceptor properties [for example, the carbon(II) oxide or carbyne ligands] because the valence occupied d -orbitals of the metal atom are closer in energy to the π^* -MOs than to the π -MOs of the ligand (Fig. 1a), whereas the $d(\text{M})-\pi$ -MO(ligand) interaction dominates the HOMOs of the complexes with ligands exhibiting weak π -acceptor properties, such as nitriles, because the energies of the highest occupied d -orbitals of the metal atoms are similar to those of the occupied π -MOs of the ligand (Fig. 1b).

Until very recently, the extended Hückel theory (EHMO) was most commonly used in calculations of MOs of nitrile and isocyanide complexes. However, higher-level approximations, viz., the Hartree–Fock method (HF), the functional density theory (DFT), the second-order Møller–Plesset theory (MP2), etc., have found application in the last few years. The next section covers the results of studies devoted to the electronic structures and the nature of coordination bonds in transition metal complexes with isocyanides and nitriles.

[‡] It should be noted that theoretical studies devoted to isocyanide complexes and, particularly, to nitrile complexes are much smaller in number than those dealing with carbonyl compounds or π -complexes.

1. Electronic structures of isocyanide and nitrile complexes

The nature of coordination bonds and reactivities of the molybdenum diisocyanide complex *trans*-[Mo(CNMe)₂(dppe)₂] (dppe = Ph₂PCH₂CH₂PPh₂) and the rhenium isocyanide complexes *trans*-[Re(CNR)Cl(dppe)₂] (R = H, Alk, Ar) were studied.^{27,28} It was found that two of the highest occupied MOs of the molybdenum complex and the HOMOs of the rhenium complexes are formed *via* interactions of the d -orbitals of the metal atom with the π - and π^* -MOs of isocyanide. The HOMO of the molybdenum complex (Fig. 2) is bonding for the Mo–C bond and antibonding for the C≡N bond due to the predominant contribution of the π^* -MO of the ligand to the HOMO responsible for the π -back donation effect. However, the π -component of the metal–ligand bond is rather weak because of the small coefficients with which the AOs of the α -carbon atom are included into the HOMO of the complex under consideration. The contributions of the π - and π^* -MOs of isocyanide to the HOMOs of the rhenium complexes are approximately equal (the HOMO is a nonbonding orbital with respect to the Re–C bond).



The electronic structures of the [Pd₂(CNR)₂(μ-η³-L)₂] (L is indenyl) and [Pd₄(μ-CNR)₄(μ-OAc)₄] complexes, the model compounds [Pd₂(μ-CNH)₂(OH)₄]⁴⁻ and [Pd₂(μ-CNH)₂(OH)₄]²⁻ and the [Ni₂(CNH)(PH₂CH₂PH₂)₂] complex were examined at the EHMO level of theory.^{29,30} The highest occupied MOs of the last two mentioned complexes consist of the π_d^* -orbitals of the {Pd₂(OH)₄}²⁻ or {Ni₂(PH₂CH₂PH₂)₂} fragment and the π^* -MO of isocyanide. It was noted that the interaction between these orbitals in the former complex is rather weak. The lowest unoccupied MO of the nickel complex is a purely $\pi^*(\text{CNH})$ -orbital. For the indenyl complexes, the energy gap between the HOMO and LUMO was demonstrated to be rather large. As a consequence, these complexes exist in the singlet state, which accounts for the formation of the Pd–Pd bond.

The MOs of the model binuclear complex [Pd₂(CNMe)₄Cl₂] were calculated by the extended Hückel method³¹ with the aim of obtaining qualitative information on the nature of the frontier MOs and examining the dependence of the compositions of the MOs on the internuclear Pd–Pd distance and the torsion angle θ between the planes of two {Pd(CNMe)₂Cl} fragments. The orbitals of the metal atom make the major contribution to the HOMO and LUMO, the orbitals of the C α atom of isocyanide also making a particular contribution (the antibonding character of the Pd–C bond), whereas the AOs of the N β and C γ atoms of the isocyanide ligand contribute insignificantly to these orbitals. The composition of the MOs is virtually insensitive to variations in the torsion angle θ and the internuclear Pd–Pd distance.

The electronic structures and the nature of the coordination bonds in the isocyanide complexes M(CNBu^t)Me(CO)₂·(η⁵-C₅R₅) and the isomeric compounds [M(η²-CMe=NR')·(CO)₂(η⁵-C₅R₅)] and [M{η³-CH₂=CHNBu^t}(CO)₂(η⁵-C₅R₅)] (M = Mo, W; R = H, Me; R' = Prⁱ, Bu^t) were discussed based on the data from photoelectron spectroscopy and the results of EHMO calculations of the molecular orbitals carried out for model compounds.³² In the isocyanide complexes, the two highest occupied MOs are centred on the metal atom but the π^* -MOs of the carbonyl and isocyanide ligands also make particular contributions to these MOs giving rise to π -back donation [the π -MO(CNR) also makes a certain contribution to these MOs of the complexes].

Although the isocyanide ligands in many complexes possess noticeable π -acceptor properties, the contributions of the π - and π^* -MOs of the ligand to the HOMOs of the complex are in some cases insignificant and the HOMOs are centred on the metal atom. Thus calculations for the frontier MOs of the model complexes

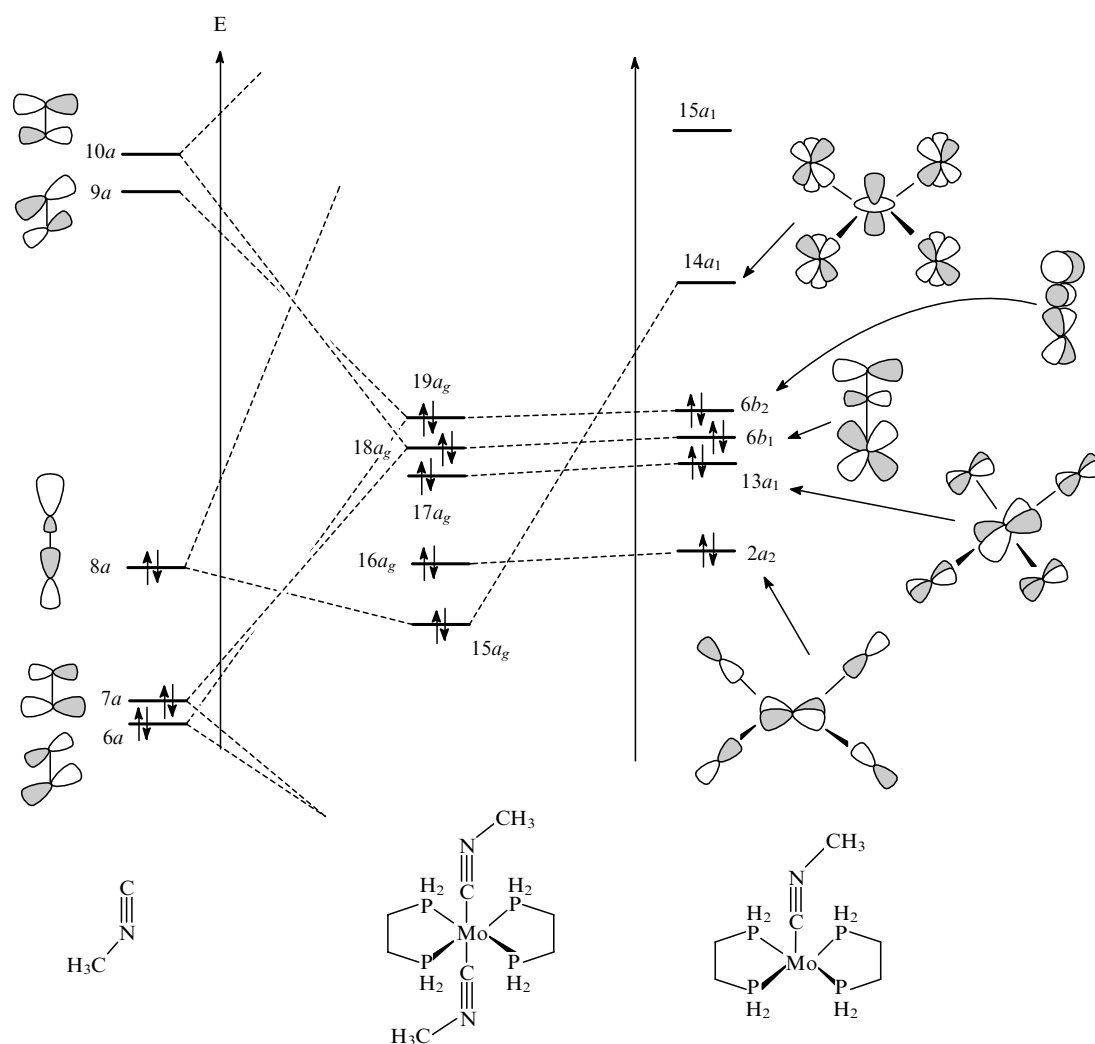


Figure 2. Correlation diagram of the MOs in the *trans*-[Mo(CNMe)₂(dppe)₂] complex.²⁷

[Ag₂(CNMe)₄X₂] (X = Cl, Br, I) (**1**),³³ [PtRh(CNBut)₂.(CN)₂(dmpm)₂]⁺ (dmpm = Me₂PCH₂PMe₂) (**2**), *trans*-[Rh(CNBut)₂(PPh₃)₂]⁺ (**3**)³⁴ and [M(CNH)₄]⁺ (**4**) (M = Cu, Ag)³⁵ demonstrated that the HOMOs are localised predominantly on the metal atoms. The orbitals of the halogen atoms in the complexes **1** and the *s*-orbitals of the carbon atom of the isocyanide ligand in the complexes **4** also make contributions to the HOMOs of these complexes. The lowest unoccupied MOs of the complexes **1** and **4** are the π^* -orbitals of the CNR fragment, whereas the LUMOs of the complexes **2** and **3** consist of the p_z (Rh), π^* (CN), p_z , d_{xz} (P) and p (Pt) atomic orbitals.

The compositions of the frontier MOs in the tetranuclear linear [M₄(CNMe)₈(PH₃)₂]²⁺ clusters (M = Pd, Pt) were studied by the EOMO method.^{36,37} The highest occupied and lowest unoccupied MOs are the σ_a^* -orbitals of the metal atom. The next 18 occupied MOs of the clusters are centred on the metal atom, whereas 4 unoccupied MOs following after the LUMO are the π^* -orbitals of CNMe.

The introduction of other ligands exhibiting strong π -acceptor properties into isocyanide complexes often leads to weakening of π -back donation of the electron density from the *d*-orbitals of the metal atom to the π^* -orbitals of isocyanide. This weakening is particularly noticeable when a strong π -acceptor is in the *trans* position with respect to the isocyanide ligand, which actually reflects the mutual trans effect of two π -acceptors. In contrast, the introduction of a ligand exhibiting pronounced donor properties (for example, the chloride ligand) in the *trans* position with respect to isocyanide leads to enhancement of the π -acceptor properties of

isocyanide and strengthening of π -back donation. Thus several highest occupied MOs in the *trans*- and *cis*-[(PH₃)₂(CO)₂W.(CNMe)($\equiv$ CCH=CH₂)]⁺ complexes containing one carbyne ligand and two carbonyl ligands (strong π -acceptors) along with the isocyanide ligand are composed predominantly of the orbitals of the metal atom and the carbonyl and carbyne ligands with a very small contribution of the AOs of the nitrogen atom of isocyanide (Figs 3 and 4).³⁸

The nature of the coordination bond in the isocyanide complexes [Cp₂Ta(CNMe)(η^2 -CH₂=CH-CH=CH₂)]⁺ (Cp is the cyclopentadienyl ligand) (**5**), [Cp₂Ta(CNMe)₂]⁺ (**6**) and [Cp₂M(CNMe)]^{0/+} (M = Ta, Zr) was examined based on the results of DFT calculations³⁹ with full geometry optimisation of different isomers of these complexes. Analysis of the theoretical and experimental structural data (the linearity of the isocyanide molecule, the equal CN bond lengths in free and coordinated isocyanides) and examination of the energy components of the coordination bond showed that π -back donation is of secondary importance in the interaction between isocyanide and tantalum in the complex **5**, which contains other strong π -acceptors. In this case, the interaction between the metal atom and the ligand is predominantly Coulombic in character. In the complex **6**, which contains no other π -acceptor ligands except for isocyanide, the Ta $\rightarrow$ CNR π -back donation becomes essential.

Three orbitals, *viz.*, the *d*-orbital of the metal atom and the π - and π^* -orbitals of isocyanide, contribute to the π -component of the coordination bond between the metal atom and the isocyanide ligand. The interactions between these orbitals give rise to three

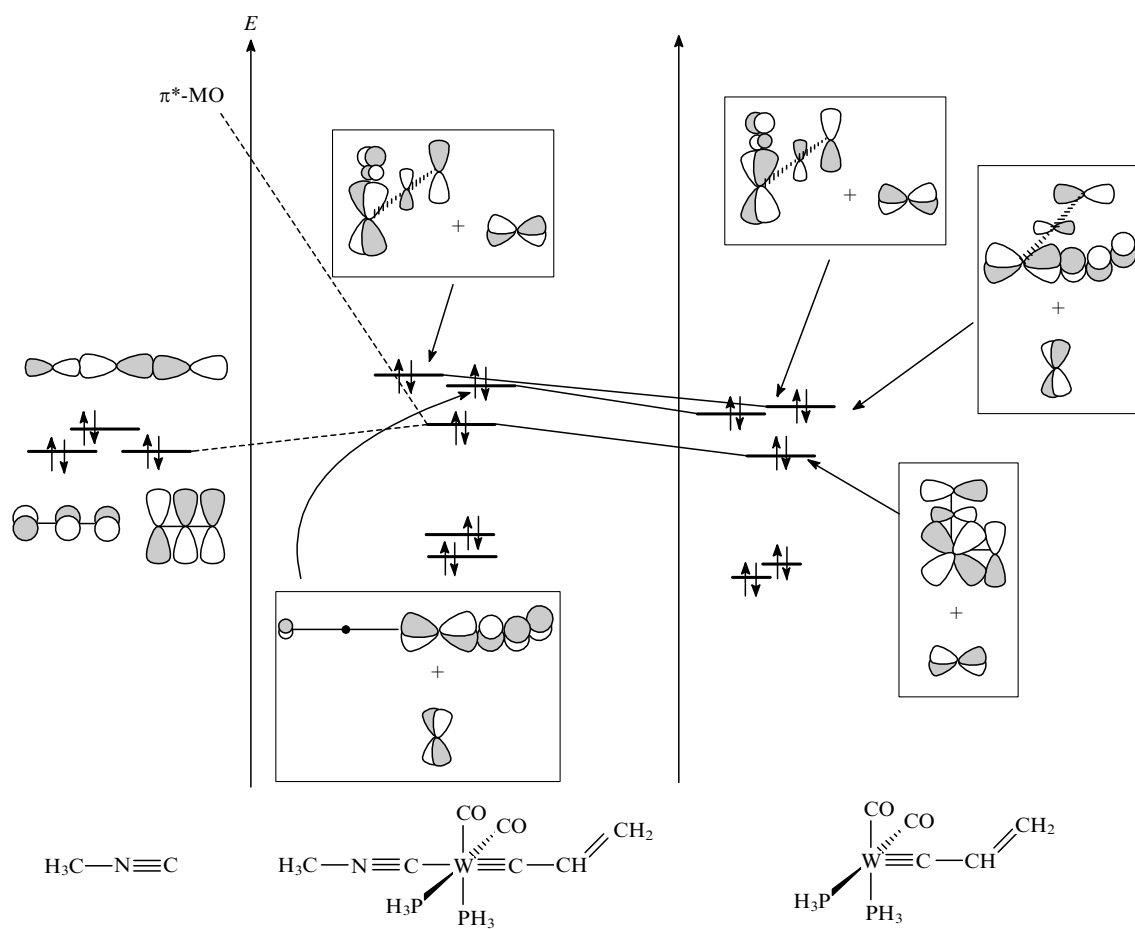


Figure 3. Correlation diagram of the MOs in the *trans*-[(PH_3)₂(CO)₂W(CNMe)($\equiv\text{CCH}=\text{CH}_2$)]⁺ complex.³⁸

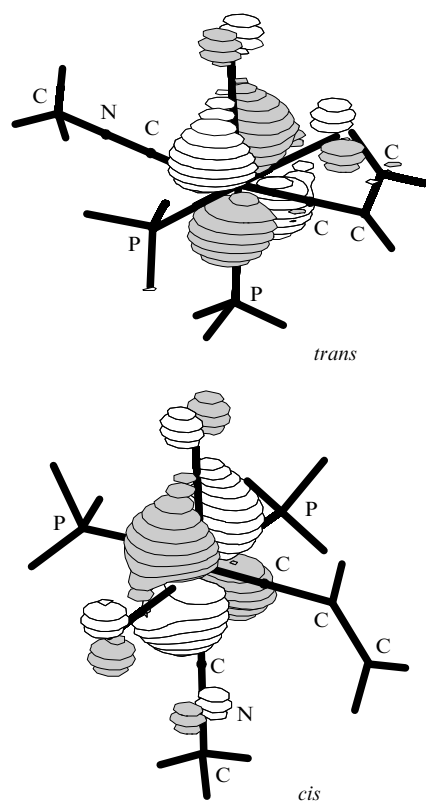


Figure 4. Composition of the HOMOs in the tungsten isocyanide complexes *trans*- and *cis*-[(PH_3)₂(CO)₂W(CNMe)($\equiv\text{CCH}=\text{CH}_2$)]⁺.³⁸

molecular orbitals two of which, viz., $\pi_{d-\pi(\text{L})}$ (MO1) and $\pi_{d-\pi^*(\text{L})}^*$ (MO3), are formed primarily from the d -orbitals of the metal atom and the π - or π^* -orbitals of the ligand. These MOs produce the bonding and antibonding combinations for the metal–ligand bond, respectively (Fig. 5). In some cases, the third orbital (MO2) is the HOMO of the complex derived from a linear combination of the $\pi_{d-\pi(\text{L})}^*$ - and $\pi_{d-\pi^*(\text{L})}$ -orbitals. The contribution of the unoccupied π^* -orbital of the ligand to the MO2 of the isocyanide complexes is often larger than the contributions of the occupied π -MOs of the ligand although the participation of the latter remains essential. As a result, the MO2 orbital either remains nonbonding with respect to the metal–ligand bond or becomes weakly bonding. Actually, as can be seen from Fig. 6, the formation of the MO2 leads to a substantial decrease in the electron density on the C^α and C^γ atoms, whereas the electron

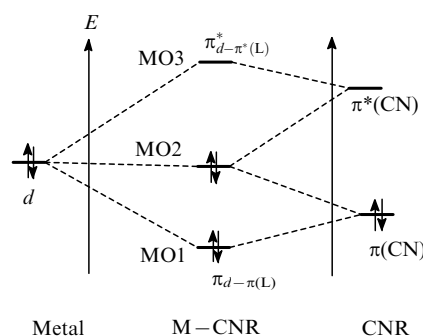


Figure 5. Three-orbital interaction between the frontier MOs of the metal atom and the ligand.

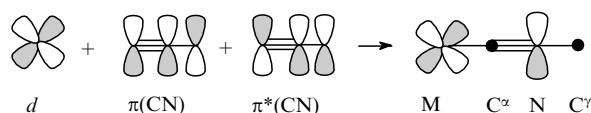


Figure 6. Polarisation effect of the nonbonding HOMO.

density on the nitrogen atom increases resulting in polarisation of the corresponding MO. This polarisation of orbitals in cyanide, carbonyl and nitrogen complexes was described by R Hoffmann⁴⁰ as early as 1977. At the same time, the contributions of the π - and π^* -MOs of isocyanide to the HOMO are very small in the presence of other (in addition to CNR) ligands possessing strong π -acceptor properties. In the latter case, the properties of such complexes are not always correctly interpreted in terms of the qualitative DCD model.

On the whole, the compositions of frontier MOs determining the π -component of the coordination metal–ligand bond in nitrile complexes is similar to those in isocyanide compounds. The EHMO calculations were carried out for the model nickel nitrile complex $[\text{Cp}(\text{PH}_3)\text{Ni}(\text{N}\equiv\text{CC}_6\text{H}_4\text{NH}_2)]^+$ (**7**).¹⁰ Figure 7 shows the correlation diagram of the MOs describing interactions between the molecular orbitals of the $[\text{Cp}(\text{PH}_3)\text{Ni}]^+$ fragment and the nitrile ligand upon the formation of the complex **7**. The most important result of this interaction is σ -donation of the

electron density from the occupied σ -orbitals of the nitrile ligand (σ_1 - and σ_2 -MOs), which are bonding with respect to the CN group, to the unoccupied d_{z^2} -orbital of the metal atom. In addition to the above-mentioned two σ -orbitals, the third lower-energy σ -orbital of the nitrile ligand (it is omitted in the figure), which is antibonding with respect to the CN bond, also makes a contribution to this interaction. The authors of the cited study believed that the last-mentioned contribution [which leads to a decrease in occupancy of the $\sigma^*(\text{CN})$ -orbital upon coordination] is mainly responsible for strengthening of the CN bond on going from the free ligand to the complex.

In addition to the σ -component, the coordination bond in the complex **7** also involves the π -component (interactions between the occupied d -orbitals of nickel and the π -orbitals of the nitrile ligand). Both π - and π^* -MOs contribute to the resulting MOs of the complex. The highest occupied MO derived from a linear combination of three orbitals $a'' + \lambda_1\pi_{||} + \lambda_2\pi_{||}^*$ is a nonbonding orbital with respect to the N and C atoms. The contribution of the $\pi_{||}$ -orbital of the ligand to the HOMO only insignificantly overrides the contribution of the $\pi_{||}^*$ -orbital from which it was concluded that the metal–ligand π -interaction has its origin in very weak π -donation of the electron density from the ligand to metal.

In transition metal complexes, nitriles exhibit both weak π -donor and weak π -acceptor properties, which is yet another important characteristic of the electronic structures of this class of

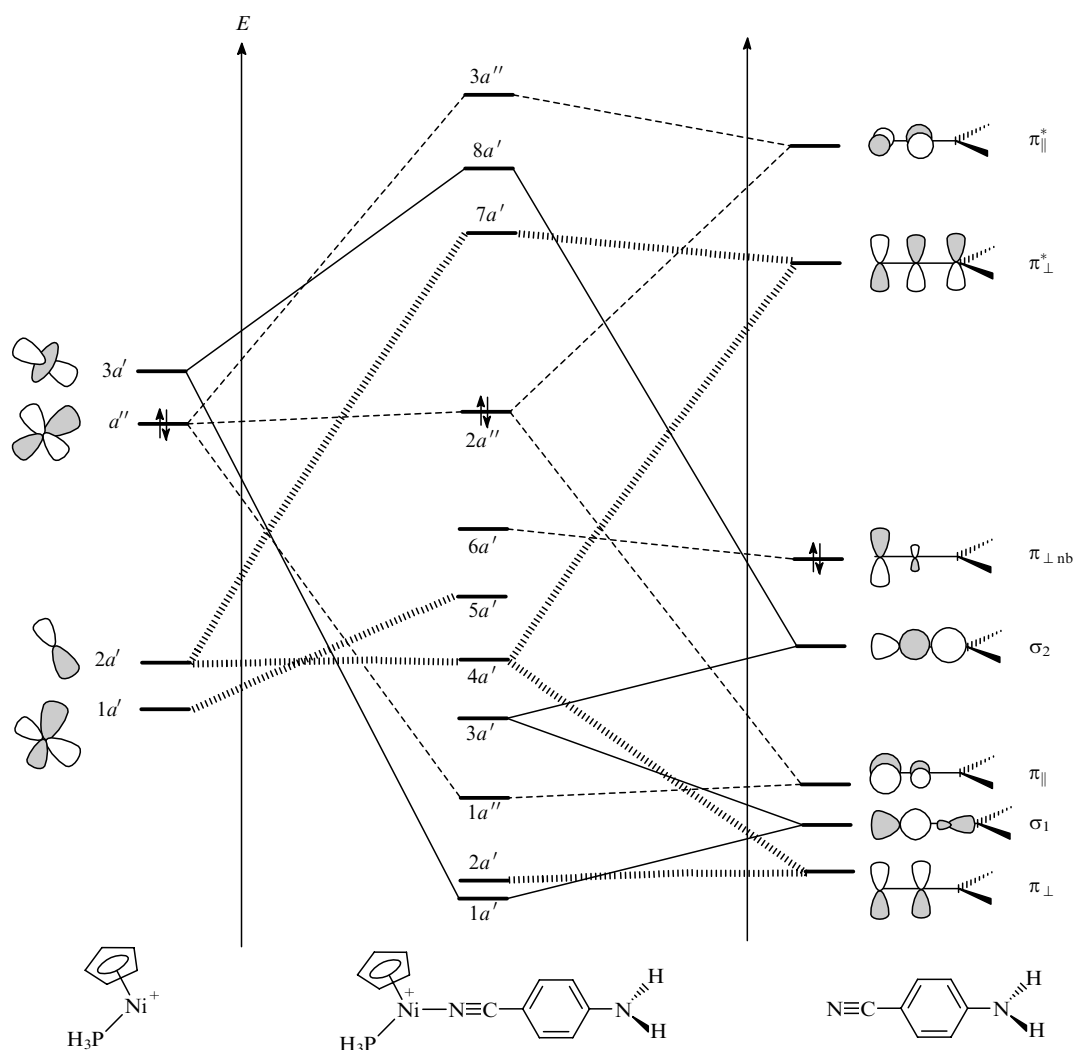


Figure 7. Scheme of the interactions between the MOs of the $[\text{Cp}(\text{PH}_3)\text{Ni}]^+$ and $\text{NCC}_6\text{H}_4\text{NH}_2$ fragments upon the formation of the complex **7**. For the nitrile ligand, only the orbitals belonging to the nitrile group are shown.¹⁰

coordination compounds. Hence, the total contribution of the π -orbitals of nitrile (both π and π^*) to the frontier MOs of the complex is, generally, insignificant and the latter orbitals are often centred on the metal atom. The results of EHMO or HF calculations of the electronic structures of the model nitrile complexes $[\text{CpFe}(\text{NCMe})(\text{PH}_3)_2]^+$, $[\text{CpFe}(\text{N}\equiv\text{CCH}_2\text{C}_6\text{H}_4\text{O}.\text{P}_3\text{N}_3(\text{OH})_5\text{-}p)(\text{PH}_3)_2]^+$ (see Ref. 41) and $[\text{CpFe}(p\text{-N}\equiv\text{C}.\text{C}_6\text{H}_4\text{NO}_2)(\text{PH}_3)_2]^+$ (see Ref. 11) indicate that the HOMOs of all complexes consist predominantly of the d -orbitals of the iron atom although the π^* -orbitals of the nitrile ligand in the latter compound also make a particular contribution to the MO, which is the closest in energy to the HOMO, thus providing the π -dative interaction. Analogous results were obtained in the DFT calculations of the molecular and electronic structures of the model nickel complexes $[\text{LNi}\{\text{N}\equiv\text{CN}=\text{C}(\text{NH}_2)_2\}(\text{NH}_3)_3]$ (**8**) and $[(\text{NH}_3)_3\text{Ni}\{\text{N}\equiv\text{CN}=\text{C}(\text{NH}_2)\text{NHNi}(\text{NH}_3)_2\text{L}\}]$ (**9**) (L is 1,2-diazolidine).⁴²

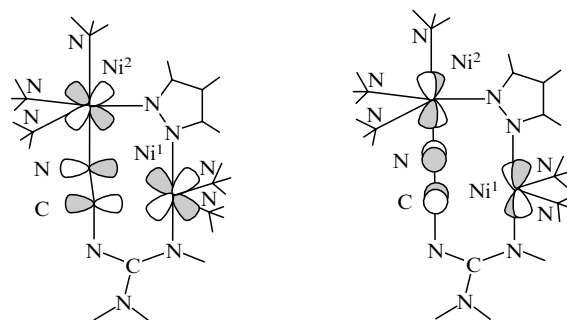
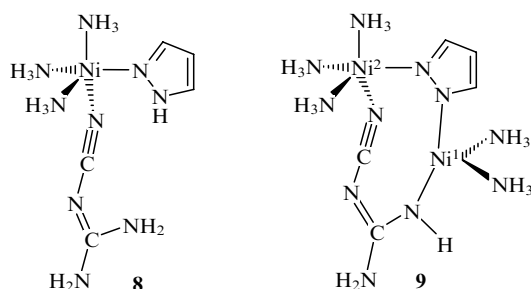


Figure 8. Interactions between the orbitals of the metal atom and the nitrile ligand in the complex **9**.⁴²

The ground state of the complex **9** is quintuplet, whereas the energies of the triplet and singlet states are higher by 46.9 and 381.4 kJ mol⁻¹, respectively. The singly occupied MOs are centred on the d_{z^2} - and d_{xy} -orbitals of Ni¹ and the $d_{z^2-y^2}$ - and $d_{x^2-y^2}$ -orbitals of Ni². The lower-energy doubly occupied MOs are composed of the d_{yz} - and d_{xz} -orbitals of the Ni¹ and Ni² atoms with a particular contribution of the π^* -MO of nitrile. The latter orbital is responsible for insignificant π -back donation of the electron density from the orbitals of the Ni² and Ni¹ atoms to the orbitals of the ligand. The side-to-side interaction between the orbitals of the Ni¹ atom and the nitrile ligand (Fig. 8) is rather unusual for the high-spin Ni(II) ion.

Kuznetsov *et al.*^{43,44} reported the results of theoretical studies of the platinum nitrile complexes *trans*-[Pt(NCMe)₂Cl₂] (**10**),

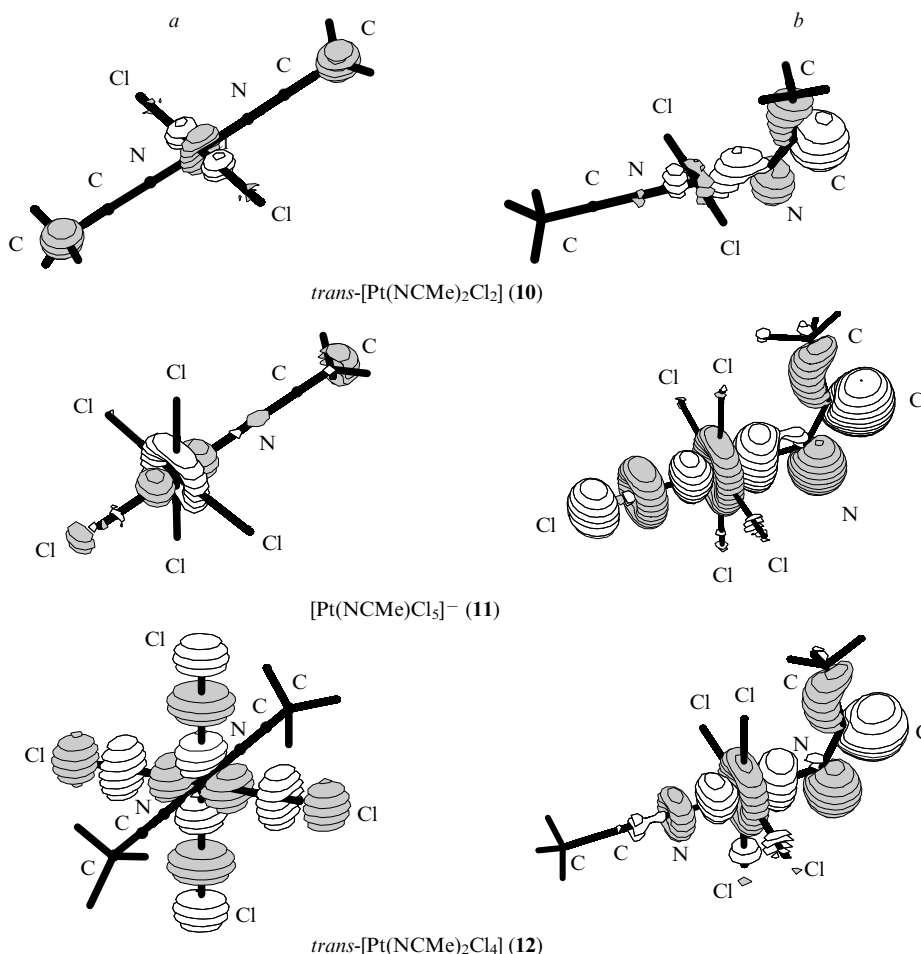


Figure 9. Compositions of the HOMOs in the complexes **10**–**12** when they contain two linear acetonitrile ligands (a) and when one of the acetonitrile ligands has an angular structure (b).⁴⁴

[Pt(NCMe)Cl₅][−] (**11**) and *trans*-[Pt(NCMe)₂Cl₄] (**12**). Figure 9 presents the compositions of the HOMOs of the complexes **10–12** when they contain two linear acetonitrile ligands (*a*) and when one of the acetonitrile ligands has a bent structure (*b*). Calculations performed for the complexes **10–12** at different levels of theory (HF and MP2) and with different basis sets demonstrated that several of the highest occupied MOs of these complexes are formed from the orbitals of the chlorine atoms or, in the case of *trans*-[Pt(NCMe)₂Cl₂], from the orbitals of the metal atom without a noticeable contribution of the orbitals of acetonitrile.

Recently, similar results were obtained by Pombeiro and co-workers³⁸ for the tungsten complexes *trans*- and *cis*-[(PH₃)₂(CO)₂W(NCMe)(≡CCH=CH₂)]⁺ (Fig. 10).

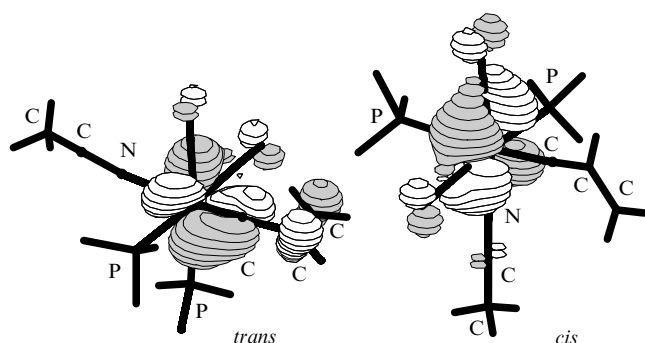


Figure 10. Compositions of the HOMOs in the tungsten nitrile complexes *trans*- and *cis*-[(PH₃)₂(CO)₂W(NCMe)(≡CCH=CH₂)]⁺.³⁸

One of the highest occupied MOs of the {(PH₃)₂.(CO)₂W(≡CCH=CH₂)}⁺ fragments (the first orbital in the case of the *trans* isomers and the second orbital in the case of the *cis* isomers) is derived from a linear combination of the *d*-orbitals of the metal atom with the π - and π^* -MOs of two CO ligands. Due to a large contribution from the π^* -orbitals, the HOMO is bonding relative to the W–C bond and antibonding with respect to the C–O bond. This is indicative of the presence of π -back donation from the metal atom to the π^* -MO of a strong π -acceptor such as CO. Two other highest occupied MOs of the {(PH₃)₂(CO)₂W(≡CCH=CH₂)}⁺ fragments of the *cis* and *trans* isomers are composed of the *d*-orbitals of the metal, which also interact with the π - and π^* -MOs of one of the CO ligands and with the orbitals of the carbyne ligand. Upon the formation of the nitrile complex [(PH₃)₂(CO)₂W(NCMe)(≡CCH=CH₂)]⁺ from the {(PH₃)₂(CO)₂W(≡CCH=CH₂)}⁺ and {NCMe} fragments, the composition of the highest occupied MOs of the former fragment remains virtually unchanged and the orbitals of the nitrile ligand make an insignificant contribution to the HOMO of the complex (see Fig. 10).

In the study,⁴⁵ calixarene complexes of Ta and Nb, including those containing the coordinated acetonitrile molecule, were synthesised, their spectroscopic parameters and structural characteristics were determined, and the molecular orbitals were calculated by the Fenske–Hall method.⁴⁶ In the [Cp*Ta(NCMe)(calix[4]arene)] complex (Cp* = η^5 -C₅Me₅), the bonding interaction between nitrile and metal involves the *d*_{z²}(Ta)- and *p*_z(N)-orbitals *via* σ -bonding (Fig. 11) and the HOMO of the complex is centred on the atoms of the calixarene ligand.

The *ab initio* calculations for the tetranuclear copper(I) clusters [Cu₄(NCMe)₂L₂] (L is 2,6-dimethylaniline, 6-ethyl-*o*-toluidine or *p*-toluidine)⁴⁷ demonstrated that the *p*-orbitals of the iodine atoms make major contribution to the HOMO of the complex, whereas the LUMO is formed from the *p*-orbitals of copper. It was noted that the orbitals of acetonitrile make no substantial contribution to the frontier MOs of the complex.

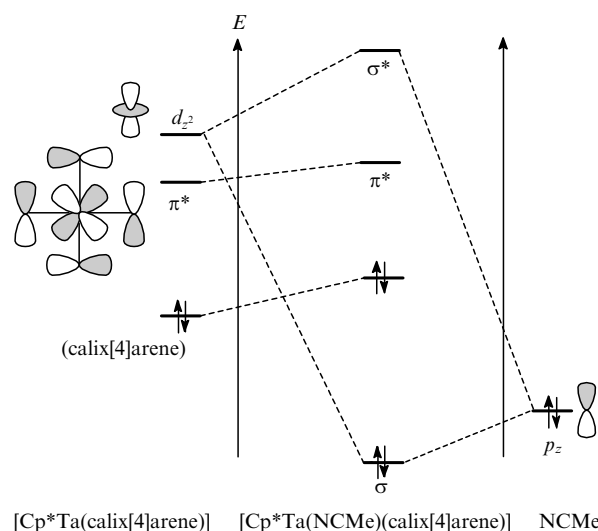


Figure 11. Correlation diagram of the MOs in the nitrile complex [Cp*Ta(NCMe)(calix[4]arene)].⁴⁵

The main difference between the nitrile and isocyanide complexes is associated with weaker π -acceptor properties of nitriles compared to those of isocyanides due to which the contributions of the π - and π^* -MOs of the ligand to the MOs of the complex compensate each other and the corresponding molecular orbital is nonbonding.

The total contribution of the π - and π^* -orbitals of the ligand to the HOMOs in nitrile complexes is smaller than that in isocyanide complexes, which is also indicative of weaker π -acceptor properties of the nitrile ligands. As a result, the π -component of the coordination bond in nitrile complexes is often negligible as compared to the σ -donor or Coulombic component (see below). Hence, the DCD model must be applied to the description of the properties of the nitrile complexes with caution. Finally, analysis of the compositions of the frontier MOs of acetonitrile and methyl isocyanide⁴⁸ demonstrated that nitriles are weaker σ -donors than isocyanides due to substantially lower energy of the valence occupied σ -orbitals of NCR compared to those of CNR.

2. Structural features of metal complexes with nitriles and isocyanides

Back π -donation of the electron density from metal to the ligand has a substantial effect on the geometric parameters of the complexes. Actually, an increase in the occupancy of the π^* -antibonding orbitals of the ligand must lead to weakening of the multiple C≡N bond in the ligand and, consequently, its length must slightly increase on going from the free ligand to the complex. To the contrary, the metal–ligand bond becomes stronger due to additional π -interaction resulting in shortening of the metal–ligand bond compared to those in the related complexes in which π -back donation is absent.

In the early studies by Sarapu and Fenske,^{49,50} the presence of π -back donation in isocyanide complexes was confirmed by the X-ray diffraction data. The Mn–C(CNMe) bond length in the [Mn(CNMe)₂(CO)₃Br] complex is 0.10–0.14 Å smaller than the sum of the covalent radii of Mn and the *sp*-hybridised carbon atom, which indicates that this bond in the complex is partially double. The results of X-ray diffraction studies are in agreement with the data from theoretical calculations of MOs by the Fenske–Hall method. In particular, the substantial occupancies of the π^* -MOs of the isocyanide ligand in the [Mn(CNMe)_n(CO)_{5–n}Br] (*n* = 0–4), [Mn(CNMe)_n(CO)_{6–n}]⁺ (*n* = 0–6), [Mn(CN)(CO)₅], [Mn(CN)₆]^{5–} and [Fe(CNMe)₆]²⁺ complexes are indicative of the efficient electron density transfer from the *d*-orbitals of metal to the π^* -MO of isocyanide in spite of

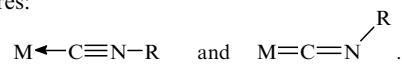
the presence of such a strong π -acceptor as the CO ligand. A comparison of the occupancies of the π^* -MOs of the isocyanide and carbonyl ligands shows that the latter is the stronger π -acceptor than isocyanide and that π -back donation of the electron density from the d -orbitals of metal to the π^* -MOs of the carbonyl ligand is more pronounced than that to the π^* -orbitals of the isocyanide ligand.

It does not always happen that the expected elongation of the $C\equiv N$ triple bond takes place on going from the free ligand to the complex. For example, the calculated $C\equiv N$ bond length in the *trans*- and *cis*- $[(PH_3)_2(CO)_2W(CNMe)(\equiv CCH=CH_2)]$ complexes (1.145 and 1.147 Å, respectively) is 0.011–0.013 Å smaller than that in the free ligand.³⁸ The interactions of the $[MCP_3]^+$ fragment (M = Ti, Zr, Hf) with such ligands as NCMe, CNMe and CO, which afford the corresponding $[MLCP_3]^+$ complexes, were examined.⁵¹ It was demonstrated that the M–L bond length calculated by the DFT method increases in the series $Ti < Hf < Zr$ and $CO < CNMe < NCMe$. The authors of the cited study attributed the former tendency to the relativistic effects, which were taken into account for Hf. An increase in the M–L bond length on going from CO to NCMe correlates with weakening of the π -acceptor properties of the ligands in this series.

The variations in the $C\equiv O$ and $C\equiv N$ bond lengths on going from the free ligand to the complex are less evident. These bond lengths depend on two opposite effects.⁵² One effect, *viz.*, σ -donation from the ligand to metal $L \rightarrow M$, must lead to shortening of the $C\equiv N(O)$ bond because the corresponding occupied σ -orbital of the ligand, which is involved in the formation of the M–L σ -bond, is antibonding. Consequently, coordination of the ligand must lead to a decrease in the electron density on the σ^* -orbital, which is antibonding for the $C\equiv N$ or $C\equiv O$ bond, resulting in its strengthening. The opposite effect, *viz.*, π -back donation from metal to the ligand, must lead to elongation of the $C\equiv N$ or $C\equiv O$ bond due to an increase in the electron density on the π^* -MO of the ligand upon coordination. Taking into account weakening of the π -acceptor properties of the ligands (more precisely, a decrease in the ratio between the π -acceptor and σ -donor abilities) on going from CO to NCMe, one would expect a decrease in $\Delta r = r(C\equiv X)_{\text{comp}} - r(C\equiv X)_{\text{free}}$ (X = O, N) in this series. However, the results of calculations demonstrated that the $C\equiv O$ bond length increases upon coordination, the $C\equiv N$ bond length in isocyanide complexes decreases, whereas the corresponding bond length in nitrile complexes remains virtually unchanged (Table 1). To account for this phenomenon, the energy characteristics of the M–L bond were analysed. The energy of this bond (E_{bond}) was divided into three components $E_{\text{bond}} = -(\Delta E_{\text{Coul.}} + \Delta E_{\text{Pauli}} + \Delta E_{\text{oi}})$, where $\Delta E_{\text{Coul.}}$ characterises the Coulombic component of the M–L interaction, ΔE_{Pauli}

represents the exchange repulsion and ΔE_{oi} accounts for the contribution of the bonding orbital interaction. The sum $\Delta E_{\text{Pauli}} + \Delta E_{\text{oi}}$ represents the orbital energy (ΔE_{orb}). The results of analysis showed that the maximum contribution of $\Delta E_{\text{Coul.}}$ to the energy of the bond E_{bond} is observed in the case of isocyanide complexes, whereas this contribution in the case of carbonyl and nitrile complexes is much lower (see Table 1), which is responsible for additional shortening of the $C\equiv N$ bond in the $[M(CNMe)Cp_3]^+$ complexes. The lowest orbital energies ΔE_{orb} were found for nitrile complexes, which results in intermediate values of Δr .

It should be noted that π -back donation sometimes leads to a bent distortion of the ligand. Thus the geometry of coordinated isocyanide can be described as intermediate between two structures:



Apparently, a predominance of a particular form is determined by the relative contributions of the π -acceptor and σ -donor components to the metal–ligand bond. When the σ -donor ($L \rightarrow M$) component substantially dominates over the π -acceptor ($M \rightarrow L$) component, the ligand adopts a linear conformation. In contrast, when π -back donation becomes dominant, the multiplicity of the M–L bond increases, whereas the multiplicity of the $C\equiv N$ bond decreases, which could cause a bent distortion of the isocyanide ligand.^{39, 53}

Actually, according to the X-ray diffraction data,^{54–58} the isocyanide ligand has a linear structure in most of isocyanide complexes of transition metals in high oxidation states in which π -back donation is manifested to only a small extent, if at all. At the same time, the isocyanide ligand has an angular structure in complexes of transition metals in low oxidation states in which efficient electron density transfer occurs from the d -orbitals of metal to the π^* -MO of the ligand,^{59, 60} the C–N–C angle being contracted to 140°.

The correlation diagrams of the MOs for linear and angular methyl isocyanide⁴⁸ show that the bent distortion of the ligand leads to an increase in the energy of the π -MO and this orbital becomes the highest occupied MO, whereas the energy of the π^* -MOs decreases (Fig. 12a). Hence, the bent distortion leads to a noticeable enhancement of the π -acceptor properties of the CNMe ligand, its σ -donor properties being virtually unchanged because the energy of the π -MO in the angular ligand is only 0.008 a.u. higher than the energy of the σ -MO in the linear ligand and the π -MO is localised on the terminal carbon atom to a much lesser extent.

Table 1. The M–L, $C\equiv N$ and $C\equiv O$ bond lengths in the $[MLCP_3]^+$ complexes (M = Ti, Zr, Hf; L = CO, CNMe, NCMe), the energies of the coordination bonds and their components.

Complex	Bond lengths / Å		E / kJ mol ^{−1}			
	M–L	$C\equiv N$ ($C\equiv O$)	$\Delta E_{\text{Coul.}}$	ΔE_{Pauli}	ΔE_{oi}	E_{bond}
$[Ti(CO)Cp_3]^+$	2.09	(1.15)	−282	476	−302	108
$[Ti(CNMe)Cp_3]^+$	2.15	1.17	−337	414	−246	169
$[Ti(NCMe)Cp_3]^+$	2.18	1.16	−233	261	−164	136
$[Zr(CO)Cp_3]^+$	2.25	(1.14)	−228	365	−247	110
$[Zr(CNMe)Cp_3]^+$	2.30	1.17	−309	345	−218	182
$[Zr(NCMe)Cp_3]^+$	2.32	1.16	−219	223	−155	151
$[Hf(CO)Cp_3]^+$	2.22	(1.15)	−288	448	−294	134
$[Hf(CNMe)Cp_3]^+$	2.25	1.17	−390	457	−274	207
$[Hf(NCMe)Cp_3]^+$	2.28	1.16	−264	186	−192	170

Note. The calculated $C\equiv O$ and $C\equiv N$ bond lengths in the free CO, CNMe and NCMe ligands are 1.14, 1.18 and 1.16 Å, respectively.

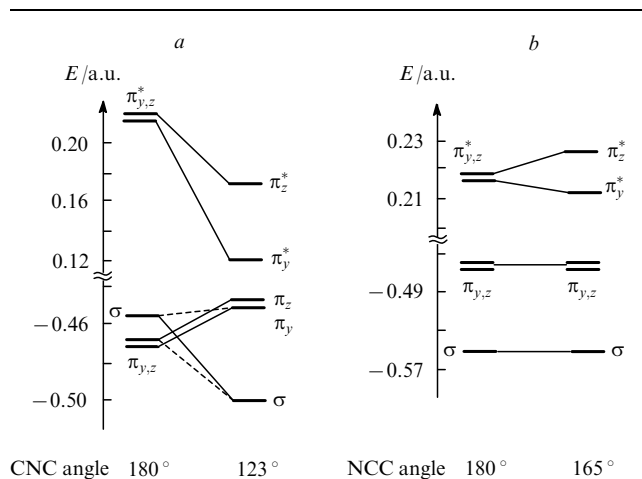


Figure 12. Walsh diagrams for the bent distortions of the methyl isocyanide (a) and acetonitrile (b) molecules (the data from the study⁴⁸).

Analysis of the linear and angular structures of the nitrile ligand NCMe (Fig. 12b) demonstrated that acetonitrile exhibits very weak π -acceptor properties due to a small degree of localisation of the π^* -MO on the terminal N atom although the energy of the π^* -MO of the nitrile ligand determined in the study⁴⁸ is comparable with the energy of the π^* -MO of the isocyanide ligand. The bent distortion of the NCMe ligand must lead to weakening of its acceptor properties due to the total destabilisation of the π^* -MO. At the same time, the authors of the cited study⁴⁸ believed that essential localisation of the π -MO(NCMe) on the C and N atoms of the $C\equiv N$ bond makes acetonitrile a potentially strong π -donor ligand. These π -donor properties of the nitrile ligand are responsible for the deviation of the $M-N-C$ fragment from linearity, which is frequently observed in experimental studies. However, as shown in Section II.1, the fact that the contributions of the π -orbitals of nitriles to the HOMOs of the complexes are small refutes this assumption.

Somewhat different distributions of the frontier MOs for acetonitrile and the model NCH structure were found in the study⁶¹ (Fig. 13). The authors believed that the bent distortion of the NCH ligand leads to mixing of the σ - and π_y -orbitals and their reorientation so that overlapping of these orbitals with the orbitals of the metal atom is enhanced in the case of the lateral coordination of the nitrile ligand through the $C\equiv N$ triple bond. Hence, the bent distortions of the nitrile ligands lead to enhancement both of their donor and acceptor properties. The lateral coordination of nitrile leads to a decrease in the energy of the LUMO of the ligand and, consequently, π -back donation in nitrile π -complexes becomes substantial.

Thus the NCC fragment of the ligand is linear in the case of the standard σ -coordination of nitriles to transition metals, whereas

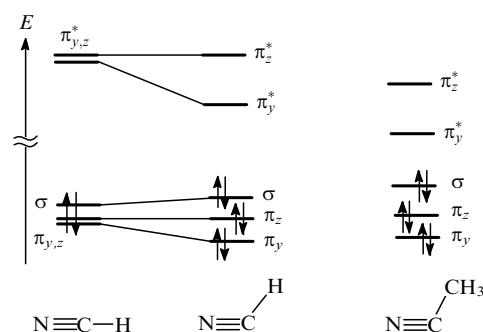


Figure 13. Walsh diagram for the bent distortion of the NCH molecule and the frontier MOs of the angular acetonitrile molecule (the data from the study⁶¹).

the nitrile ligand undergoes a bent distortion due to substantial π -back donation in the case of the lateral π -coordination through the $C\equiv N$ triple bond. Actually, geometry optimisation of the model complex $[CpW(\eta^2-NCH)(CO)(HC=C=O)]$ by the DFT method⁶¹ gave the $N-C-H$ angle of 135.6° .

Analysis of the electronic structures of the tungsten complexes $[W(NCH)Cl_2(PH_3)_3]$ and $[CpW(NCMe)(CO)\{C(SiH_3)=C=O\}]$ demonstrated that the π^* -MOs of the ligand contribute significantly to the highest occupied MOs of the complexes (in the case of $[CpW(NCMe)(CO)\{C(SiH_3)=C=O\}]$, to the highest occupied MO, which is the closest in energy to the HOMO) (Fig. 14).

The effect of the nature of the ligand, primarily, of its donor and acceptor properties, on the geometric parameters of other

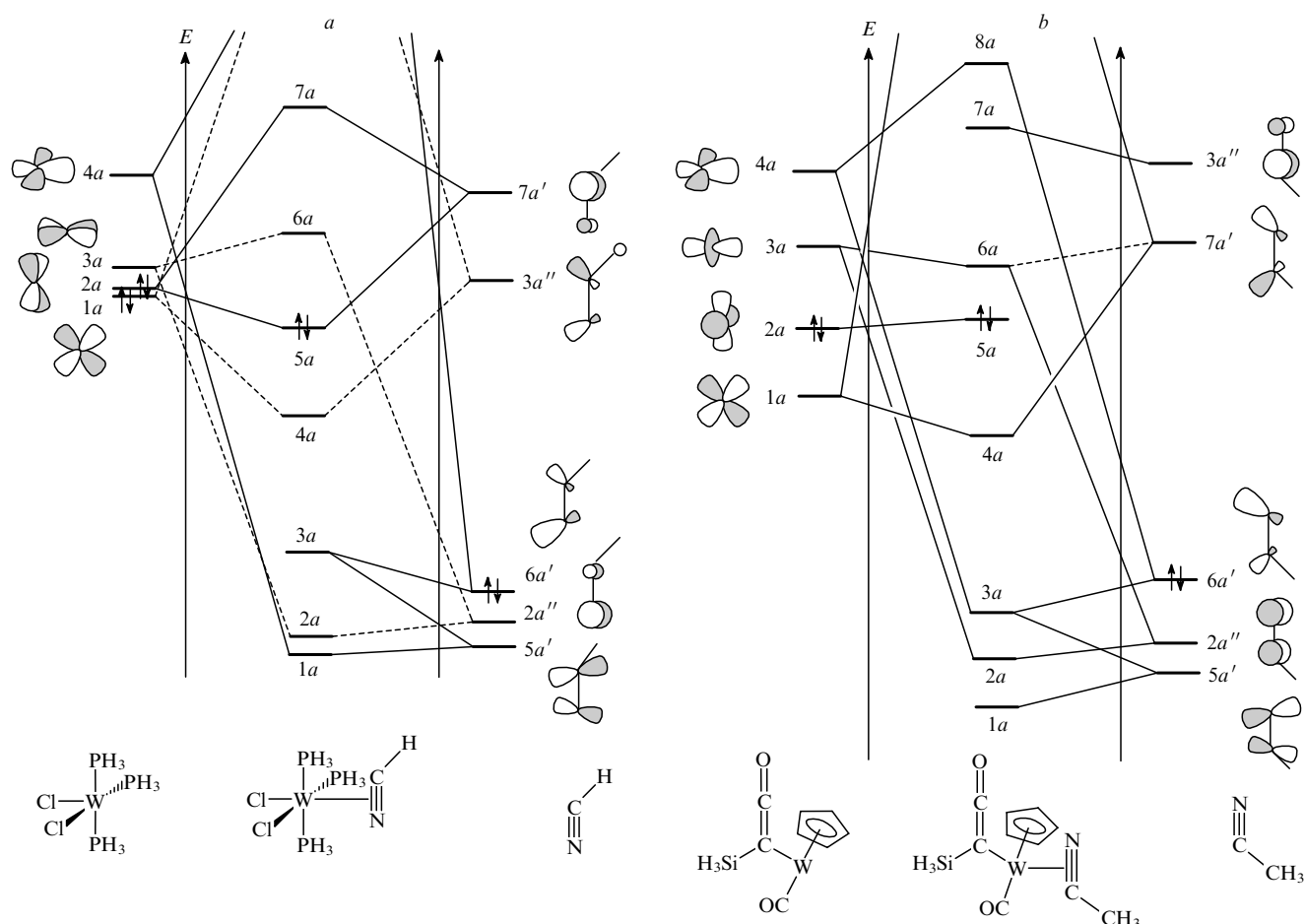
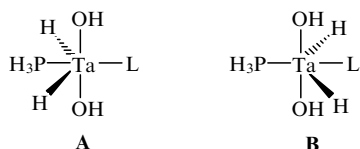


Figure 14. Correlation diagrams of the MOs in the $[W(NCH)Cl_2(PH_3)_3]$ (a) and $[CpW(NCMe)(CO)\{C(SiH_3)=C=O\}]$ (b) complexes.⁶¹

fragments in complexes was considered in the study.⁶² In the cited study, the results of *ab initio* calculations for a series of $[\text{TaL}'(\text{OH})_2\text{H}_2]^+$ complexes with various L and L' ligands, including NCMe, were discussed (the geometry optimisation was carried out by the MP2 method). The trans effect of the ligand L on the phosphine ligand (the Ta–P distance was used as a measure of the trans effect) was considered using the $[\text{TaL}(\text{PH}_3)(\text{OH})_2\text{H}_2]^+$ complexes as an example.

Depending on the nature of the ligand L, the Ta–P distance was found to decrease in the series $\text{CH}_3^- > \text{H}^- > \text{NH}_2^- > \text{BF} > \text{CS} > \text{PH}_3(\text{A}) > \text{OH}^- > \text{CO} > \text{CN}^- > \text{F}^- > \text{NC}^- > \text{Cl}^- > \text{Br}^- > \text{I}^- > \text{NH}_3 > \text{NCMe} > \text{PH}_3(\text{B}) > \text{N}_2$. The relative stabilities of the isomers **A** and **B**



($\Delta E_{\text{AB}} = E_{\text{A}} - E_{\text{B}}$) change in the following series: $\text{F}^- < \text{OH}^- < \text{Cl}^- < \text{Br}^- < \text{NC}^- < \text{I}^- < \text{CH}_3^- < \text{CN}^- < \text{NCMe} < \text{NH}_3 < \text{N}_2 < \text{H}^- < \text{NH}_2^- < \text{PH}_3 < \text{CO} < \text{CS} < \text{BF}$ (Table 2). The ligands exhibiting strong π -donor properties reside in the left side of this series, *i.e.*, the π -donor ability of the ligands L decreases from left to right. From the above series it follows that there is no correlation between the σ -donor properties (trans effect) and the π -donor (acceptor) properties of the ligands.

It was found that the hydride atoms in the complexes **A** and **B**, which are located in the *trans* positions with respect to each other, are shifted from the stronger π -donor toward the stronger π -acceptor. If the ligands possess both weak π -acceptor and weak π -donor properties, the bent distortion is caused by the ligand exhibiting the strongest static trans effect and the hydride atoms are shifted toward the weaker σ -donor. It was proposed⁶² that the unusual bent distortion of the H–Ta–H fragment is determined by these π -donor and π -acceptor (rather than by σ -donor) properties of the ligands L.

From the above-considered data, it is evident that π -back donation sometimes has a substantial effect on the structural parameters of the complexes. One of the indicators of the efficient π -back donation is the bent distortion of the CNC or NCC fragment. However, in actual practice this distortion is uncommon even in the case of transition metal complexes in low oxidation states and, hence, the linearity of CNC or NCC cannot serve as proof of weak π -acceptor properties of the ligand in the complex.

In the general case, the relative length of the $\text{C}\equiv\text{N}$ multiple bond in transition metal complexes with nitriles and isocyanides also cannot be considered as a reliable criterion for the degree or even existence of π -back donation because the length of this bond is substantially influenced not only by two opposite effects, *viz.*, σ -donation and π -back donation, but also by the Coulombic component.^{39,51} A comparison of a series of related complexes showed that the M–L bond length is a more reliable criterion for the degree of π -back donation.

Table 2. Relative energies of the **A** and **B** isomers of the $[\text{TaL}(\text{PH}_3)(\text{OH})_2\text{H}_2]^+$ complexes.

L	ΔE_{AB} /kJ mol ^{−1}	L	ΔE_{AB} /kJ mol ^{−1}	L	ΔE_{AB} /kJ mol ^{−1}
Cl [−]	−111.33	CN [−]	−57.32	NH ₂ [−]	−19.43
Br [−]	−101.24	NCMe	−36.84	PH ₃	0.00
NC [−]	−90.43	NH ₃	−35.21	CO	10.76
I [−]	−89.47	N ₂	−24.99	CS	16.08
CH ₃ [−]	−68.91	H [−]	−19.93	BF	53.55

III. Spectroscopic properties of coordinated ligands

1. Vibrational spectra

Stretching vibrational frequencies of the $\text{C}\equiv\text{N}$ and $\text{C}\equiv\text{O}$ bonds in transition metal complexes with nitriles and carbonyls[§] are influenced by several factors, including σ -donation of the electron density from the ligand to the metal atom, π -back donation from metal to the ligand and the Coulombic component of the coordination bond. σ -Donation from the ligand to metal leads to strengthening of the $\text{C}\equiv\text{N}$ and $\text{C}\equiv\text{O}$ bonds and, consequently, to an increase in their vibrational frequencies, whereas π -back donation from metal to the ligand causes weakening of these bonds and, hence, a decrease in the corresponding vibrational frequencies. In complexes with strong π -acceptor ligands, such as CO (and in some cases CNR), the latter effect generally dominates over the former as a result of which the $\nu(\text{CN})$ and $\nu(\text{CO})$ frequencies for the complexes are lower than those for the free ligands.

Actually, lowering of the $\nu(\text{CO})$ and $\nu(\text{CN})$ vibrational frequencies on going from the free ligand to the complex was predicted theoretically and observed experimentally for many carbonyl complexes as well as for a series of transition metal complexes with isocyanides (predominantly, with metals in low oxidation states).^{39,59,63,64} However, complex formation with isocyanides possessing weaker π -acceptor properties as compared to CO often leads to an increase in the $\nu(\text{CN})$ frequency. Thus theoretical analysis of the force constants and $\nu(\text{CN})$ vibrational frequencies for the $[\text{Mn}(\text{CNMe})_n(\text{CO})_{5-n}\text{Br}]$ ($n = 0-4$), $[\text{Mn}(\text{CNMe})_n(\text{CO})_{6-n}]^+$ ($n = 0-6$) and $[\text{Fe}(\text{CNMe})_6]^{2+}$ complexes demonstrated that the $\nu(\text{CN})$ frequency for the complexes is higher than that for the free ligand, which indicates that σ -donation dominates over π -back donation.⁵⁰

At the same time, detailed theoretical studies of the nature of coordination bonds in transition metal complexes demonstrated that the $\nu(\text{CN})$ and $\nu(\text{CO})$ stretching vibrational frequencies generally cannot serve as a reliable criterion for the degree of $\text{L} \rightarrow \text{M}$ donation and $\text{M} \rightarrow \text{L}$ π -back donation even for complexes with such a strong π -acceptor as carbon(II) oxide. Examples are provided by the so-called 'non-classical' carbonyl complexes, for instance, $[\text{Os}(\text{CO})_6]^{2+}$ and $[\text{Ir}(\text{CO})_6]^{3+}$. In their spectra, the $\nu(\text{CO})$ frequency is higher than that in the spectrum of the free ligand. The reason is that Coulombic interactions are of paramount importance in the formation of coordination bonds in non-classical carbonyl complexes and these interactions ultimately determine the $\nu(\text{CO})$ frequency.^{65,66} In transition metal complexes with isocyanides, which are weaker π -acceptors than CO, Coulombic interactions can exert a stronger effect on the $\nu(\text{CN})$ frequency compared to that of π -donation, which often leads to an additional increase in this vibrational frequency upon complex formation.

In nitrile complexes, the above-described tendencies are further enhanced because the nitrile ligands exhibit very weak π -acceptor properties and rather weak σ -donor properties. In this case, the Coulombic component of the metal–ligand interaction often exerts primary control over the $\nu(\text{CN})$ frequency. This fact is confirmed by the preliminary data from analysis of the natural bond orbitals performed for the *cis*- $[\text{Re}(\text{NCMe})\text{Cl}(\text{PH}_3)_4]$ and *trans*- and *cis*- $[\text{Re}(\text{NCMe})\text{Cl}(\text{PH}_3)_4]^{+/2+}$ complexes.⁶⁷ Generally, the $\nu(\text{CN})$ vibrational frequencies for nitriles are shifted to the high-frequency region on going from the free ligand to the complex.^{68–78} At the same time, there are examples of low-frequency shifts of this band upon coordination of nitriles with metals in the lowest oxidation states^{79–81} but these shifts are much smaller than those in the spectra of analogous isocyanide complexes. Finally, it should be noted that the low-frequency

[§]Spectroscopic properties of carbonyl compounds are considered for comparison.

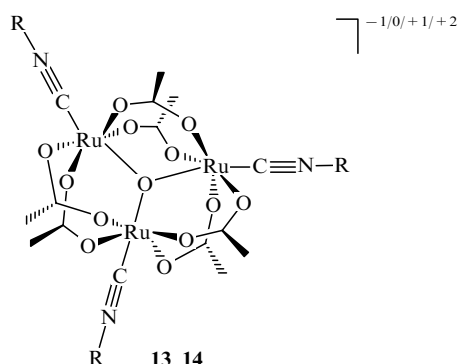
shifts of $\nu(\text{CN})$ for nitrile η^2 -complexes in which the ligand is coordinated through the $\text{C}\equiv\text{N}$ bond are rather high,^{82–84} which indicates that this is virtually a double bond.

The spectroscopic properties of nitrile complexes were examined in several theoretical studies. Thus the vibrational spectra of the platinum complex $[\text{Pt}(\text{NCMe})\text{Cl}_3]^-$ were calculated and described in detail.⁶⁹ The $\nu(\text{CN})$ band in the spectrum of the complex is shifted by 113 cm^{-1} to the high-frequency region as compared to its position in the spectrum of free acetonitrile. Interestingly, analogous high-frequency shifts of $\nu(\text{C}\equiv\text{N})$ ($95\text{--}117\text{ cm}^{-1}$) were found for the adducts of acetonitrile with Lewis acids BF_3 and BCl_3 (Ref. 85) in which π -back donation is, in principle, impossible.

It was demonstrated that the calculated $\nu(\text{CN})$ frequency decreases from 2209 cm^{-1} for the free $\text{N}\equiv\text{C}-\text{N}=\text{C}(\text{NH}_2)_2$ ligand to 2189 and 2143 cm^{-1} upon coordination of the ligand to nickel (complexes **8** and **9**, respectively).⁴² The calculated $\text{C}\equiv\text{N}$ bond length increases from $1.163\text{ \AA}$ (in the free ligand) to 1.178 and $1.187\text{ \AA}$ (in the complexes **8** and **9**, respectively), which correlates with a change in the $\nu(\text{CN})$ vibrational frequency. However, the order in which the calculated $\nu(\text{CN})$ frequencies change is inconsistent with the experimental series $\mathbf{8} > \text{N}\equiv\text{C}-\text{N}=\text{C}(\text{NH}_2)_2 > \mathbf{9}$.

The vibrational spectra of acetonitrile coordinated to the Li^+ and Na^+ ions were calculated at the HF/6-31G and HF/6-31G** levels of theory.⁸⁶ Coordination leads to a substantial increase in the intensities of the $\nu(\text{C}\equiv\text{N})$, $\nu(\text{C}-\text{C})$ and $\delta(\text{CH}_3)$ vibrations but calculations demonstrated that their frequencies change only slightly.

Finally, mention may be made of the study⁸⁷ in which the vibrational spectra and the nature of the Fermi resonance for ruthenium isocyanide complexes **13** and **14** were analysed by the DFT method.



$\text{R} = \text{MeC}_6\text{H}_4$ (**13**), Bu^t (**14**).

In the case of the neutral complexes and their reduced forms, Fermi resonance appears due to the interaction between the fundamental frequency $\nu(\text{C}\equiv\text{N})$ [2094 (**13**), 2010 (**13**⁻), 2131 (**14**) and 2028 cm^{-1} (**14**⁻)] and the vibrational overtone B_2 (**13** and **13**⁻) or E (**14** and **14**⁻) involving deformation of the $\text{C}\equiv\text{N}-\text{C}$ fragment as the major component.

In some experimental studies (see, for example, the review⁴), it was found that the change in the $\nu(\text{C}\equiv\text{N})$ frequency correlates with the reactivities of nitrile and isocyanide complexes with respect to nucleophilic and electrophilic addition. It was shown that complexes for which the parameter $\Delta\nu(\text{C}\equiv\text{N}) = \nu(\text{C}\equiv\text{N})_{\text{comp}} - \nu(\text{C}\equiv\text{N})_{\text{free}}$ is negative are readily subjected to electrophilic attack. If $\Delta\nu(\text{C}\equiv\text{N}) > 0$, complexes are involved in nucleophilic addition at the β -carbon atom. If the contribution of π -back donation to the coordination bond is essential, the β -atom of the ligand becomes more nucleophilic due to the electron density transfer from the d -orbitals of metal to the π^* -MO of the ligand thus facilitating electrophilic attack. In contrast, if π -back donation makes only an insignificant contribution upon the formation of the coordination bond, the electron density transfer from the σ^* -orbitals of the ligand to the d -orbitals of metal leads

to enhancement of electrophilicity of the β -atom of the ligand, which facilitates the nucleophilic attack. However, detailed theoretical studies providing the interpretation of this correlation are lacking.

2. Electronic spectra and excited states

Theoretical and experimental investigations devoted to the electronic spectra and the nature of excited states of nitrile and isocyanide complexes are rather scarce. Most of the calculations were carried out in a one-electron approximation. Several electronic states of the bis(isocyanide) complexes of nickel(II) peroxo $\text{NiO}_2(\text{CNH})_2$ were studied by the unrestricted HF and CI methods.⁸⁸ It was demonstrated that the singlet state $^1A_1$ is the ground electronic state of the complex. The first excitation state is the triplet $^3B_1$ with the energy parameter $\Delta E(^3B_1-^1A_1) = 47.60\text{ kJ mol}^{-1}$. The authors of the cited study considered the electron density distribution (ρ) and its Laplacian ($\nabla^2\rho$) and analysed the natural orbitals.

Photophysical properties of the model mononuclear copper clusters CuL_n^+ ($\text{L} = \text{NH}_3$, NCMe , $\text{C}_5\text{H}_5\text{N}$; $n = 1\text{--}4$) were described.⁸⁹ These properties were interpreted with the use of the Hartree–Fock method. The nature of the low-energy excited states was examined, their energies were determined, and the assignments of the metal-to-ligand charge transfer (MLCT) bands in the spectra of these complexes were made. The first excited state of the $[\text{Cu}(\text{NCMe})_4]^+$ complex ($^3B_3$) is formed due to MLCT and the second excited state ($^3B_1$) is formed through electron transfer from the $3d$ - to $4s$ -orbitals of the metal (Table 3). The assignments of these bands in the emission spectra of these complexes were performed.⁸⁹

Table 3. Energies of the first excitation states (ΔE) and changes in the Mulliken electronic populations of the $4s$ -, $4p$ - and $3d$ -orbitals of the copper atom with respect to the ground state for the $[\text{Cu}(\text{NCMe})_4]^+$ complex.

State	ΔE /a.u.	ΔCu			
		$4s$	$4p$	$3d$	total
$^3B_3$	0.159	0.062	0.393	-0.786	-0.331
$^3B_1$	0.164	0.900	0.050	-0.796	0.156
$^3A_1$	0.179	0.905	0.056	-0.827	0.135

The nature of the low-energy excited states of the $[\text{Ag}_2(\text{dmb})_2\text{X}_2]$ complexes ($\text{X} = \text{Cl}$, Br , I ; dmb is 1,8-diisocyanop-menthane) was discussed based on the experimental data and the results of EHMO calculations.³³ The charge-transfer bands in the electronic absorption spectra were assigned and their nature was studied. The broad band in the region of $250\text{--}350\text{ nm}$ was assigned to the electron transfer from the HOMO ($\text{HOMO} - n$) to the LUMO ($\text{LUMO} + n$): $d(\text{Ag}_2)/p(\text{X}) \rightarrow \pi^*(\text{CNR})$.

A comparison of the photoelectron spectra of the $[\text{CpM}(\text{CNBu}^t)(\text{CO})_2\text{Me}]$ and $[\text{CpM}(\text{CO})_3\text{Me}]$ complexes ($\text{M} = \text{Mo}$ or W) showed³² that the replacement of the carbonyl ligand by isocyanide leads to destabilisation of the d -orbitals of the metal atom, which is manifested in shifts of stretching bands in the spectrum of the isocyanide complex to lower energies by $0.73\text{--}0.83\text{ eV}$. An analogous result was obtained in the study⁹⁰ dealing with iron pentacarbonyl $\text{Fe}(\text{CO})_5$ and the iron isocyanide complexes $\text{Fe}(\text{CNR})(\text{CO})_4$ ($\text{R} = \text{Me}$, Bu^t , SiMe_3 , Ph). The higher energies of the occupied π -MOs of the isocyanide ligand compared to those of CO (the electron ionisation energy for the π -MOs of the corresponding free ligands are 12.46 and 16.91 eV) leads to enhancement of the destabilising interaction between the valence occupied d -orbitals of metal and the occupied π -MOs of the isocyanide ligand and to weakening of the stabilising $d(\text{M})-\pi^*(\text{L})$ interaction in the pentacarbonyl complexes resulting in an increase in the HOMO energy. Hence, it was concluded that

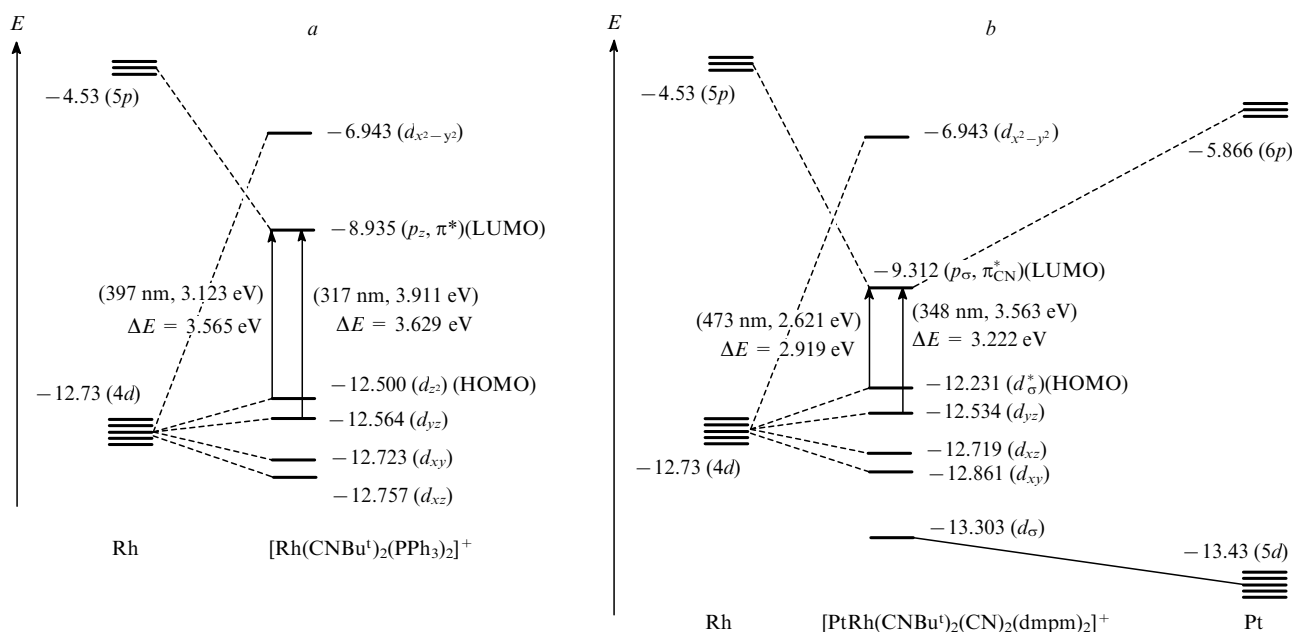


Figure 15. Correlation diagram of the MOs in the $\text{trans-}[\text{Rh}(\text{CNBUt})_2(\text{PPh}_3)_2]^+$ (a) and $[\text{PtRh}(\text{CNBUt})_2(\text{CN})_2(\text{dmpm})_2]^+$ (b) complexes.³⁴

the isocyanide ligand is a better π -donor but a poorer π -acceptor as compared to the carbonyl ligand.

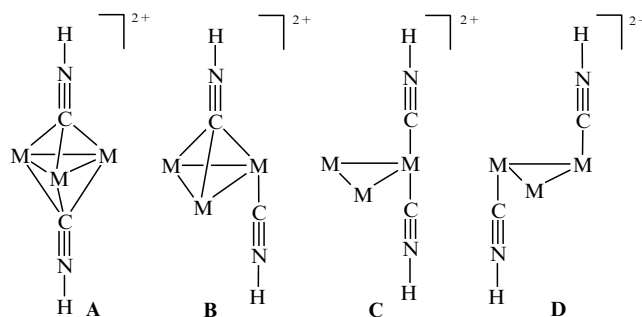
Analysis and the assignments in the electronic spectra of the $\text{trans-}[\text{Rh}(\text{CNBUt})_2(\text{PPh}_3)_2]^+$ and $[\text{PtRh}(\text{CNBUt})_2(\text{CN})_2(\text{dmpm})_2]^+$ complexes (dppm = $\text{Ph}_2\text{PCH}_2\text{PPh}_2$) were carried out based on the results of EHMO calculations for the model compounds $\text{trans-}[\text{Rh}(\text{CNBUt})_2(\text{PPh}_3)_2]^+$ and $[\text{PtRh}(\text{CNBUt})_2(\text{CN})_2(\text{dmpm})_2]^+$ (Fig. 15).³⁴ Two intense absorption bands at 397 and 317 nm in the spectrum of the former complex were assigned to the transitions $d_{z^2}(\text{Rh}) \rightarrow p_z(\text{Rh})/\pi^*(\text{CNR})/p_z, d_{xz}(\text{P})$ and $d_{yz}(\text{Rh}) \rightarrow p_z(\text{Rh})/\pi^*(\text{CNR})/p_z, d_{xz}(\text{P})$, respectively. The bands at 473 and 348 nm in the spectrum of the latter compound were assigned to the transitions $d_{z^2}(\text{Rh})/d_{z^2}(\text{Pt}) \rightarrow p_y(\text{Rh})/\pi^*(\text{CNR})/p_z, d_{xz}(\text{P})$ and $d_{yz}(\text{Rh}) \rightarrow p_y(\text{Rh})/\pi^*(\text{CNR})/p_z, d_{xz}(\text{P})$, respectively, the electron transfer from the d -orbitals of Rh to the π^* -MO of the ligand contributing significantly to the former band.

Among other studies devoted to examination of the spectroscopic properties of the complexes under consideration, noteworthy is the investigation⁹¹ in which the spin-spin coupling constants J_{HD} for the $[\text{OsL}(\text{NH}_3)_4(\eta^2\text{-H}_2)]^{(\epsilon+2)+}$ compounds (where $\text{L} = \text{Me}_2\text{CO}$, H_2O , MeCOO^- , Cl^- , H^- , $\text{C}_5\text{H}_5\text{N}$, NCMe , NH_3 , NH_2OH or CN^-) were calculated by the DFT method. For the acetonitrile complex, the constant J_{HD} is 20.8 Hz. The dependence of J_{HD} on the internuclear H–H distance was discussed.

IV. Reactivities and mechanisms of reactions with coordinated ligands

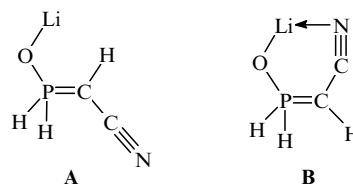
1. Isomerism and coordination modes

The coordination modes of ligands in complexes were discussed in theoretical studies.^{38, 67, 92–94} The relative stabilities of the trinuclear platinum and palladium isocyanide clusters $[\text{M}_3(\text{CNH})_2(\mu\text{-dppm})_3]^{2+}$ ($\text{M} = \text{Pt}$, Pd) with different coordination modes of the CNH ligand (isomers A–D) were studied based on the results of EHMO calculations:⁹²



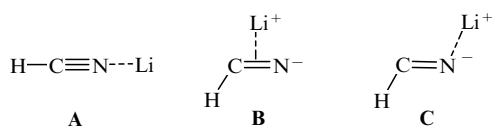
According to these results, the stability of the clusters A–D changes in the series $\text{A} > \text{B} > \text{C} > \text{D}$. This order is inconsistent with the experimental data, which provided evidence that the configuration C is most stable for the platinum complex. Apparently, more precise calculation methods are necessary for the correct description of the energy characteristics.

The stabilities of the monodentate (A) and chelate (B) configurations of the model complex $[\text{Li} - \text{O} - \text{PH}_2 = \text{CH} - \text{C} \equiv \text{N}]$ were analysed theoretically (HF/6-31G*⁹³).



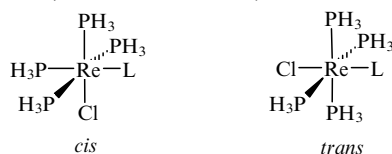
Calculations demonstrated that the chelate configuration of the complex is 112.6 kJ mol^{−1} more stable than the monodentate form in spite of the fact that it is characterised by the unusual Li–N≡C angle (91°).

The reactions of the Li⁺ ion with the NCH and NCMe molecules were studied by the semiempirical MNDO method and EPR spectroscopy.⁹⁴ Geometry optimisation of the LiNCH complexes revealed three minima corresponding to the structures A–C.



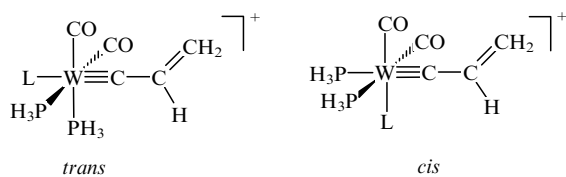
The heats of formation of these isomers are 46, 163 and 113 kJ mol⁻¹, respectively. The activation energy of the **C** → **B** conversion is 8 kJ mol⁻¹, which indicates that there is little likelihood that the structure **C** exists under the experimental conditions.

The geometric isomerisation of transition metal complexes was examined in the studies.^{38,67} The preliminary study of the rhenium(I) complexes *trans*- and *cis*-[ReLCl(PH₃)₄] (L = NCMe, CNMe or CO) revealed that the *cis* isomers are more stable in the presence of weak π -acceptor ligands (L = NCMe), whereas the *trans* isomers are more stable in the presence of strong π -acceptor ligands (L = CO and CNMe).⁶⁷

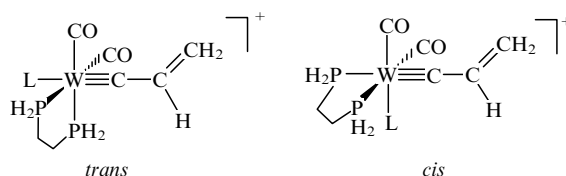


L = NCMe, CNMe, CO.

The opposite tendency was found for the model tungsten complexes [(PH₃)₂(CO)₂WL(≡CCH=CH₂)]⁺ (**15**) and [(H₂PCH₂CH₂PH₂)(CO)₂WL(≡CCH=CH₂)]⁺ (**16**) (L = Cl⁻, NCMe, CNMe or CO),³⁸ which contain such a strong π -acceptor as the carbyne ligand in addition to the nitrile or isocyanide ligands. If the ligand L is a strong π -acceptor (L = CO, CNMe), the *cis* isomers are more stable (L and the carbyne ligands are in the *cis* positions) (Table 4). In contrast, if the ligand L is a weak π -acceptor (L = NCMe) or an efficient σ -donor (L = Cl⁻), the *trans* isomers become more stable. The relative stabilities of the *cis* isomers compared to those of the *trans* isomers increases in the series Cl⁻ < NCMe < CNMe < CO in accordance with enhancement of the π -acceptor properties of the ligands (more precisely, with the net π -acceptor minus σ -donor abilities of the ligand). Theoretical predictions about the relative stabilities of the geometric isomers were confirmed by the experimental data on the *trans* → *cis* isomerisation of the tungsten isocyanide complexes.



L = Cl⁻, NCMe, CNMe, CO.



L = NCMe, CNMe, CO.

Based on the results of theoretical investigations^{38,67} and experimental studies,^{95–98} it can be assumed that configurations with σ -donor ligands and strong π -acceptor (in particular, CNR) ligands or with weak π -acceptor ligands (for example, NCR) and strong π -acceptor ligands in the *trans* positions are thermodynamically more stable for octahedral transition metal complexes in low oxidation states. Structures containing two strong π -acceptors, a weak π -acceptor and a σ -donor or two weak π -acceptors in the *trans* positions are less stable than the corresponding *cis* isomers. In contrast, for complexes with metals in

Table 4. Relative energies of the *trans*- and *cis* isomers of the complexes **15** and **16**.

L	$\Delta E = E_{trans} - E_{cis} / \text{kJ mol}^{-1}$	
	HF//HF	MP2//HF
[(PH ₃) ₂ (CO) ₂ WL(≡CCH=CH ₂)] ⁺		
Cl ⁻	-26.08	-27.05
NCMe	-12.56	-14.49
CNMe	11.60	10.63
CO	35.71	35.71
[(H ₂ PCH ₂ CH ₂ PH ₂)(CO) ₂ WL(≡CCH=CH ₂)] ⁺		
NCMe	-18.34	
CNMe	4.81	
CO	36.68	

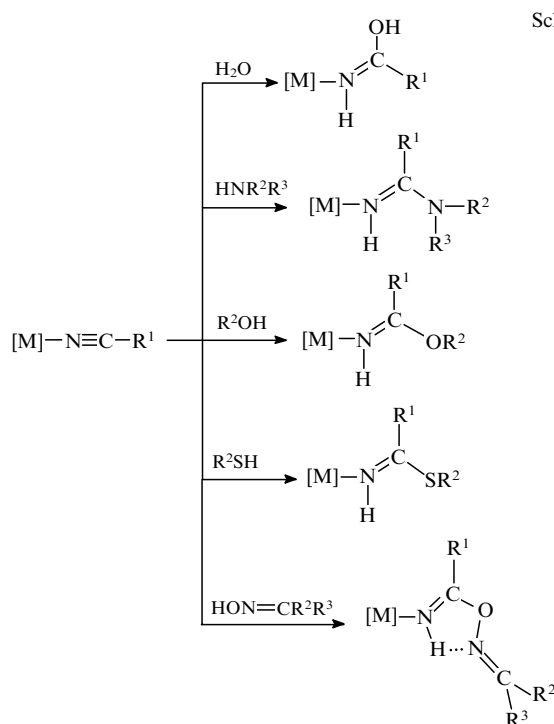
high oxidation states, structures with σ -donor ligands and weak π -acceptor ligands in the *trans* positions or with σ -donor ligands and strong π -acceptor ligands in the *cis* positions appear to be stable. The question of whether these conclusions have a general character calls for further investigations.

2. Nucleophilic addition reactions

Theoretical studies of the reactivities of compounds, in general, and complexes, in particular, are usually carried out with the use of frontier orbital theory.⁹⁹ According to this theory, if the reactivity of the compound is determined predominantly by the energies and compositions of the highest occupied and lowest unoccupied MOs (the so-called frontier orbitals) whose interactions are responsible for the formation of new bonds, the reaction is orbital-controlled. If the reaction (in particular, nucleophilic and electrophilic addition) is determined predominantly by the distribution of the effective charges on the atoms involved in formation of a new chemical bond, the reaction is charge-controlled.

Among various reactions with coordinated nitriles, the nucleophilic addition at the nitrile C≡N group is of paramount importance. These reactions were considered in numerous experimental studies and reviews. The reactions of such nucleophiles as water, amines, alcohols,^{4, 100–104} thiols,^{105, 106} phosphines,^{107–109} hydrazines¹¹⁰ and oximes^{111–114} with nitrile complexes lead to the addition of the nucleophile at the carbon atom of the C≡N group, which is generally accompanied by migration of the proton from the nucleophile to the nitrile nitrogen atom. Examples of the reactions of coordinated nitriles with a number of nucleophiles are presented in Scheme 1 (all products are arbitrarily shown in the *E* configurations). It was noted that coordinated nitriles are more reactive in nucleophilic addition reactions than the free ligands, the complexes of metals in high oxidation states being more reactive than those bearing metals in low oxidation states.

Theoretical studies concerned with activation of nitriles with metals and the reactivities of coordinated nitriles in nucleophilic addition reactions are few in number. The reactions of oximes with nitriles and hydrolytic processes have received the most study (see Section IV.3). Activation of nitriles upon complex formation is often qualitatively explained by a decrease in the electron density on the carbon atom of nitrile upon its coordination to the metal atom and, as a consequence, by the enhancement of electrophilicity of the β -carbon atom thus facilitating the attack of the nucleophile on this atom. However, theoretical studies^{43, 44, 69} demonstrated that this interpretation is in doubt. Thus it was found⁶⁹ that the effective charges on the C and N atoms of the nitrile ligand, which were calculated according to Lowdin scheme, are increased on going from free acetonitrile to the [Pt^{II}(NCMe)Cl₃]⁻ complex (Table 5), i.e., the electron density on these atoms decreases due to which the ligand becomes more accessible to nucleophilic attack. However, calculations of the



effective charges according to Mulliken gave another charge density distribution and opposite results. Thus the effective charge on the carbon atom of nitrile was found to decrease on going from NCMe to $[\text{Pt}^{\text{II}}(\text{NCMe})\text{Cl}_3]^-$.

The reactivities and activation of platinum nitrile complexes in the nucleophilic addition at the $\text{C}\equiv\text{N}$ triple bond were examined.^{43,44} The *ab initio* calculations of the effective charge distributions in free acetonitrile and three platinum complexes, viz., *trans*- $[\text{Pt}^{\text{II}}(\text{NCMe})_2\text{Cl}_2]$ (**10**), $[\text{Pt}^{\text{IV}}(\text{NCMe})\text{Cl}_5]^-$ (**11**) and *trans*- $[\text{Pt}^{\text{IV}}(\text{NCMe})_2\text{Cl}_4]$ (**12**), by the HF and MP2 methods with differ-

Table 5. Effective charges on the atoms in the NCMe and $[\text{Pt}(\text{NCMe})\text{Cl}_3]^-$ molecules.

Atom or ligand	NCMe				$[\text{Pt}(\text{NCMe})\text{Cl}_3]^-$	
	M ^a	L ^a	M ^b	L ^b	M ^a	L ^a
N	-0.09	-0.13	-0.08	-0.10	0.18	0.11
C	-0.05	-0.04	-0.05	-0.05	-0.16	0.13
CMe	0.14	0.17	0.11	0.15	0.10	0.20
NCMe	0	0	0	0	0.12	0.44
Pt					0.43	-1.15
Cl ^{trans}					-0.49	-0.05
Cl ^{cis}					-0.53	-0.12

Note. M is the analysis of the Mulliken populations, L is the analysis of populations according to Lowdin.

^a Without considering the electron correlation. ^b Taking into account the electron correlation.

ent basis sets demonstrated that the effective positive charge on the carbon atom of nitrile calculated according to Mulliken changes only slightly on going from the free ligand to the complex and is virtually independent of both the oxidation state of the metal atom and the total charge on the complex ion (Table 6).

Activation of nitriles in the complexes **10–12** can be partially accounted for by the orbital control. In the context of the theory of frontier orbitals, the formation of a new chemical bond upon nucleophilic addition results from the interaction between the HOMO of the nucleophile and the LUMO of nitrile. In this case, the reactivity must depend on the relative energies of these orbitals. If the reaction involves the same nucleophile, the reactivity must be governed by the energy of the LUMO of nitrile. Actually, calculations showed that the energies of the LUMOs of the complexes **10–12** are 1.5–3.5 eV lower than the energy of the LUMO (π^* -MO) of acetonitrile, which provides an explanation for the activation of MeCN in complexes. At the same time, the energy of the LUMO changes non-monotonically and insignificantly on going from **10** to **12** in spite of the noticeable enhance-

Table 6. Mulliken effective charges on the atoms calculated for the free NCMe ligand and the complexes **10–12**.

Atom	ECP ^a	3-21G ^b	6-31G ^b	6-31G(<i>d</i> -Cl) ^b HF	6-31G(<i>d</i> -Cl) ^b MP2	6-31G* ^b	DH ^b
NCMe							
N	-0.02	-0.51	-0.32	—	-0.25	-0.45	-0.09
C	-0.16	0.31	0.12	—	0.11	0.30	-0.05
<i>trans</i> - $[\text{Pt}(\text{NCMe})_2\text{Cl}_2]$							
Pt	0.75	0.51	0.59	0.66	0.24	0.62	0.27
Cl	-0.52	-0.44	-0.41	-0.43	-0.31	-0.43	-0.36
N	-0.16	-0.77	-0.39	-0.38	-0.25	-0.45	0.06
C	0.03	0.64	0.18	0.18	0.19	0.34	0.01
$[\text{Pt}(\text{NCMe})\text{Cl}_5]^-$							
Pt	0.82	0.32	0.09	0.34	-0.18	0.30	0.02
Cl	-0.40; -0.34	-0.33; -0.21	-0.26; -0.14	-0.31; -0.18	-0.22; -0.11	-0.31; -0.18	-0.26; -0.15
N	-0.14	-0.72	-0.36	-0.35	-0.20	-0.42	0.07
C	0.04	0.63	0.17	0.15	0.16	0.32	-0.05
<i>trans</i> - $[\text{Pt}(\text{NCMe})_2\text{Cl}_4]$							
Pt	0.84	0.59	0.44	0.67	0.07	0.59	0.29
Cl	-0.31	-0.26	-0.19	-0.24	-0.15	-0.23	-0.19
N	-0.17	-0.81	-0.39	-0.39	-0.21	-0.42	0.10
C	0.07	0.69	0.20	0.19	0.20	0.34	-0.03

^a Stuttgart quasi-relativistic pseudopotentials and the corresponding basis sets on the Pt, C, N and Cl atoms (for the hydrogen atoms, the 6-31G basis set was used). ^b Stuttgart quasi-relativistic pseudopotentials and the corresponding basis sets on the Pt atom.

ment of the reactivity in this series of compounds. In addition, the LUMOs of the starting nitrile complexes do not virtually involve the orbitals of acetonitrile although the nucleophilic attack occurs at the carbon atom of the nitrile group (see Fig. 9a).

The nucleophilic addition reactions of oximes with the complexes **10**–**12** were accompanied by a change in the geometry of the acetonitrile fragment from linear to angular, which corresponds to a change in hybridisation of the β -C atom from sp to sp^2 . Apparently, the change in hybridisation must cause the rearrangement of the valence molecular orbitals and substantial variations in their composition and energy. Analysis of the Walsh diagrams⁴⁴ demonstrated that the change of the conformation of coordinated acetonitrile from linear to angular leads to a decrease in the energy of the LUMOs of the complexes by 0.3–0.8 eV and to variations in the compositions of the lowest occupied MOs such that the orbitals of the carbon and nitrogen atoms of nitrile contribute significantly to the LUMOs (Fig. 9b). According to the theory of frontier orbitals, this bent distortion of acetonitrile facilitates the nucleophilic addition at the β -C atom.

With the aim of providing the more rigorous description of the relative reactivities of nitriles and their platinum complexes **10**–**12**, the activation and reaction energies of the interaction of formaldoxime with these complexes were calculated. It was found that the activation energy decreases and the absolute value of the reaction energy increases in the series NCMe–**10**–**11**–**12** (Table 7), which is consistent with the enhancement of the reactivity of these compounds. Hence, activation of nitriles in complexes and their relative reactivities can be described on the basis of kinetic (a decrease in the activation energy) and thermodynamic (an increase in the reaction energy) factors.

Table 7. Activation energies of the rate-limiting step (E_a /kJ mol^{−1}) and the energy effects (ΔE /kJ mol^{−1}) of the reactions of NCMe and the complexes **10**–**12** with formaldoxime.

Compound	E_a	ΔE
NCMe	275.16	−3.85
10	265.53	−66.61
11	253.93	−75.32
12	237.52	−91.73

The mechanism of nucleophilic addition of oximes to acetonitrile and the complexes **11** and **12** was examined in detail.^{43, 115} The possible transition states and the reaction coordinates were calculated. Under non-catalytic conditions, these reactions proceed through the formation of the four-membered cyclic transition state **A** (Scheme 2).

Nucleophilic and electrophilic addition to coordinated nitriles and isocyanides at the $C \equiv N$ triple bond are of great practical importance because these reactions allow one to prepare com-

pounds possessing valuable properties, which cannot be synthesised without the use of transition metals. Nowadays, these processes call for further extensive theoretical investigations.

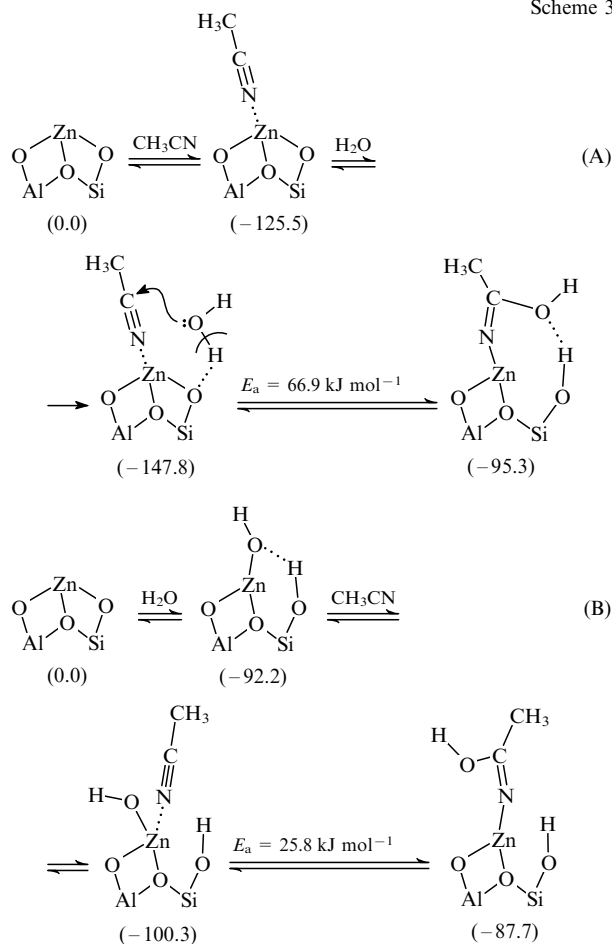
3. Catalytic reactions

One of the most promising and practically important directions in the theoretical chemistry of transition metal complexes is concerned with catalytic reactions whose mechanisms often cannot be studied in detail without application of theoretical methods. Actually, the idea of metal complex catalysis assumes that intermediates formed in the course of the reaction are highly labile due to which they often cannot be detected experimentally.

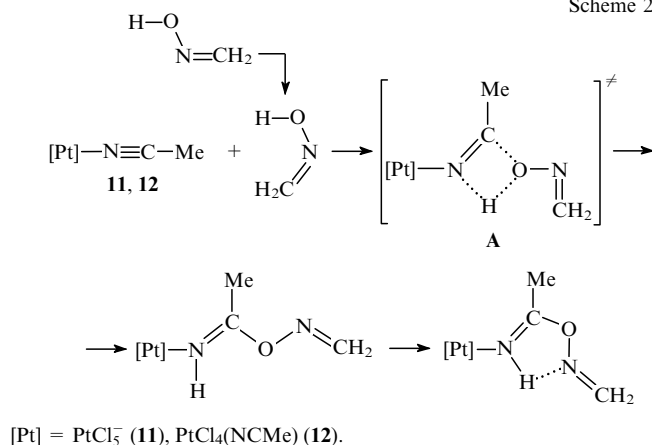
The mechanisms of catalytic reactions with the use of transition metal complexes have been the subject of much investigation, but the studies devoted to reactions involving nitrile complexes are few in number. Thus the mechanism of hydrolysis of acetonitrile adsorbed on Zn^{2+} ion-exchange zeolite was studied in detail by the DFT method.¹¹⁶ The reaction involves three main steps, *viz.*, hydration, isomerisation and desorption of the product. The first step includes two different processes, *viz.*, the initial activation of the reagents and the primary nucleophilic attack of the water molecule on Zn or nitrile. Of eight possible mechanisms of the first step (involving one water molecule), two mechanisms (A and B) shown in Scheme 3 are preferable (in this scheme and in Scheme 4, the calculated heats of formation of intermediates (in kJ mol^{−1}) are given below the formulae in parentheses).¹¹⁶

The first mechanism involves activation of nitrile upon coordination followed by the nucleophilic attack of the water molecule on the oxygen atom of zeolite and concerted elimination of the OH group with the simultaneous nucleophilic attack at the carbon atom of nitrile. The second mechanism (in the presence of an excess of water) consists in primary adsorption of the H₂O molecule on zeolite followed by the cleavage of the O–H bond

Scheme 3



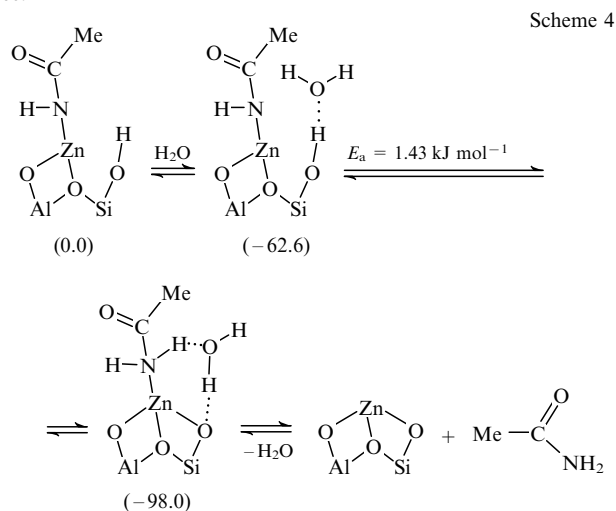
Scheme 2



and migration of the proton on the oxygen atom of zeolite, coordination of acetonitrile to the zinc atom and migration of the OH group from metal to the carbon atom of nitrile.

The second step (isomerisation) involves conformational changes of the iminol fragment and migration of the proton from the OH group to the N atom through the formation of a four-membered transition state (or a six-membered state with the participation of the water molecule).

The third step, *viz.*, desorption of acetamide, consists in the formation of the hydrogen bond between the hydrogen atom of the OH group and the new water molecule followed by the proton transfer from the water molecule to the nitrogen atom (Scheme 4) and desorption of acetamide by itself, which either occurs directly or proceeds with the participation of acetonitrile or water molecules.



The mechanism of nickel-catalysed hydrogenation of nitriles giving rise to amines was proposed.¹¹⁷ According to the results of EHMO calculations, the addition of the first hydrogen atom most probably leads to the attack at the carbon atom of nitrile to produce imidoethylidenes $\text{CH}_3\text{CH}=\text{N}=[\text{Ni}]$. Then either the second proton adds to the β -carbon atom to form the nitrene intermediate $\text{CH}_3\text{CH}_2-\text{N}=[\text{Ni}]$ or the imidoethylidene products undergo dimerisation.

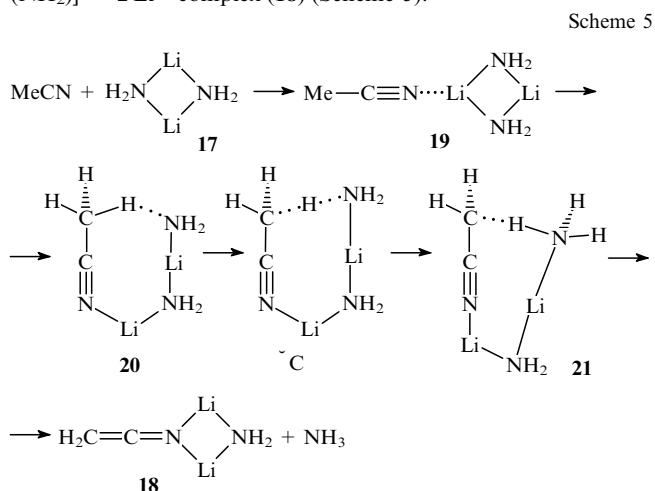
4. Other reactions

Hydrogenation of quinoline (Q) catalysed by $[\text{Ru}(\text{NCMe})_2(\text{CO})] \cdot \text{H}(\text{PR}_3)_2[\text{BF}_4]$ was studied by the CNDO/2 method.¹¹⁸ The bond between the metal atom and the acetonitrile ligand, which is located in the *trans* position with respect to the hydrogen atom, is weaker than that with another acetonitrile ligand located in the *cis* position with respect to this hydrogen atom. This arrangement facilitates the replacement of the former nitrile ligand in the reaction with Q although the reaction at the latter ligand also

can proceed to a considerable extent. Based on the results of calculations and taking into account the data from kinetic and chemical studies,¹¹⁹ the mechanism of this reaction was suggested.

In the experimental and theoretical investigation of the coordination transformations of the indenyl (Ind) ligand in the $[(\eta^5\text{-Ind})\text{MoL}_2(\text{CO})_2]^{0/+}$ complexes (L are various ligands, including NCMe and CNMe),¹²⁰ the $\eta^5 \rightarrow \eta^3$ -transformation of indenyl due to the addition of one more acetonitrile molecule to the $[(\eta^5\text{-Ind})\text{Mo}(\text{NCMe})_2(\text{CO})_2]^+$ complex was considered {this reaction did not proceed with the $[(\eta^5\text{-Ind})\text{Mo}(\text{CNMe})_2(\text{CO})_2]^+$ complex}. The driving forces for these processes were discussed based on the results of DFT and EHMO calculations.

The mechanism of the reaction of acetonitrile with dimeric lithium amide $[\text{LiNH}_2]_2$ (**17**) was examined by the MP2 and DFT methods and by the semiempirical methods (PM3 and MNDO).¹²¹ The reaction involves deprotonation of acetonitrile accompanied by the formation of the dianionic $[(\text{CH}_2\text{CN})/(\text{NH}_2)]^{2-} \cdot 2 \text{Li}^+$ complex (**18**) (Scheme 5).



The first step of the reaction affords the adduct of NCMe with the dimer of lithium amide (adduct **19**). This adduct is transformed into the 'open' dimeric complex **20**, which requires energy consumption of 47.7 kJ mol^{-1} (the MP2/6-31 + G*/MP2/6-31 + G* level, Table 8). Then, the migration of the proton from the CH_3 group of acetonitrile to the amino group occurs through the formation of a transition state (TS) to produce complex **21**. Finally, elimination of NH_3 gives rise to the reaction product **18**. Calculations by the PM3 method demonstrated that the intramolecular mechanism (including solvation) is 37.7 kJ mol^{-1} energetically more favourable than the intermolecular mechanism involving two dimeric molecules of lithium amide.

The driving forces for the chemical, electrochemical and photochemical activation of CO_2 by transition metal (Ir or Ni) complexes containing the isocyanide ligands were discussed relying on analysis of frontier molecular orbitals.³⁰

Table 8. Relative energies of formation of the compounds **17–21** and the transition state (TS) (kJ mol^{-1}).

Compound	PM3	6-31G*/6-31G* ^a	6-31 + G//6-31 + G ^a	MP2/6-31 + G*// MP2/6-31 + G* ^b	B3LYP/6-311 + G*// B3LYP/6-311 + G* ^b	DGauss/DZVP A1 ^b
NCMe + 17	0.0	0.0	0.0	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)
19	−107.10	−45.97	−42.96	−49.82 (−51.79)	−42.45 (−44.25)	−42.79 (−47.23)
20	−2.80	10.26	9.42	−4.14 (−4.10)	−4.14 (−3.06)	—
PS	18.92	40.74	46.81	8.37 (0.75)	−1.42 (6.11)	−13.98 (−11.30)
21	−68.08	−40.44	−46.39	−55.43 (−59.62)	−63.81 (−68.75)	−63.60 (−67.70)
18	42.08	51.37	34.29	49.91 (47.90)	23.36 (27.63)	24.24 (29.64)

^a The Hartree–Fock approximation; ^b the values, which were corrected for the zero-point energy scaled by a factor of 0.91, are given in parentheses.

V. Conclusion

To summarise, theoretical methods can successfully be used for the solution of practically important problems, such as investigations of electronic and geometric structures, spectroscopic properties, reactivities and reaction mechanisms of coordination compounds containing nitrile and isocyanide ligands. However, in spite of the fact that transition metal complexes with nitriles and isocyanides belong to an important class of coordination compounds (from both fundamental and applied standpoints), the theoretical chemistry of these compounds remains a poorly studied field of the modern coordination chemistry and applied quantum chemistry due, apparently, to the difficulties in describing coordination bonds in isocyanide and, particularly, in nitrile complexes.

In most cases, complexes with strong π -acceptor ligands, such as carbonyls, in which π -back donation most often prevails, are successfully described with the use of the Dewar–Chatt–Duncanson (DCD) model. However, this model must be applied to the interpretation of the properties of isocyanide complexes and, particularly, of nitrile complexes with caution because, being weak π -acceptors, nitriles and often isocyanides, form coordination bonds in which π -back donation is of secondary importance. The σ -component and Coulombic interactions make a large (and often the major) contribution to the coordination bonds in these compounds. As a result, there are often no direct correlations of the properties of these complexes with the π -acceptor ability of the ligand or with the difference between the π -acceptor and σ -donor properties.

Studies of the reactivities of coordination compounds are of paramount importance in modern chemistry. This problem is most efficiently solved by the combined employment of experimental and theoretical methods. Early in the development of applied quantum chemistry, theoretical analysis of the reactivities was restricted to examination of the electronic structures of the starting compounds. However, recent studies demonstrated that detailed data on the reaction mechanisms with consideration for all possible transition states and intermediates are necessary for the correct description of the chemical properties. A knowledge of the mechanisms and driving forces for chemical reactions helps essentially in the design of chemical experiments and target-directed syntheses. Modern computation tools and theoretical methods allow one to study the reactivities of complexes using high-level approximations. There is no doubt that theoretical studies of transition metal complexes, including those with nitrile and isocyanide ligands, will attract ever increasing interest in the near future.

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^b — *Russ. J. Coord. Chem. (Engl. Transl.)*

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Microwave radiation in analytical chemistry: the scope and prospects for application

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Abstract. The key aspects of the effect of microwaves on the physicochemical processes in solutions and heterogeneous systems are analysed. Good prospects for the use of microwave radiation for intensifying various types of interaction are demonstrated in relation to dissolution, hydrolysis of organic and inorganic substances, complex formation by metal ions in solution and in the sorbent phase, oxidation of organic compounds, and synthesis of coordination and organic compounds. Specific features of analytical operations with microwave treatment are considered and the trends of development of analytical methods using microwaves are discussed. The bibliography includes 137 references.

I. Introduction

In recent years, a breakthrough has taken place in the development of instrumental methods used in inorganic and organic analysis, such as electrothermal atomic absorption spectrometry (ETAAS), inductively coupled plasma atomic emission spectrometry (ICP AES), inductively coupled plasma mass spectrometry (ICP MS), chromatographic and GC/MS techniques, *etc.* This is due to the need for more stringent control of technological processes, development of the analytical groundwork for the search for new raw material sources, aggravation of the environmental problems related to industrial environment pollution. Meanwhile, traditional methods used to prepare samples for analysis, which are time-consuming, comprise many stages and require large amounts of reagents, held up the elaboration of modern quick analytical procedures and hampered implementation of the most important parameters of instrumental methods. Development of more advanced methods for preparing a substance for determination of its composition has become a highly topical task in modern analytical chemistry.

The efficiency of analysis is largely determined by the rate and completeness of the underlying physicochemical processes. The search for ways of affecting these processes and controlling them in various fields of chemistry and technology has resulted in

extensive use of physical fields¹ and in the design of photochemical, catalytic and ultrasonic methods. Nevertheless, an increase in temperature has the most crucial effect on reactions in solutions and heterogeneous systems. However, slow heat transfer from the source to the sample and within the sample creates insurmountable obstacles which preclude substantial acceleration of processes under conditions of conventional (thermal) heating. An alternative way of raising the temperature of reaction mixtures is fast bulk heating on exposure to electromagnetic radiation of the microwave range.

Microwave heating differs from the traditional one by the greater volume and time gradients involved and by the fact that solutions and components of heterogeneous systems differing in composition possess unequal abilities to absorb the energy of radiation. In addition, charged species and dipoles present in the solution become oriented in the electromagnetic microwave field, which has an influence on their interaction.² This changes the yields of reaction products³ and gives rise to some specific effects² observed only under microwave heating conditions. No unambiguous interpretations of these phenomena have been proposed; an approach to investigation of chemical processes induced by microwave radiation (MW) includes comparison of the reaction rates, the compositions and yields of the resulting compounds, and the activation energies of reactions proceeding under thermal and microwave heating.⁴

This review describes systematically the available data on the use of MW for the intensification of chemical reactions, first of all, those which underlie analytical operations.

II. Some aspects of the influence of electromagnetic fields on solutions

Numerous chemical reactions proceed in aqueous solutions or, at least, in the presence of water.⁵ The processes taking place in solutions, in particular, in aqueous ones, are mediated by interactions of the reactants with the solvent. These electrostatic interactions result in the formation of ions, solvation shells and assembled structures; this may prevent the initial substances from reacting with each other. The application of external physical fields, including electromagnetic fields, not only activates diffusion and mass transfer in solutions but also gives rise to additional effects upon electrostatic interactions, namely, it changes the degree of ordering of the solvent and the structure of solvation shells of ions, deforms the electron shells of atoms and molecules, facilitates reactions between species, increases the reaction efficiency, and accelerates chemical reactions. These phenomena can be of different natures such as the influence of the field on

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electrostatic interactions in solutions (an additional effect of external field), an increase in the system's intrinsic energy due to heating or the direct effect on charged species. An increase in temperature and the electric field effect have the most pronounced influence on the structure of water and solutions. Under exposure to MW, these factors are closely interrelated.

Now we consider the mechanisms of microwave heating in more detail. Microwave radiation is a form of non-ionising electromagnetic radiation whose frequency is intermediate between the infrared (IR) and radio-frequency ranges, namely, 300 to 30 000 MHz (wavelengths from 1 m to 1 cm). Since these waves are actively used in radio- and telecommunications, for industrial purposes, in science and in medicine, four frequencies are stipulated by international rules, a frequency of 2450 MHz (12.2 cm) being utilised most often. In recent years, radiation of this type is so widely employed to accelerate chemical processes and to solve applied analytical problems that some researchers have spoken about a new line of research called microwave chemistry;^{2,6} nevertheless, the data on the chemical aspects of the action of MW on reaction systems are sparse.

The mechanism of interaction of MW with matter involves absorption of the electromagnetic radiation energy by the material and scattering of the energy as heat. Although the microwave frequency corresponds to the rotational movement of molecules, in the condensed state where no free molecular rotations take place, as opposed to the gas phase, the absorption of energy immediately results in its redistribution between molecules and homogenous heating of the medium. Thus, microwave heating is a bulk phenomenon; the physical aspects of the effect of MW on a substance are described in detail in monographs dealing with the theory of dielectrics (see references in Ref. 2) and in some other studies.⁷⁻⁹

As MW passes through solutions, the transfer of energy occurs by two mechanisms, namely, due to re-orientation of the solvent dipoles in an alternating electric field and due to migration of ions of the solute, *i.e.*, through dipole rotation and ion conduction. The induced thermal motion is superimposed onto the solvent structure disordering, which is due to the orienting action of the field. The significance of each factor is dictated by the nature of the process and the reactants. It is worth noting that back in 1933, Bernal and Fowler,¹⁰ introduced the notion of 'structural temperature', according to which the influence of ions (*i.e.*, charged species which form some electric field) on water (solvent) can be likened to the action of an increase or decrease in temperature. These views can be useful for the understanding of the specific features of chemical reactions under microwave heating when the same outcome is attained at the same or even lower temperature than upon thermal heating.²

The mechanism of dipole rotation is the major one in the case of pure water or other solvents with low degrees of dissociation. The heating rate and the temperature that can be obtained largely depend on the radiation frequency, the initial temperature of the solution and on the solvent properties, in particular, the dielectric constant. Figure 1 shows the experimental curves characterising the microwave heating of water and some organic solvents.

The dielectric properties of free and bound (present as aggregates in a substance) water molecules are somewhat different;¹¹ as a consequence, they possess different capacities for absorbing the microwave radiation energy. This difference can be clearly seen when examining drying in a microwave oven of ferrimanganese concretion samples (FMC),¹² which are layered structures binding water molecules in different ways. When dried under conventional conditions, FMC initially lose the absorbed water and then the water incorporated in the structure of the minerals.¹³ A similar stepwise removal of water also occurs in a microwave field, and the curves for the loss of weight by the samples during microwave heating for several minutes reveal the presence of different H₂O forms. This selectivity in the absorption of the radiation energy by the solvent molecules bound in different ways has also been used^{11, 14, 15} in microwave extraction techni-

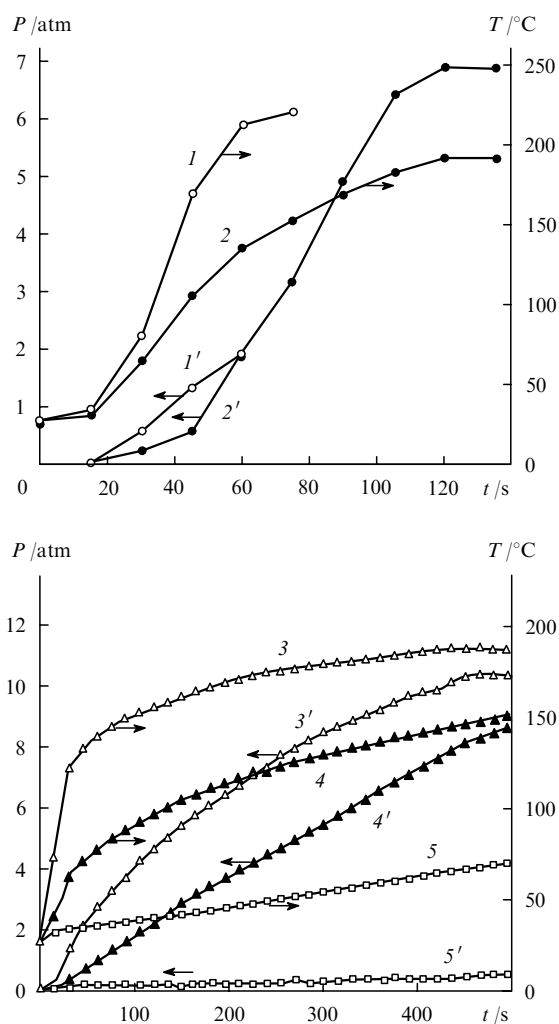


Figure 1. Effect of microwave radiation on the variation in the temperature (T) of solvents (1–5) and the pressure (P) of the vapour (1'–5') in a closed vessel: (1, 1') dimethyl sulfoxide; (2, 2') water; (3, 3') propan-2-ol; (4, 4') dichloromethane; (5, 5') hexane (t is the time of microwave treatment).

ques.[†] The stepwise pattern of variation of the absorptivity of aqueous solutions of alcohols, indicating the presence of different molecular structures, has also been noted in other publications.^{16, 17}

Yet another mechanism of the microwave heating is related to the effects of conduction, which may be due to electrophoretic ion migration in solution or the transfer of charged species in a solid upon application of an electromagnetic field. The contribution of the ion conduction mechanism in solutions is determined by the sizes, charges and the electrical conductivity of ions;⁸ in addition, this value depends on the interaction of ions with solvent molecules. The ion conductivity depends on the concentration, ion mobility and the solution temperature. Compounds with high dissociation constants absorb efficiently the microwave energy.

The relative contribution of each of the two mechanisms of transformation of the MW energy (dipole rotation and ion conduction) depends substantially on the temperature. For small molecules such as water molecules or molecules of other solvents, the dielectric loss caused by the contribution of the dipole rotation

[†] The term 'microwave extraction' is often used in the literature to describe the extraction of useful components of different natures by any solvent on exposure to MW. Here, this term is used to imply the extraction of organic components by organic solvents.

decreases with an increase in the temperature.^{8, 18} Conversely, the dielectric loss due to ion conduction increases with an increase in the sample temperature, and the effect of MW on charged species becomes more significant. Due to the diversity of factors which influence the warming-up of a solution exposed to MW, modelling of this process is currently considered to be impossible,² although a physical model that allows the calculation of the change in the solution temperature in an open system has been proposed, the mechanisms of gaining and losing energy through the solution have been analysed,¹⁹ and the theoretical aspects of the microwave heating of solids have been considered.^{20, 21}

It is generally believed among the analysts who use laboratory microwave systems mainly for the routine digestion of samples that fast heating is the major or the only consequence of action of a microwave field on solutions. Indeed, the MW frequency approximately corresponds to the frequency of the rotation of molecules but the energy of a quantum per mole ($\sim 1 \text{ J mol}^{-1}$) is too low to cleave not only chemical bonds (the energy of a C–H bond is 350 kJ mol^{-1}) but also hydrogen ($\sim 20 \text{ J mol}^{-1}$) and even van der Waals bonds (2.5 J mol^{-1}).¹¹ However, regarding chemical transformations, the changes in the structures of the solvent and solvated ions are especially important because, as noted above, it is the solvation shells that hamper the occurrence of reactions involving ions and molecules; the electron density redistribution in molecules and conformational changes induced by an electromagnetic field are equally important.

It can be seen from Fig. 2 that an electromagnetic field brings about a substantial change in the state of the ion shell; as a consequence, the ion should become much more reactive and accessible for a nucleophilic attack. The electron density shifts very rapidly (in 10^{-14} s)²³ (electron polarisation), and then it is 'fixed' in the field with the given frequency over a period of $2.5 \times 10^{-9} \text{ s}$; the positions of the ions and molecules themselves change to a much lesser extent. During the indicated period, a field-activated ion present in aqueous solution can participate in $10-10^3$ collisions. This is important, for example, when microwave heating is used to accelerate substitution in the inner coordination spheres of complexes with inorganic ligands or in the molecules of organic compounds where steric factors and configurations of the reacting species are rather significant. In particular, acceleration of complexation caused by microwave

treatment has been observed for various elements and sorbents in different sorption regimes at the same temperature as in the case of traditional heating.²⁴⁻²⁶ Note that the displacement of the electron density in an electromagnetic field does not depend on the temperature and can be attributed to so-called non-thermal effects.

Direct evidence for the change in the state of solvated (hydrated) species in a microwave field has also been obtained. Circular dichroism measurements provided experimental data on the change in the spatial structure of protein molecules, which is known to be largely formed due to hydration of polar groups in the polypeptide chains by water molecules. Experiments carried out[‡] at different temperatures with either thermal or microwave heating of an aqueous solution of erythropoietin demonstrated that thermal heating at 65°C is equivalent to exposure to MW at 45°C over a period of time which makes only 7% of the overall experiment duration (recall the Bernal and Fowler's structural temperature).

We have also observed destruction of colloid particles of soil in an MW field; thus the microstructure of the particles formed by hydrated layers was identified; the solution temperature did not exceed 50°C .

Microwave treatment can induce additional thermal effects related to the nature of the influence of the radiation on the system. In the case of conventional heating, the number of boiling centres in the solution bulk is much smaller than that near the surface. The microwave heating takes place from the inside, uniformly throughout the whole bulk; therefore, the temperature of the solution is higher than the temperature of the surroundings (vessel walls, the gas phase above the solution, *etc.*).²⁷ As a result, the solution can be heated to a temperature exceeding its boiling point under atmospheric pressure, which has been shown experimentally using various physical methods^{2, 3} (Table 1).

Table 1. Change in the boiling point (b.p.) of liquids of different natures under microwave radiation conditions.^{2, 3}

Solvent	b.p. /K		$\Delta \text{b.p. /K}$
	traditional heating	microwave heating	
Water	373	377	4
Methanol	338	357	19
Ethanol	352	376	24
Propan-2-ol	355	373	18
Tetrahydrofuran	339	354	15
Dichloromethane	313	328	15
Acetonitrile	354	380	26
Acetone	329	354	25
Diglyme	435	448	13
Ethyl acetate	351	368	17
Dimethylformamide	426	443	17
Diisopropyl ether	342	358	16

One more mechanism of interaction of MW with the matter is possible in heterogeneous systems, which is due to interface phenomena (interfacial polarisation). The thermal effects thus arising are used to heat mixtures of dielectrics with compounds that poorly absorb the MW energy.²⁸ The non-uniformity of heating caused by different abilities of substances to absorb the MW energy gives rise to non-trivial results upon bulk removal of water, synthesis on solid surfaces and the preparation and use of catalysts.^{2, 29} The difference in the ability of the initial reactants

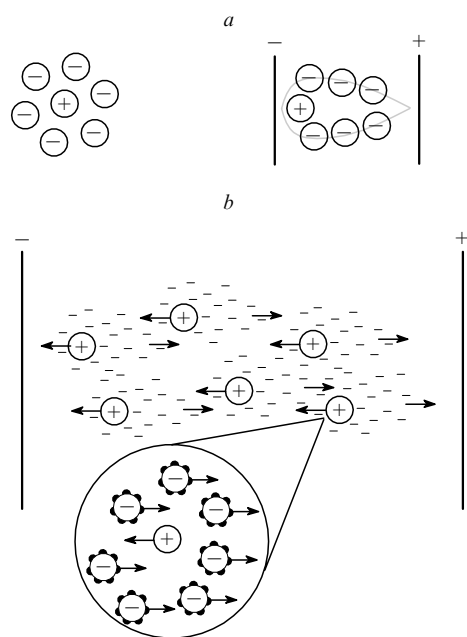


Figure 2. Change in the state of the ionic environment in a microwave field (a) and electrophoretic effect (b).²²

[‡] We carried out these studies together with N V Bovin (Institute of Bioorganic Chemistry, Russian Academy of Sciences).

and reaction products to absorb the MW energy can give rise to self-catalysed reactions.³⁰

The course of chemical processes and the composition of the resulting products are influenced by one more important factor, the time gradient of heating ($\Delta T/\Delta t$), which is much higher in the case of microwave treatment than in the case of conventional heating of solutions. When several competing reactions with different rate constants take place simultaneously, the probabilities of formation of particular products in the very narrow temperature range under the action of MW can differ appreciably from those observed under conventional heating. The same is true for equilibrium processes in which the rate constants for the forward and back reactions are different. This fact has been considered³¹ as the reason for the higher selectivity of some processes of organic synthesis under microwave heating.

III. Specific features of chemical reactions in a microwave field

This Section covers the main types of reactions widely used in analytical practice.

1. Hydrolysis of inorganic and organic compounds

The effect of MW on reaction systems is most pronounced in the case where the radiation energy is absorbed directly by a reactant. In some cases, a reactant acts simultaneously as the reaction medium. Evidently, MW should have a substantial influence on hydrolysis because water efficiently absorbs energy of electromagnetic radiation.

Hydrolysis induced by MW has been used to synthesise organic compounds,^{32,33} to cleave the peptide bonds in proteins when determining their amino acid composition,^{34,35} and to study the composition of a number of other natural compounds.^{35,36}

Hydrolysis of inorganic compounds in a microwave field has been studied³⁷ in relation to the exceptionally stable polynuclear iridium sulfate complexes. The uncertainty in elucidation of the composition of these complexes is the main cause for the analytical problems arising during determination of iridium in sulfate solutions by various methods. The mononuclear chloride complex of iridium was prepared upon hydrolysis and destruction of the iridium sulfate complex on exposure to MW with subsequent transformation of the resulting aqua hydroxo complex into the chloride complex on treatment with NaCl in HCl. Microwave irradiation accelerates deprotonation and hydrolysis. The degree of transformation of sulfate complexes of iridium into the chloride complexes is linearly dependent on temperature, which indicates a substantial contribution of thermal effects to acceleration of the reaction. However, it has not yet been explained why the metal is stabilised in the higher oxidation state under the action of MW.

The rigorous conditions of hydrolysis, namely, concentrated acid and elevated temperature, ensure the cleavage of most of hydrolysable bonds in organic compounds. However, in many cases, these conditions also promote undesirable side processes, in particular, destruction of either initial compounds or reaction products. The efficiency of using microwave treatment for performing such reactions was first demonstrated by Majetich and Hicks.³⁸ Of special importance is the choice of conditions for mild and, simultaneously, selective hydrolysis for the removal of protective groups. Under microwave heating, the occurrence of these reactions is markedly facilitated.³³

Microwave-enhanced hydrolysis has been used for analytical purposes in the synthesis of macrocyclic compounds³⁹ that have found application as reagents for determination of metals. Acid hydrolysis of *p*-toluenesulfonyl protective groups under conditions of thermal or microwave heating has been studied in relation to a number of macrocyclic compounds and their linear fragments.^{40,41} The possibility of stepwise hydrolysis under the action of radiation and, hence, targeted control of reaction products has been demonstrated. Compounds have been synthesised that could not be prepared in the given reaction system

upon thermal heating. The achieved effects are caused, most likely, by the sharp increase in the temperature of the reaction mixture under conditions of microwave heating (to 200 °C for 2 min), which is due, to some extent, to the absorption of the radiation energy by the substrate;⁴ according to some views,⁴² this substantially activates the reactions.

2. Complexation of metal ions with organic reagents

The kinetic inertness of the coordination compounds of a number of metals towards substitution is often an obstacle hampering the practical use of complexation reactions.⁴³ The use of MW for the solution of various problems related to complexation has been described only in a few publications. For example, it was demonstrated that coordination compounds of transition and noble metals, in particular, chromium, ruthenium, iridium, platinum and gold, with organic ligands can be synthesised efficiently under microwave heating.^{44,45} The analytical aspects of complexation of inorganic ions in solutions and in the phase of complexing sorbents under the action of MW (sorptional collection of palladium and rhodium⁴⁶ and chromium²⁶ using nitrogen-containing sorbents, the formation of complexes by the platinum metal and chromium in solutions) have been considered.^{25,47–50} A reaction with microwave heating between cadmium or cobalt ions and immobilised reagents, bromothiazole and 1-(2-pyridylazo)-2-naphthols,⁵¹ prepared using MW, has been described.⁵² The possibility of synthesising coloured compounds of platinum metals for spectrophotometric determination of metals in a flow system on exposure to radiation has been demonstrated.^{53,54} A study⁵⁵ has been devoted to the targeted synthesis of binuclear tetraacetate, the initial compound for the coulometric determination of rhodium, in the solution to be analysed. The general regularities of MW-assisted complexation identified for the above-listed systems are considered below.

a. Complex formation in solutions

The reactions of metal ions with nitrogen-, sulfur- or oxygen-containing reagents under routine conditions can involve ligand desolvation and conformational changes, hydrolysis and desolvation of metal ions, changes in the metal oxidation state (usually, reduction to a more labile state), and the formation of a complex (metal–ligand interaction), which is complicated in some cases by the formation of polynuclear complexes.^{47,49,56} For complexation under microwave heating conditions, it is most often impossible to separate the contributions of thermal effects and the field effects on the electrostatic interactions of particles. According to the Arrhenius equation, the rate constants of the slowest reactions increase most appreciably as the temperature rises. The orienting action of the field can play a crucial role in the case of sterically hindered transformations, for example, those involving large molecules of organic compounds which react with metal ions according to the nucleophilic substitution mechanism.

The most comprehensive information on the intensification of complexation under the action of MW has been obtained for platinum metal compounds (Table 2) some chemical forms of which are extremely inert towards ligand substitution.⁴³ It was found that radiation substantially intensifies the reduction of metals (at the same temperature),^{25,50,57} markedly shortens the reaction time and often makes it possible to exclude the use of stabilising additives. The composition of complexes thus formed does not change. The labilising action of MW is so pronounced that the efficiency of complexation does not depend on the initial form of the metal. This allows the use of MW for reagent-free activation of inert coordination compounds.⁵⁸

b. Complex formation in the sorbent phase

The sorption of metal ions on sorbents with fixed complexing groups depends not only on the chemical reaction but also on the diffusion of metal ions both from the solution to the sorbent (outer diffusion) and in the sorbent pores (inner diffusion). It was noted that in the reaction of cobalt ions with the modified silicic

Table 2. Effect of microwave radiation on the time (*t*) of metal complexation with organic reagents in solution.

Metal	Reagent	Hypothetical composition of the complex	<i>t</i> /min		Ref.
			usual conditions	microwave treatment	
Pd(II)	chlorophosphonazo-mN	PdR ₂	1	0.5	54
Rh(III)	5-chloro-2-pyridylazo-2,4-diaminobenzene	unknown	does not react	0.5 ^a	53
Ru(III)	the same	the same	the same	0.5 ^a	53
Os(IV)	"	"	"	0.5 ^a	53
Ir(IV)	"	"	"	0.5 ^a	53
Pt(IV)	"	"	"	0.5 ^a	53
Ir(IV)	2,2'-bipyridine	[Ir(H ₂ O)R ₃] ²⁺	220	10	47–49
Os(IV)	1,10-phenanthroline	[OsR ₃] ²⁺	180	15	47
Ru(IV)	the same	[RuR ₃] ²⁺	45	6	47
Ru(IV)	sulfochlorophenolazorhodanine	[RuCl ₄ R ₂] [–]	30 ^b	4	25, 48
Al(III)	sulfonaphtholazorhodanine	[AlR ₃] ³⁺	60 ^b	4	25, 48

^a Complexation in the presence of a reducing agent. ^b Complexation in the presence of an acetate buffer solution.

acid xerogel, microwave heating increases the rates of both the outer and inner diffusion.⁵¹ Acceleration of diffusion processes on treatment with physical fields of various natures has also been described in other publications.^{20, 21, 59–61}

The extraction of noble metals by the POLYORGS IV sorbent containing 3(5)-methylpyrazole groups has been studied under static conditions.^{12, 46} The action of MW substantially accelerates the process (which takes place at the solution boiling point) both for rhodium, which reacts with sorbent groups by a complex-formation mechanism,⁶² and for palladium and platinum (which react by the ion-exchange mechanism⁸). Similar results have been obtained for sorption on POLYORGS XI-H,²⁴ the degree of rhodium collection in a microwave field being higher than that with conventional heating. The observed acceleration of sorption has been explained by the influence of the electromagnetic field on the state of the complex ion and electrostatic interactions in solution. Under conventional conditions, similar results can be attained by adding alkali metal salts, which destroy the structure of the solvation shells of ions; however, the effect of a microwave field is much greater.¹²

Microwave treatment has markedly enhanced the efficiency of collection of chromium ions, especially Cr(VI), by the DETATA sorbent.^{26, 63} Almost complete separate extraction of Cr(III) and Cr(VI) from solutions with pH 7 and 3, respectively, can be attained only using MW. An EPR study of the possible changes in the Cr(III) coordination sphere during the reaction with the aminocarboxy groups of the sorbent showed that the spectra of the complexes obtained at room temperature with conventional heating and in a microwave field are identical. This indicates that the same complex species of Cr(III) are formed under different conditions and that the factors influencing the reaction rate make the predominant contribution to the increase in the efficiency of sorption extraction of chromium on exposure to MW. Obviously, the same factors increase the efficiency of preconcentration of chromium ions by sorption in a flow regime and make it possible to increase the solution flow rate from 0.4–0.5 to 10 ml min^{–1}. Similar results have been obtained in a study of the reaction of cadmium ions with silicic acid xerogels modified by organic reagents.⁵¹

3. Oxidation of organic compounds by inorganic acids

Oxidation of an organic matrix with nitric acid is a widely used analytical operation. Study of the mechanism of oxidation of organic compounds including natural products in a microwave field^{64–67} showed that, as in the case of traditional heating, the

major reaction products include, apart from carbon dioxide and water, nitro-substituted aromatic acids, which decompose at temperatures above 260 °C. The same composition of the oxidation products obtained in the conventional and microwave heating modes suggests that the reactions follow the same pathways. However, the rates of oxidation are substantially different: decomposition of organic matrices at the same temperature is much faster with microwave heating than with traditional heating both in open and closed systems.^{67, 68} No unambiguous interpretation of this fact can be found in the literature; therefore, it seems important to compare the quantitative characteristics, for example, the activation energies (*E*_a) of the processes that take place under different conditions. The first attempt to solve this complicated experimental problem was made by Pratt,⁶⁹ who showed that the *E*_a values for the oxidation of amino acids (phenylalanine and tryptophan) with nitric acid under conditions of conventional and microwave heating are equal.[¶]

Bacci *et al.*⁷¹ were the first to use heating of the reaction system by microwave radiation when determining the thermodynamic functions and kinetic parameters. Microwave heating at a rate of 6.0–7.5 K min^{–1} was combined with simple photometric recording of the absorbance of the resulting complex. This technique appears efficient because the experiment can be carried out quickly and no temperature gradients exist in the solution; however, special experimental equipment is required.

In recent years, continuous temperature variation⁷² has been used to estimate the activation energies of various processes ranging from enzymic reactions to evaporation of atoms in electrothermal atomic-absorption spectrometry (dynamic method). This method is based on a logarithmic dependence of a parameter proportional to the concentration of an element or a substance in the analytical volume on the reciprocal temperature. This dependence is used to calculate the activation energy of the process using the Arrhenius equation from the slope of the straight line plotted in the ln *P*–*T*^{–1} coordinates, where *P* is the sought-for parameter (in particular, pressure) and *T* is absolute temper-

¶ Only sparse data on determination of *E*_a under conditions of microwave treatment can be found in the literature. The researchers' opinions concerning the coincidence of the activation energies of processes carried out with traditional and microwave types of heating are different. For example, the activation energy for sintering of alumina calculated for microwave heating⁷⁰ is several times lower than the *E*_a value for this process carried out with traditional heating. Apparently, this is due to the specific character of microwave heating, namely, high temperature and time gradients and a change in the ratio of contributions of various reactions to the overall process under these conditions. A refined mathematical model describing the temperature–time distribution in solid metal oxides heated by MW has been reported.²⁰

§ Acceleration of cation exchange processes has also been described by Mingo and Baghurst.⁷

ature. An important aspect in using the dynamic method is substantiation of the applicability of experimental results to the construction of the Arrhenius plot and determination of the thermodynamic characteristics of the processes.

Modern commercially produced laboratory microwave systems are equipped with fibre-optics sensors for direct measurement of the temperature of the reaction mixture, by monitoring systems of the pressure in the vessel and facilities for data recording in graphical and digital forms at 1–30 s intervals. Hence, this equipment can be used to study processes during which the pressure in the system varies together with the temperature, in particular, due to the formation of gaseous reaction products. This formed the basis of a mathematical model for the kinetics of a chemical reaction⁴ proceeding in a closed vessel under the action of MW, which was developed in the simple approximation of homogeneous distribution of the temperature and pressure in the system. The above-considered dynamic method for determination of the activation energy for the oxidation of organic compounds by nitric acid from the experimental exponential dependence of the system pressure on the reciprocal temperature of the reaction mixture was substantiated.

Microwave oxidation of individual organic compounds (amino acids, stearic acid, monosaccharides) forming the basis for the most important natural products (proteins, fats and carbohydrates) has been studied.^{73,74} Figure 3 shows the temperature and pressure variation in the system vs. time during the oxidation of phenylalanine by nitric acid; Figure 4 presents the Arrhenius dependence of the total pressure in the system, which is proportional, in the chosen approximation,⁴ to the rate constant

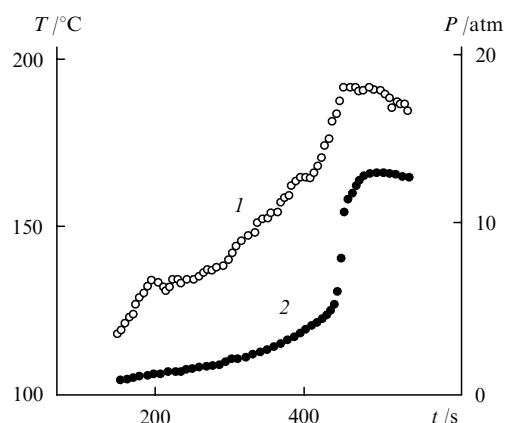


Figure 3. Effect of microwave radiation on the variation of temperature (1) and pressure (2) in a closed vessel during oxidation of phenylalanine by nitric acid.⁷⁴

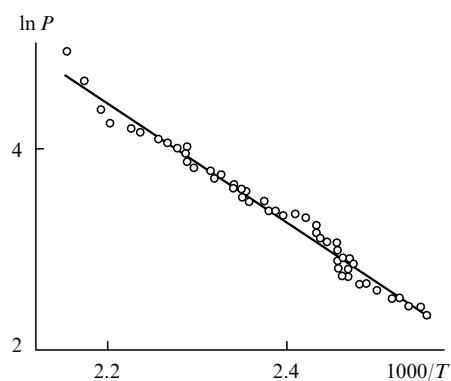


Figure 4. Arrhenius dependence of pressure on temperature during oxidation of phenylalanine by nitric acid under conditions of microwave heating ($E_a = 50.1 \text{ kJ mol}^{-1}$).⁷⁴

Table 3. Experimental values of the activation energy (E_a) for the oxidation of organic compounds determined under microwave heating conditions.⁷⁴

Class	Compound	$E_a / \text{kJ mol}^{-1}$
Sugars	saccharose	73.3
	galactose	73.5
Amino acids	lysine	24.0
	phenylalanine	50.1 (50.0 ^a)
	tryptophan	32.0 (29.8 ^a)
Fatty acids	stearic acid	76.4

^a The data were obtained with electrochemical detection of the products of decomposition of amino acids at constant temperatures (static method).⁶⁹

for the oxidation, on the reciprocal temperature. The data for the calculation of the activation energies for the oxidation of some model compounds and natural products are listed in Table 3. These values fall in the normal range of the E_a values typical of reactions of this type carried out with traditional heating (40–120 kJ mol^{-1})⁷⁵ and are correlated with the strengths of chemical bonds in the molecules of these compounds.

The approach to the determination of the activation energy of oxidation used in this work was implemented within the framework of formal kinetics and the views of the collision theory in which the pre-exponential factor $A = zN$ in the Arrhenius equation $k = A \exp[-E_a/(RT)]$ reflects the influence of the steric factors (N) and the number of collisions (z). In addition, this approach does not contradict interpretation of the results obtained in terms of the transition state theory. In this case, the activation energy correlates with the enthalpy of formation of the activated complex, and the pre-exponential factor is correlated with entropy. The former correlation leads tacitly to a fundamentally important conclusion stating that the reaction pathway remains invariant irrespective of whether it is induced by microwave or traditional thermal heating, and the latter correlation attests to an important role of the entropy factor, *i.e.*, the orienting influence of the electrical component of a microwave field on the reacting species. Thus, acceleration of chemical reactions by microwave radiation is due to kinetic factors. Hence, microwave heating can be used not only to affect physicochemical processes in solutions or heterogeneous systems but also for fast determination of the quantitative characteristics of reactions and modelling of kinetically hindered transformations.

4. Synthesis of organic compounds

Within the scope of this review, which is mainly devoted to the processes used in the chemical analysis and accelerated by microwaves, it is also pertinent to touch upon some aspects of organic synthesis. First, for many reactions involving organic compounds, the reaction mechanisms, the roles of the solvent and the composition of the reaction mixture and reaction conditions have been studied in sufficient detail. This makes easier the identification of the effects caused by the additional external treatment and promotes the understanding of the general mechanisms of the microwave influence on chemical transformations. Most of the results unexplainable in terms of thermal effects alone and most studies analysing the patterns of MW influence on the course of reactions refer to the processes of organic synthesis.^{2,3,42} Second, diverse compounds of the organic nature (solvents, extractants, polymer-based sorbents, complexing reagents including macroheterocycles) play an enormous role in analytical research, and development of methods for preparing them remains a topical task.

The extensive use of MW for synthetic purposes started in 1986.^{76,77} Acceleration in a microwave field of many organic reactions such as elimination, esterification, cycloaddition, isomerisation, substitution, hydrolysis, dehydration, condensation, *etc.*, has been noted.^{2,3,42} In some cases, the reaction time

determined on the basis of the product yield can be shortened by three orders of magnitude.⁷⁸ The reaction conditions are exceptionally diverse — at atmospheric or elevated pressure, in a flow, in aqueous or non-aqueous solutions, on a solid surface^{2, 42, 79} and in the solid phase.⁸⁰ A laboratory setup has been elaborated for microwave organic synthesis⁸¹ carried out at high pressures (up to 100 atm) and at a temperature of up to 260 °C.

The decrease in the solution viscosity, heating of the solution to a temperature higher than the boiling point, change in the electron density distribution in the molecules of organic compounds and in the contribution of the products of competing reactions are, apparently, the main factors inducing the effects observed when organic reactions are carried out under microwave radiation. It has been shown⁸² that the kinetics and the order of reactions do not depend on the method of heating. However, some abnormal features may arise on exposure to MW.⁸³ In competing reversible reactions,³¹ the rate of warming-up of the reaction mixture plays the most important role because the ratios of the products formed are different at different temperatures. Fast microwave heating allows one to perform the reaction at a strictly specified temperature and to minimise the duration of the temperature variation step and, hence, to avoid conditions that may bring about the formation of undesirable products. In some cases, the abnormally high selectivity and substantial yields of the reaction products for the reactions taking place in the presence of catalysts or on supports after the removal of a solvent, can be explained by the selective heating of separate sections of the surface on which the reaction takes place, due to the microwave irradiation. A sharp increase in the yield (from 2% to 92%) of the product of intramolecular rearrangement of unsaturated ketones has been noted⁸⁴ (the results were obtained from conventional and microwave heating, respectively, at the same temperature; the publication cited contains no kinetic data⁸⁴). The synthesis of acetylene in a yield of >90% by microwave cracking of benzene has been reported⁸⁵ (the thermal cracking of benzene scarcely takes place). The reaction mode also has a certain influence on the product yields. For example, the increase in the yields of products in some organic reactions induced by microwave radiation was reported to be more pronounced in the flow mode than in closed vessels.⁸⁶ This fact was attributed² to the higher surface area of the reaction mixture in the case of flow systems, because the action of MW on the surface increases the contribution of the interfacial polarisation mechanism.

It has been suggested in a review⁴² generalising the results of a large number of synthetic studies dealing with the use of MW that, if the radiation energy is absorbed only by the solvent, the acceleration of reactions with respect to those proceeding by conventional heating will not be significant. If the radiation interacts with either the reactants or intermediate compounds, the increase in the reaction rate can be appreciable. The absorption of the radiation energy by not only the solvent but also the reacting substances is observed, in particular, for polymerisation processes.^{87–89} This makes it possible to control the conditions of synthesis with high accuracy and to reduce the energy expenditure by a factor of 10–20. The polymers produced in this way often possess better physical properties, for example, higher strengths,³ than the polymers synthesised with conventional thermal heating,⁴² although the structures of both types of polymer are similar.

The conditions used to conduct reactions are diverse, and the outcome depends appreciably on the type of the process, the nature of the solvent and the reactants, the radiation power and the way of irradiation,⁴² because these factors determine the degree of action of MW on the reaction system. For example, variation of the conditions of emulsion polymerisation of acrylates allows, apart from shortening of the polymerisation time by a factor of 60,⁹⁰ the synthesis of poly(*p*-nitrophenyl acrylates) with molecular masses ranging from 40 000 to 180 000.

IV. Microwave-assisted sample preparation in chemical analysis

The preparation of samples for the measurement of the analytical signal from a particular component can include drying, ashing, mineralisation, decomposition (dissolution) and preconcentration (matrix separation). The sample pretreatment operations are based on various chemical reactions and physicochemical interactions involving components of the sample. Many of these reactions (hydrolysis, oxidation, complexation) have been considered above; their typical features observed under microwave heating also remain valid for sample pretreatment processes. Despite the obvious similarity of the occurrence of chemical reactions under thermal and microwave heating, significant additional effects can be attained in the latter case by using the specificity of warming-up induced by radiation. The development of microwave-assisted sample preparation techniques has been the subject of hundreds of papers, two monographs^{2, 8} and several reviews.^{11, 15, 18, 58, 63, 91–95}

1. Drying

Owing to the direct absorption of the MW energy by H₂O molecules, heating and vaporisation of water present in the pores of a material proceed much faster than under conventional conditions. Unlike the situation with traditional heating, warming-up of the material becomes less pronounced as water is removed, and by the end of the process, the sample temperature decreases.

It is expedient to carry out microwave-induced drying for individual substances, for example, in the preparation of inorganic specimens,⁹⁶ or in those cases where the accuracy of analysis is not subject to stringent requirements. This is due to the fact that it is difficult to select conditions for the microwave drying of materials with mixed or variable composition⁹⁷ because water molecules bound to the matrix in different manners absorb the MW energy to different extents. If a determination reproducibility equal to several percent is admissible, drying in microwave ovens has a substantial effect.^{2, 12, 98} The results of early studies on the use of microwave drying are summarised in a monograph,² and the most recent achievements along this line have been reported.⁹⁹ An interesting way of using MW for drying of silicic acid gels in the preparation of modified xerogels has been proposed.⁵¹

2. Ashing and fusion

These operations involve no direct action of MW on the substance under analysis; as in the case of conventional heating, the material is warmed up by the muffle furnace walls, which are heated extremely rapidly (in several minutes) to 1200 °C due to the efficient absorption of the radiation energy by silicon carbide, which is the material of the internal walls.⁸ As a consequence, the time required for the furnace to be heated is markedly shortened and the efficiency of the method increases. The duration of the ashing decreases several-fold because of the use of forced convection; fusion can also be carried out 1.5–2.0 times faster.

3. Digestion

One of the most important applications of microwave systems in analysis is to decompose samples having highly diverse compositions and origins. Since the first publication¹⁰⁰ dealing with the use of a microwave oven to accelerate the sample pretreatment appeared in 1975, numerous expedients and techniques of microwave decomposition suitable for virtually any type of object have been developed; they are covered in the above-mentioned monographs^{2, 8} and reviews.^{18, 58, 63, 91–95} We shall note only typical features of this method for sample digestion.

Decomposition of substances on treatment with inorganic acids is a heterogeneous reaction the rate of which can be determined by either diffusion processes or interactions at the solid–solution interface. In both cases, treatment with MW substantially accelerates the processes involved. The regularities

considered above established for individual reactions (shortening of the reaction time, decrease in the reactant ratio down to stoichiometric amounts, an increase in the completeness of reactions) are clearly manifested in decomposition processes.

Microwave digestion is carried out using the same reagents (most often, acids and their mixtures) as that induced by conventional heating.[†] Treatment can be carried out both in usual open vessels made of materials which slightly absorb MW (glass, quartz or fluoroplastic) and in closed systems at elevated temperatures and pressures. This allows the mixture under analysis to be heated to a temperature markedly exceeding the boiling point of the used acid under normal pressure; therefore, both the rate and the degree of transfer of the sample into a solution become much higher. An important advantage of microwave-assisted digestion in closed vessels is low pressure with a relatively high temperature (see Figs 1, 3), due to the fact that radiation causes heating of the liquid but not of the gas phase.

Since the temperature of decomposition dictates the range of applicable acids, an increase in this temperature often makes it possible to replace high-boiling perchloric, sulfuric or phosphoric acid by hydrochloric or nitric acid, which are more convenient for digestion. In some cases, the higher degree of sample dissolution at higher temperatures makes it possible to eliminate the stage of fusion of the residue after sample dissolution in acids.

It is fairly useful to apply microwave heating for decomposition of organic matrices (biological and clinical objects, pharmaceutical preparations, foodstuffs, forages, food raw materials and ecosystem components). In this case, the time of analysis can be appreciably reduced. Decomposition of organic matrices can be carried out in both closed and open systems. The use of open systems is recommended for working with large amounts (up to 10 g) of materials when considerable amounts of gaseous products of oxidation are evolved during the process. In combination with modern, highly sensitive methods of analysis (for example, atomic spectroscopy techniques such as ETAAS, ICP AES or ICP MS) in which determination of elements at a level of $10^{-6}\%$ – $10^{-5}\%$ can be accomplished using fractions of a gram of the material, closed or flow systems are used more frequently. Flow setups represent a step towards automation of the analysis, attained by connecting a flow system for sample digestion to the injecting device of a spectrometer. The samples are commonly introduced in the systems as suspensions in acids.^{101,102} The publications describing the use of microwave heating for decomposition of organic matrices are devoted, most of all, to determi-

nation of trace elements and identification of the species containing them in environmental and biological objects by instrumental methods.^{18,26,65–67,103–106}

Decomposition of inorganic matrices often requires drastic conditions; therefore, for this purpose, it is expedient to use closed vessels, which are applicable up to a temperature of $\sim 350^\circ\text{C}$ and a pressure of 200 atm.^{107–109} These conditions may ensure dissolution of the most complex geological specimens (for example, those containing noble metals), poorly soluble oxides (such as niobium and tantalum oxides), metals, alloys or catalysts.^{18,110,111} The use of microwave setups including automated or robotised ones acquires special significance in the analysis of radioactive specimens.¹¹² Data on the time required for preparation of some substances for the analysis using traditional and microwave heating procedures are compared in Table 4.

The main causes for the intensification of sample digestion in the case of microwave treatment include high rate and uniformity of heating of the reaction mixture; exceeding of the boiling point corresponding to the given pressure; and local effects (warming-up of the solvent in the sample pores, *i.e.*, actually, in a confined space, and sample destruction under high pressure; selective heating of components of heterogeneous systems; reflection of the radiation to the near-surface layer of the solution in the case of digestion of metallic samples). Indeed, according to our data, the dissolution of gold alloys under microwave heating is twice as fast as that at the same temperature achieved by conventional heating.

The specific features of microwave digestion have a substantial influence on the metrological characteristics of the results. Due to good reproducibility of decomposition conditions, it is possible to obtain solutions of virtually identical compositions from identical samples, which is favourable for the reproducibility of the subsequent determination. The work with stoichiometric or nearly stoichiometric reactant ratios leads to a considerable decrease in the blank correction. A decrease in this value is also attained owing to use of closed or flow systems, which eliminates the loss of the analyte as volatile compounds and the ingress of contaminants from air; in combination with the use of high-purity chemicals, this brings the analysis closer to the 'clean room' conditions.¹¹³ In addition, simplification of the composition of the reaction mixture allows some sample pretreatment operations to be avoided, which also improves the metrological characteristics of the analysis as a whole. Mention should be made of high productivity and economic efficiency of the microwave techniques, and their flexibility in combination with preconcentration and instrumental determination.^{2,4,58}

The most promising approach to the substantiated selection of digestion conditions consists in modelling with the use of individual compounds of various classes. This approach was used, for example, to establish the conditions for the oxidation of model organic compounds by nitric acid. Kingston and Jassie¹¹⁴ showed

[†] However, due to specific features of microwave heating and the change in the kinetics of chemical reactions, the conditions chosen for thermal digestion can be regarded only as the starting point in microwave procedures.

Table 4. Comparison of the times of digestion of various samples in the conventional and microwave heating modes.^{4,22}

Sample type	t_1 /h ^a	Microwave digestion conditions	t_2 /min ^b	t_1 / t_2
Biological objects (trace components)	8	HNO ₃ or its mixtures with HF and HCl, closed systems	1.5–30	16–100
Geological objects (macrocomposition)	6	HNO ₃ , HCl, closed systems	4	90
Geological objects (trace components)	4–16	HF and HCl, HF and HNO ₃ , closed or open systems	10–20	24–32
Objects with an organic matrix (trace components)	8–16	HNO ₃ , closed systems	10–20	24–64
Biological objects, Kjeldahl determination of nitrogen	2–6	H ₂ SO ₄ , open systems	3–6	20
Alumina	24	H ₂ SO ₄ , H ₃ PO ₄ , closed systems	40	36
Steels	1	HCl, HF, HNO ₃ , closed systems	1–2	45
Soils, dust	8	HF, HNO ₃ , closed systems	20	24
High-purity compounds	8–24	HF, HNO ₃ , closed systems	12	40–120
Waste water	6	HNO ₃ , closed systems	10	60

^a Time of traditional sample pretreatment. ^b Time of microwave pretreatment.

that carbohydrates, proteins and fats are oxidised on exposure to MW at 140, 150 and 160 °C, respectively. Later, the activation energies for the oxidation of a number of model organic compounds were determined; these data were shown to be suitable as the basis in choosing for conditions for decomposition of natural products.⁷⁴

The principles of selection of the conditions for microwave decomposition depending on the sample weight, the rate of temperature rise, the volume of the reaction mixture and the total volume of the vessel have been considered in detail by Knapp.¹¹⁵

4. Preconcentration of traces of elements

Exposure to radiation permits fast preconcentration of trace amounts of metals by evaporation⁹⁹ or by using organic sorbents that react with metal ions according to complex-formation or ion-exchange mechanism. Preconcentration by sorption is carried out in either the static or dynamic mode. Preconcentration of platinum group metals and chromium on nitrogen-containing complexing sorbents has been reported.^{104, 110}

5. Identification of the element forms (speciation)

Analysis with the use of MW, which provides simultaneously specific chemical treatment and fast heating of the system, permits selective isolation of analytical forms of elements without changing their chemical composition in the sample. The compounds are collected using organic solvents or mixtures based on inorganic acids.¹¹⁶ This expedient was used for mass-spectrometric identification of chemical species containing mercury,¹¹⁷ tin¹¹⁸ and heavy metals.¹¹⁹

6. Extraction of organic impurities

Of special interest are recent studies dealing with the selective microwave-assisted extraction of toxic organic compounds into organic solvents.¹¹ These studies would undoubtedly serve as a significant stage in the development of organic analysis methods, first of all, chromatographic techniques. The advantages (considerable acceleration and an increase in the degree of extraction of the organic impurities to be determined) are caused in this case by the increase in the temperature of the extraction system by several tens of degrees. A highly important specific feature of microwave extraction is the fact that this method allows selective collection of components either through selective heating of the phase or a separate component of the system (for example, free water molecules in plant cells), depending on its dielectric properties, or through choosing an organic solvent that would selectively extract one or another component. In addition, the consumption of organic solvents and, hence, the amount of toxic wastes markedly decrease, which is beneficial from the environmental standpoint.^{14, 15}

An interesting version of microwave-assisted extraction is the withdrawal of volatile organic compounds to the gas phase through microwave heating of a matrix containing a polar solvent (water). The gas phase which does not absorb MW does not warm up, and under certain conditions, it virtually does not contain solvent vapour due to the non-equilibrium character of the system. Determination of the impurities of relatively volatile organic compounds in solid matrices such as soils is also possible; the most polar substances are the first to be evaporated. Upon irradiation of solid materials containing moisture, the selectivity of determination is due to the separate transition to the gas phase of components characterised by different vapour pressures.^{11, 14}

The principles of selection of the conditions for the extraction of organic impurities (biologically active nutritional compounds, antioxidants, UV stabilisers of plastics, pesticides, polyaromatic hydrocarbons, phenols, organometallic compounds and other contaminants) in microwave systems and comparison of the results with traditional methods have been reported.^{11, 14, 15}

7. Determination of the contents of total nitrogen and phosphorus

Under conditions of traditional heating, sample digestion, which is the limiting step in determination of the total nitrogen, takes 2 to 6 h. Since sulfuric acid, used in the Kjeldahl method, efficiently absorbs microwave radiation, the time it takes for the reaction mixture to warm up to 400 °C can be shortened from 45 min to 3–6 min. The introduction of an additional oxidant (Caro's acid) and the use of special techniques make it possible to reduce both the duration of decomposition of the organic matrix and the time of cooling the mixture and also to simplify titration. The problems of the traditional Kjeldahl determination of nitrogen and the capabilities of the microwave modification of this analysis have been considered quite comprehensively in a publication.¹²⁰ The results of application of microwave methods for determination of nitrogen¹²¹ and phosphorus¹²² in the analysis of environmental objects have been generalised.

V. Conclusion

The significance of MW for analytical chemistry grows continuously and rapidly. In the 1970s, there were only seven publications devoted to analysis using MW; in the 1980s, the number of publications increased to 132, while over a period of only four years, from 1991 to 1995, according to the data of a review,¹⁸ 166 more studies were published. About 1000 studies related to the application of MW in analysis have now been published. The main topics considered in these studies are related to sample digestion, drying and ashing under the action of MW. The microwave-assisted sample preparation has underlain new-generation analytical techniques — fast and highly efficient methods having good metrological characteristics; this reduces the gap between the existing power of instrumental determination of elements and the level of sample pretreatment techniques and extends the range of objects that can be analysed by routine methods. Due to the versatility of microwave methods, it is possible to design integrated analytical sequences consisting of inseparably connected operations and meant for the determination of a wide range of substances and materials, instead of separate procedures. This field of analytical chemistry is being vigorously developed.

The design of multipurpose analytical schemes on the basis of minimisation of the number of operations and integration of operations in space and in time¹²³ implies, first of all, improvement of the sample preparation step and convenient combination of this step with instrumental determination. The most promising lines of development of inorganic analysis with the use of MW were outlined by Matusiewicz and Sturgeon.⁹¹ They believe that the goals of using MW should include the decrease in the number of analytical operations and the time required to perform them through intensification of chemical processes, integration of operations, development of on-line analysis and speciation methods and implementation of rational hybrid methods. Generally, these trends correspond to the general principles of the development of analysis discussed in a number of publications.^{123–129}

Attempts to develop general approaches to the design of analytical schemes based on the microwave sample pretreatment, to improve individual stages and to implement integrated sequences of operations in a microwave field within a single system have been undertaken.^{6, 130, 131} An approach proposed in our study¹² and developed further under the name 'total microwave sample preparation' (which implies sample pretreatment in which all operations are carried out under the action of MW, are interrelated and often combined with one another)¹³² is regarded to be one of the major directions in the microwave-assisted sample preparation.² In the development of hybrid methods and analytical schemes for analysing unique samples by high-sensitivity instrumental methods, non-traditional combinations (in particular, those with the use of micromethods, *i.e.*, techniques and expedients for working with small amounts of the analyte) are

fairly promising. The methods of sample preparation with the use of MW are suitable for complex analytical objects, both for elements and matrices such as geological (ores, rocks), environmental (foodstuffs and raw materials, biological preparations, natural water, soil), industrial (high-purity substances, concentrates, metals, alloys, second-hand raw materials) containing heavy, rare and noble elements as macro- and micro- components. The use of MW substantially improves characteristics of analysis, not only that carried out by advanced instrumental methods but also of the analysis performed by well-known traditional methods, thus providing an increase in the potential of the existing analytical equipment. Owing to the microwave pretreatment, it is possible to reduce several-fold the duration of analysis, decrease the consumption of chemicals and energy expenditure, and to reduce the required man-hours.

In addition to ultra-trace analysis of components, which is associated with specific conditions (clean chemistry), one more important analytical problem that has appeared quite recently is elaboration of methods for determination of the forms in which elements exist. Microwave methods, which possess great potential due to the diversity of operations carried out in a microwave field and the flexibility of combinations with instrumental methods, are undoubtedly promising in this respect. Microwave systems are used to increase the efficiency of multistep procedures of successive selective acid extraction of various chemical forms of metals, sample digestion and extraction with organic solvents. Sample derivatisation, *i.e.*, preparation of a derivative convenient for the subsequent instrumental determination of the element, is also carried out directly in the microwave oven; this is done in open, closed or flow systems.^{2, 116, 117} By combining microwave pretreatment with atomic and mass spectrometry or liquid and capillary gas chromatography, hybrid methods have been developed, which shorten the time of analysis by a factor of 20–100.^{130, 131, 133, 134}

Yet another important feature of microwave methods is the possibility of preparing metals as convenient analytical forms and as complexes that are difficult to prepare by traditional methods due to kinetic restrictions. A simple procedure for preparation of the required analytical forms under the action of MW increases the efficiency of rather long-lasting classical spectrophotometric, fluorescence, luminescence, sorptional, electrochemical and other methods that are sensitive to the form of element existence in solution. The correlation between the specified conditions of reactions and the quantitative and qualitative composition of the products provides the possibility of targeted synthesis of both inorganic complexes and macrocyclic reagents^{40, 41} or polymers.^{4, 90}

The embodiment of the potential of microwave methods is determined by the development of instrumentation, increase in the efficiency of the control of process parameters, and the decrease in the cost of equipment. Thus an increase in the speed of analysis can be achieved by two methods: by increasing the number of samples treated simultaneously [in closed systems, this can be 52 (see Ref. 135)] and by using flow systems in which, according to the data of CEM company, 180 samples can be prepared over a period of 3 h. The metrological characteristics of analysis can be improved, for example, by using steel autoclaves in combination with microwave heating by focused radiation; in Matusiewicz's opinion,¹⁰⁸ this ensures faster heating, a higher pressure, and a better reproducibility of results. A promising technique is the use of microwave flow setups for digestion and preconcentration coupled with automated determination. The scopes of the two approaches are analysed in a publication.⁶⁶ Flow setups appear to be the optimal devices for the design of automated systems, although other facilities (for example, open and robotised devices^{2, 136, 137}) can also serve as parts of these systems used to solve particular analytical problems. Undoubtedly, with the advent of new technologies and materials, novel engineering solutions for the implementation of microwave heating will also arise (the ways of radiation supply; the design of the vessels, flow systems, automated injection units and types of coupling with instrumental

determination) and new ways of controlling the parameters (temperature, pressure) and of the 'parameter–process' feedback will appear. This will give rise to a new generation of laboratory microwave systems.

The possibility of conversion of microwave devices from a fairly advanced facility used for routine sample pretreatment into a tool for investigation of the regularities of chemical transformations appears to be of fundamental importance.^{69, 71, 73, 80} The change in the kinetic parameters of reactions on exposure to radiation with maintenance of invariable thermodynamic properties of the system allows quantitative investigations of the slow physicochemical processes, simulation of various reactions in model systems and, thus, provides a way for predicting the results of processes taking place under real conditions. This is of interest from both theoretical and practical standpoints, for example, for the perfection of complex technological processes involving a series of reactions with participation of many components.

The development of the theoretical basis of microwave sample pretreatment is a topical subject. Further studies along this line should probably be related to in-depth investigations of the interaction of MW with substances of different chemical nature (solvents, analytes, structural components of microwave systems); research into the influence of physical parameters of MW (frequency and intensity) on the course of physicochemical processes in solutions or heterogeneous systems. This would enable researchers to ensure selective transfer of energy to the reaction system components and, thus, to propose new in kind routes to the solution of analytical problems. In addition, extension of the range of chemical processes taking place under the action of MW, in particular, study of the influence of MW on catalytic and enzymic processes, organic synthesis, preparation of coordination compounds and polymerisation is also important for modern analytical methods.

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^e — *Russ. J. Bioorg. Chem. (Engl. Transl.)*

Titanocene derivatives containing titanium – carbon σ -bonds

V A Knizhnikov, N A Maier

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Abstract. The published data on the major methods for the synthesis and chemical conversions of titanocene derivatives containing titanium – carbon σ -bonds are systematised. The bibliography includes 288 references.

I. Introduction

The chemistry of dicyclopentadienyltitanium (titanocene) derivatives is one of the most rapidly developing branches of the chemical science. The interest in titanocene derivatives is partly due to their ability to catalyse various chemical processes, *e.g.*, polymerisation, isomerisation and hydrogenation of alkenes, cyclotrimerisation of acetylene derivatives, fixation of molecular nitrogen under mild conditions and many other reactions. These compounds acquire increasing popularity as additives to fuels and high-temperature lubricants, rubber accelerators, lacquer and water-repellent components, antiknock compounds, *etc.*

Among other compounds of the titanocene series, titanocene derivatives containing Ti – C σ -bonds are still the least known due to the thermal instabilities of the majority of representatives of this class and, to some extent, their high sensitivities to oxygen and atmospheric moisture. High reactivities of titanocene derivatives containing Ti – C σ -bonds with various organic and inorganic substrates and the presence of several reaction centres in some of them open broad prospects for their application in both organic synthesis and in the preparation of diverse organometallic compounds including novel representatives of the known types of titanocene derivatives. The published data on the major methods for the synthesis of titanocene derivatives containing Ti – C σ -bonds isolated from various reaction mixtures in individual state and the most typical chemical transformations are considered. The principal characteristics of titanocene derivatives (colour, solubility, air resistance, thermal stability, structure, *etc.*) have been described in the majority of the original papers and therefore fall outside the scope of this review.

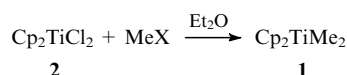
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II. Methods for the synthesis of titanocene derivatives containing Ti – C σ -bonds

1. Reactions of titanocene halides with organic derivatives of non-transition metals

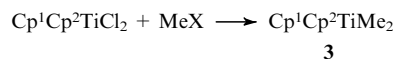
Reactions of titanocene dihalides with organolithium, -sodium, -magnesium or -aluminium compounds constitute a classical method for the synthesis of titanocene σ -derivatives; depending on the reagent ratio, both mono- and dialkyl- or diaryl derivatives can be prepared.

Dimethyltitanocene (**1**) was prepared by the reaction of titanocene dichloride (**2**) with an excess of methylolithium, methylmagnesium halides or lithium tetramethylaluminium at reduced temperatures. Diethyl ether is the most convenient solvent for such syntheses.^{1–5}



Cp = C₅H₅; MeX = MeLi, MeMgHal, LiAlMe₄.

Dimethyltitanocene derivatives **3** containing various substituents in π -bound cyclopentadienyl ligands are prepared from the corresponding dichlorides.



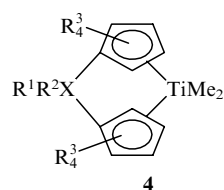
MeX = MeLi, MeNa, MeMgHal, Me₃Al.

Cp ¹	Cp ²	Ref.
C ₅ H ₄ Me	C ₅ H ₄ Me	6
C ₅ Me ₅ (Cp*)	C ₅ Me ₅	2, 6
1,2,3-Me ₃ C ₅ H ₂	1,2,3-Me ₃ C ₅ H ₂	6
C ₅ Me ₄ H	C ₅ Me ₄ H	6–8
C ₅ Me ₄ (CH ₂ CH ₂ CH = CH ₂)	C ₅ Me ₄ (CH ₂ CH ₂ CH = CH ₂)	9
C ₅ H ₅	C ₅ Me ₅	10
C ₅ H ₃ (SiMe ₃) ₂	C ₅ H ₂ (SiMe ₃) ₃	11
1,3-Bu ^t ₂ C ₅ H ₃	C ₅ H ₅	12
C ₅ Me ₅	C ₅ Me ₄ (CH ₂) ₂ NMe ₂	13
C ₅ Me ₅	C ₅ H ₄ CMe ₂ C ₁₃ H ₉	14

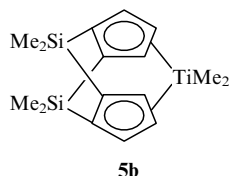
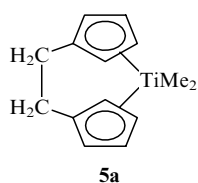
Dimethyltitanocene derivatives with bridges between the cyclopentadienyl ligands, such as compounds **4**,^{15–19} **5a**²⁰ and **5b**,^{21,22} are known.

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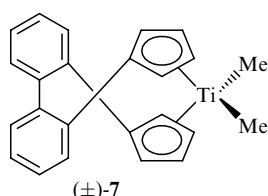
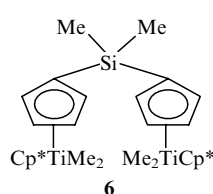
Uspekhi Khimii 71 (4) 341–362 (2002); translated by R L Birnova



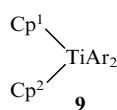
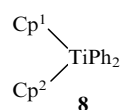
R ¹	R ²	R ³	X	Ref.
Me	Me	H	C	15
H	Bu ⁿ	H	C	16
Me	Me	H	Si	17, 18
Me	Me	Me	Si	19



The binuclear titanocene-like complex **6**²³ with a bridging (dimethylsilylidene)dicyclopentadiene ligand and the complex **7**²⁴ in which the role of a bridge is played by biphenyl-2,2'-diyl have been synthesised.



The reaction of titanocene dichloride (**2**) with phenyllithium or phenylmagnesium halides gave diphenyltitanocene Cp_2TiPh_2 .^{4, 25–28} Diphenyltitanocene derivatives containing substituents in both π -bound cyclopentadienyl ligands, such as compound **8**, and σ -bound phenyl rings, such as compounds **9**, have been described.

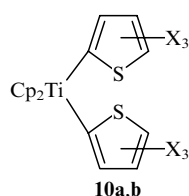


Cp ¹	Cp ²	Ref.	Cp ¹	Cp ²	Ar	Ref.
C ₅ H ₅	C ₅ Me ₅	10	C ₅ H ₅	C ₅ H ₅	3(4)-MeC ₆ H ₄	27, 28
C ₅ H ₅	C ₅ HMe ₄	7, 8	C ₅ H ₅	C ₅ H ₅	2-Me ₂ NC ₆ H ₄	27
C ₅ Me ₅	C ₅ Me ₅	7, 8	C ₅ H ₅	C ₅ H ₅	C ₆ F ₅	4, 29, 30
			C ₅ HMe ₄	C ₅ HMe ₄	4-MeC ₆ H ₄	7, 8
			C ₅ H ₅	C ₅ Me ₅	4-MeC ₆ H ₄	7, 8

The reaction of titanocene dichloride (**2**) or its derivatives with benzylmagnesium chloride or benzyl lithium results in dibenzyltitanocene derivatives Cp_2TiBn_2 ,^{31–33} $(\text{C}_5\text{H}_4\text{Me})_2\text{TiBn}_2$,³³ $(\text{C}_5\text{H}_4\text{SiMe}_3)_2\text{TiBn}_2$ ³³ and $[(\text{C}_5\text{H}_4)_2\text{SiMe}_2]\text{TiBn}_2$.¹⁶

Syntheses of titanocene derivatives in which σ -bound organic radicals contain a heteroatom, *e.g.*, $\text{Cp}_2\text{Ti}(\text{CH}_2\text{SiMe}_3)_2$,^{34–37} $[(\text{C}_5\text{Me}_4)_2\text{SiMe}_2]\text{Ti}(\text{CH}_2\text{SiMe}_3)_2$,¹⁹ $[(\text{C}_5\text{H}_4)_2\text{SiMe}_2]\text{Ti}(\text{CH}_2\text{SiMe}_3)_2$,²¹ $\text{Cp}_2\text{Ti}(\text{CH}_2\text{GeMe}_3)_2$,³⁷ $\text{Cp}_2\text{Ti}(\text{CH}_2\text{SPh})_2$,^{38, 39} $\text{Cp}_2\text{Ti}(\text{CH}_2\text{PPh}_2)_2$,⁴⁰ $\text{Cp}^*(\text{Cp})\text{Ti}(\text{CH}_2\text{PPh}_2)_2$,⁴¹ *etc.*, have been described.

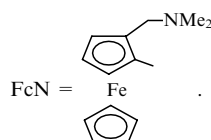
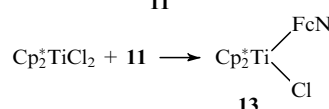
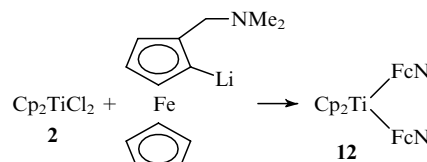
Thiophene⁴² or trichlorothiophene (compounds **10a,b**) can be used as σ -bound substituents.⁴³



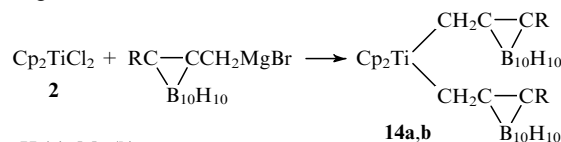
X = H (**a**), Cl (**b**).

The reaction of titanocene dichloride (**2**) with cyclopentadienylsodium afforded tetracyclopentadienyltitanium in which two cyclopentadienyl ligands were linked by π -bonds, whereas the other two ligands, by σ -bonds.^{44–47} Presumably, this complex underwent rapid (on an NMR time scale) $\pi \rightleftharpoons \sigma$ rearrangement of the ligands at 20 °C.^{46, 48}

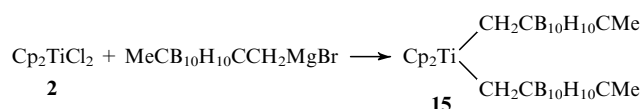
The reaction of an excess of ferrocenyllithium with titanocene dichloride (**2**) results in diferrocenyltitanocene Cp_2TiFc_2 ($\text{Fc} = \text{C}_5\text{H}_5\text{FeC}_5\text{H}_4$).⁴⁹ The reaction of titanocene dichloride (**2**) with an excess of 2-(dimethylaminomethyl)ferrocenyllithium (**11**) yields the symmetrical complex **12**. Under similar conditions, bis(pentamethylcyclopentadienyl)titanium dichloride yields the monoferrocenyl-substituted complex **13**.⁵⁰



The reaction of titanocene dichloride (**2**) with *o(m)*-carboran-1-ylmethylmagnesium bromides leads to carboranyl-substituted titanocenes **14a,b** and **15**.^{51, 52} Dicyclopentadienylbis(*o*-carboranyl-methyl)titanium **14a**, contrary to the majority of titanocene derivatives containing Ti–C σ -bonds, is stable in air at 20 °C over a long period of time and is decomposed only on melting at 185 °C.



R = H (**a**), Me (**b**).

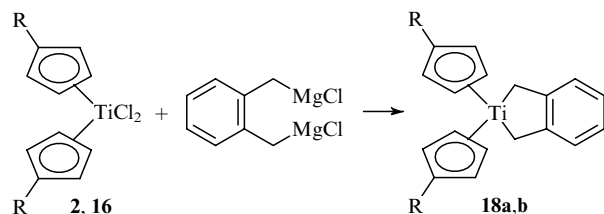


Titanocene dichloride (**2**) reacts with an excess of sodium, lithium or magnesium acetylenide to give titanocene diacetylenides $\text{Cp}_2\text{Ti}(\text{C}\equiv\text{CR})_2$, where R = Ph,^{53–55} SiMe_3 ,^{56, 57} CF_3 ,⁵⁸ Et, Prⁿ, Buⁿ, Bu^t (see Ref. 56), cyclo-C₆H₁₁, Ph₂CHCH₂, *n*-C₆H₁₃,⁵⁵ Fc, Rc (Rc = C₅H₅RuC₅H₄),⁵⁹ $(\text{C}\equiv\text{CR})_2 = (\text{C}\equiv\text{C}-2-\text{C}_6\text{H}_4-\text{C}\equiv\text{C}-2-\text{C}_6\text{H}_4-\text{C}\equiv\text{C})$.⁶⁰ Similar compounds were prepared from titanocene dichloride derivatives containing substituents in cyclopentadienyl rings, *viz.*, $\text{Cp}'_2\text{Ti}(\text{C}\equiv\text{CR})_2$, where Cp' = C₅H₄Me: R = Ph, cyclo-C₆H₁₁, *n*-C₆H₁₃, Ph₂CHCH₂,⁵⁵ SiMe_3 ,⁵⁶ Cp' = C₅H₄SiMe₃: R = Ph, SiMe_3 ,⁵⁶ $\text{C}\equiv\text{C}-\text{C}\equiv\text{C}-\text{C}\equiv\text{C}$,⁶¹ Fc,^{59, 62} Rc;⁵⁹ Cp' = C₅H₂Me₃, R = SiMe_3 ,⁶³ Cp' = Cp*, $(\text{C}\equiv\text{CR})_2 = (\text{C}\equiv\text{C}-2-\text{C}_6\text{H}_4-\text{C}\equiv\text{C}-2-\text{C}_6\text{H}_4-\text{C}\equiv\text{C})$,⁶⁰ Cp' = C₅H₄CH₂CH₂NMe₂: R = SiMe_3 ,⁶⁴ Cp' = C₅H₄X (X = Ph₂P, Ph₂P=O, Ph₂P=S), R = Bu^t (see Ref. 65).

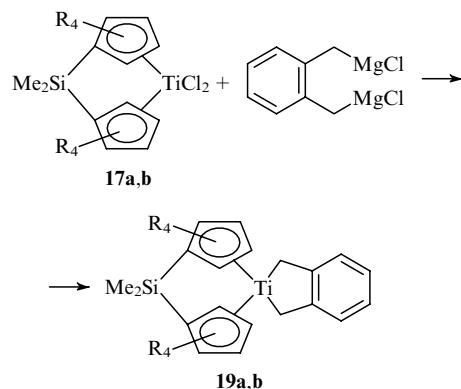
Symmetrical dicyclopentadienyltitanium derivatives with other σ -bound organic groups, *e.g.*, Cp_2TiBu^n (see Ref. 66), Cp_2TiEt_2 ,⁶⁷ $\text{Cp}_2\text{Ti}[\text{C}(\text{Ph})=\text{CMe}_2]_2$,⁶⁸ $\text{Cp}_2\text{Ti}(\text{CF}=\text{CF}_2)_2$,⁶⁹ and $[\text{Me}_2\text{Si}(\text{C}_5\text{H}_4)_2]\text{TiBu}^n_2$ (see Ref. 18), have been synthesised.

The reactions of titanocene dichloride (**2**) or its derivatives containing substituents in the cyclopentadienyl ligands with

organodilithium or -dimagnesium compounds yield metalla-cycles. Thus titanaindans **18a,b**,⁷⁰ **19a**¹⁸ and **19b**¹⁹ were prepared from the dichlorides **2**, **16**, **17a,b** and 1,2-bis(chloromagnesio-methyl)benzene.

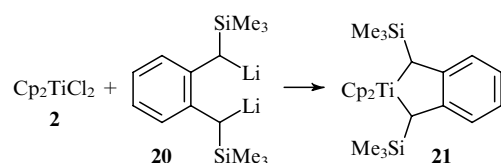


R = H (**2**, **18a**), SiMe₃ (**16**, **18b**).

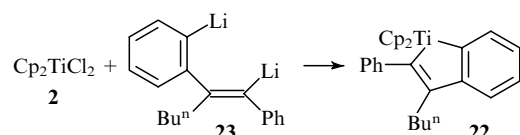


R = H (**a**), Me (**b**).

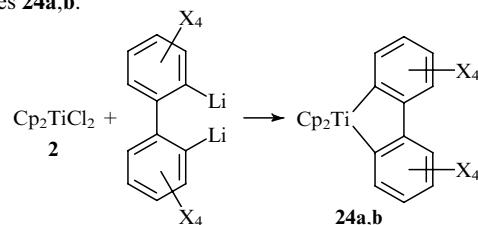
The dilithium derivative **20** was used for the preparation of substituted titanaindan **21**.⁷¹



Titanaindene **22** is produced by the reaction of titanocene dichloride (**2**) with the dilithium derivative **23**.⁷²



The reaction of titanocene dichloride (**2**) with 2,2'-dilithiobiphenyl⁷² or 2,2'-dilithiooctafluorobiphenyl⁷³ gave titanafluor- enes **24a,b**.

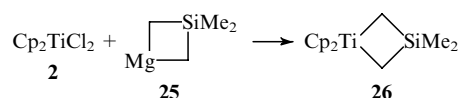


X = H (**a**), F (**b**).

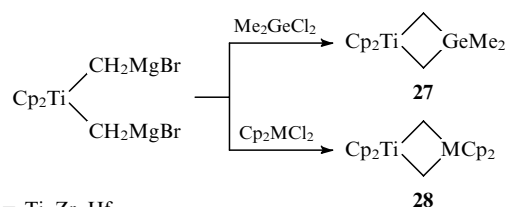
Diverse titanacyclic compounds Cp₂TiL₂ have been described in which the cyclic structures are formed owing to the ligands L₂.

L ₂	Ref.	L ₂	Ref.
	74	(CH ₂) ₄	77, 78
		CH ₂ CH(Me)CH ₂	79
		CH ₂ SiMe ₂ XSiMe ₂ CH ₂ (X = CH ₂ , O, SiMe ₂)	80
	75, 76	CH ₂ SiMe ₂ SiMe ₂ CH ₂	80

Titanocene dichloride (**2**) reacts with 1,1-dimethyl-1-sila-3-magnacyclobutane (**25**) to give thermally stable 3,3-dimethyl-1,1-dicyclopentadienyl-1-titana-3-silacyclobutane (**26**).⁸¹

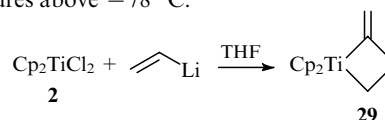


1-Titana-3-metallacyclobutanes **27** and **28** were prepared by the reactions of bis(bromomagnesiomethyl)titanocene with dichlorodimethylgermane⁸² or titanocene, zirconocene and hafnocene dichlorides.⁸³

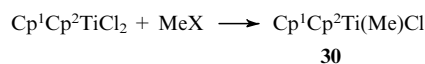


M = Ti, Zr, Hf.

1,1-Dicyclopentadienyl-1-titana-2-methylidenecyclobutane (**29**) was synthesised by the reaction of titanocene dichloride (**2**) with vinyltitanium in THF in the reagent ratio of 1:2.^{84,85} Presumably, this reaction proceeds *via* divinyltitanocene, which is rearranged into 2-methylidenetitanacyclobutane **29** at temperatures above -78°C .

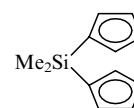


Monoalkyl- or monoaryl titanocene chlorides are formed upon treatment of titanocene dichloride (**2**) with equimolar amounts of organolithium or -magnesium compounds. Thus methyltitanocene chloride derivatives **30** were prepared using methyltitanium, methylmagnesium chloride or trimethylaluminium.



MeX = MeLi, MeMgCl, Me₃Al.

Cp ¹	Cp ²	Ref.	Cp ¹	Cp ²	Ref.
C ₅ H ₅	C ₅ H ₅	86–89	C ₅ H ₅	1,3-Bu ₂ C ₅ H ₃	12
C ₅ H ₅	C ₅ H ₄ CH(Me)Ph	90			
C ₅ H ₅	C ₅ H ₄ Me	91			
C ₅ H ₄ Me	C ₅ H ₄ Me	91			



17, 18

The complexes Cp¹Cp²Ti(Me)ClAlMe₂Cl where Cp¹ = C₅H₅, Cp² = C₅H₄Me, C₅H₄SiMe₃; Cp¹ = Cp² = C₅H₄SiMe₃, have also been synthesised.⁹²

Reactions of titanocene dichloride (**2**) or its derivatives containing substituents in the cyclopentadienyl ligands with trimethylsilylmagnesium chloride (1 : 1) yield the trimethylsilylmethyl derivatives **31a–d**. Compounds **31e–h** were prepared in a similar way.

**31a–h**

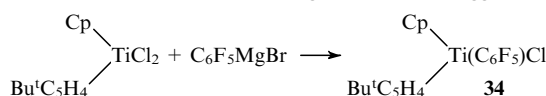
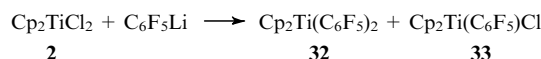
Compound 31	Cp ¹	Cp ²	E	Ref.
a	C ₅ H ₅	C ₅ H ₅	Si	33, 93, 94
b	C ₅ H ₄ Me	C ₅ H ₄ Me	Si	33
c	C ₅ H ₄ SiMe ₃	C ₅ H ₄ SiMe ₃	Si	33
d		Me ₂ Si(C ₅ H ₄) ₂	Si	17, 18
e	C ₅ H ₅	C ₅ H ₅	C	93
f	C ₅ H ₅	C ₅ H ₅	Ge	93
g	C ₅ H ₅	C ₅ H ₅	Sn	93
h	C ₅ H ₄ Me	C ₅ H ₄ Me	C	33

The reaction of titanocene dichloride (**2**) or its analogue containing a bridging dimethylsilylene group with an equimolar amount of benzylmagnesium chloride gave Cp₂Ti(Bn)Cl (see Ref. 86) and [Me₂Si(C₅H₄)₂](Bn)TiCl.¹⁷

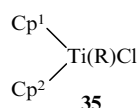
Chlorotitanocene derivatives Cp₂TiCl(L) containing bulky ligands [e.g., L = CH₂CH₂CHR¹CR²=CH₂, where R¹ = R² = H; R¹ = H, R² = Me; R¹ = Ph, R² = H; L = CH₂CMe₂CHCR¹=CR²CR³=CH₂, where R¹ = R² = R³ = H; R¹ = R² = H, R³ = Me; R¹ = Me, R² = R³ = H; R¹ = R³ = H, R² = Me; R¹ = R² = Me, R³ = H] were synthesised by the reaction of titanocene dichloride (**2**) with the corresponding organomagnesium compounds.⁹⁵

Titanocene dichloride derivatives containing substituents in the cyclopentadienyl ligands react with sodium acetylenides (charge ratio 1 : 1) to give the monoacetylenides Cp₂TiCl(C≡CR) [Cp' = C₅H₄Me, C₅H₄SiMe₃, R = Ph, SiMe₃ (see Ref. 56); Cp' = C₅H₄SiMe₃, R = C≡CEt (see Ref. 61)].

The reaction of titanocene dichloride (**2**) with pentafluorophenyllithium in ether yields bis(pentafluorophenyl)titanocene (**32**) and pentafluorophenyltitanocene chloride (**33**).²⁹ The monopentafluorophenyl titanocene derivative **34** was prepared by treatment of cyclopentadienyl(*tert*-butylcyclopentadienyl)titanium dichloride with pentafluorophenylmagnesium bromide.⁹⁶



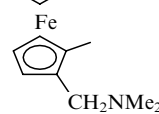
The chlorotitanocene derivatives **35** containing various alkyl-, aryl-, alkenyl- and other σ-bound ligands were synthesised by reactions of equimolar amounts of the corresponding dichlorides with organomagnesium or -lithium compounds.

**35**

Cp ¹	Cp ²	R	Ref.
C ₅ H ₅	C ₅ H ₅	Ph	86
C ₅ H ₅	C ₅ H ₅	Et	86, 97
C ₅ H ₅	C ₅ H ₅	Pr ⁿ	86
C ₅ H ₅	C ₅ H ₅	CH ₂ PPh ₂	40
C ₅ H ₅	C ₅ H ₅		98

Cp ¹	Cp ²	R	Ref.
C ₅ H ₅	C ₅ H ₅	CH ₂ OMe	99
C ₅ H ₅	C ₅ H ₅	CF ₂ =CF	69

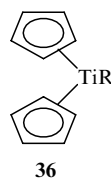


C ₅ H ₅	C ₅ H ₅		100

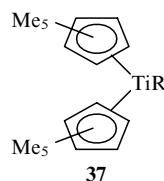
C ₅ H ₅	C ₅ Me ₅	CH ₂ PPh ₂	41
C ₅ H ₄ Me	C ₅ H ₄ Me	CH ₂ OMe	99
C ₅ Me ₅	C ₅ Me ₄ (CH ₂) ₂ NMe ₂	CH ₂ =CH	13

The bromotitanocene derivative Cp₂TiBr(CH₂MgBr) was prepared from titanocene dibromide and CH₂(MgBr)₂.¹⁰¹

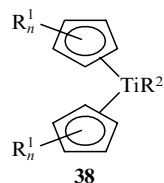
The alkyl- and aryl(dicyclopentadienyl)titanium(III) derivatives **36–38** have been described. They are prepared by treating dicyclopentadienyltitanium(III) chloride or its derivatives containing substituents in the cyclopentadienyl ligands with organolithium, -sodium or -magnesium compounds at –78 °C.



R	Ref.	R	Ref.
Me	102–104	CHCMe ₂ CH ₂ CH ₂ C(R)=CH ₂	95
Et	102	(R = H, Me)	
Bu ⁿ	102	2(3,4)-MeC ₆ H ₄	105
Ph	105	2,6-Me ₂ C ₆ H ₃	105, 106
2,4,6-Me ₃ C ₆ H ₂	105	C(Me)=CHMe	107
C ₆ F ₅	104, 105	Bn	108

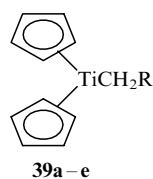


R	Ref.	R	Ref.	R	Ref.
Me	108, 109	Pr ⁿ	108	C ₂ D ₅	108
Et	108, 109	Bn	108	C ₃ D ₇	108
CH ₂ Bu ^t	108	CH ₂ =CH	108	CMe=CHMe	109
Ph	108	CD ₃	108		



R _n ¹	R ²	Ref.
Me ₄	Me	110
Me ₄	Ph	110
1,3-Bu ₂ ¹	Me	111

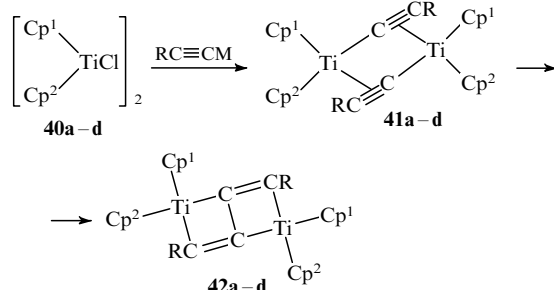
The dicyclopentadienyltitanium(III) derivatives **39a–e** containing a heteroatom in the alkyl substituent have been obtained.



Compound 39	R	Ref.
a	SiMe ₃	104
b	PPh ₂	40
c	(CH ₂) ₂ OMe	112
d	(CH ₂) ₂ SMe	112
e	CH ₂ OMe	112

It is assumed that the titanium atom in compounds **39b–e** is additionally coordinated by the heteroatom of the σ -bound ligand.^{40, 112}

Treatment of the dicyclopentadienyltitanium(III) chloride dimer or its derivatives containing substituted cyclopentadienyl ligands **40a–d** with lithium or sodium phenyl- or trimethylsilylacetylenides at -78°C yields the paramagnetic complexes **41a–d** which are converted into the dimagnetic complexes **42a–d** upon heating.^{17, 54, 57, 113, 114}

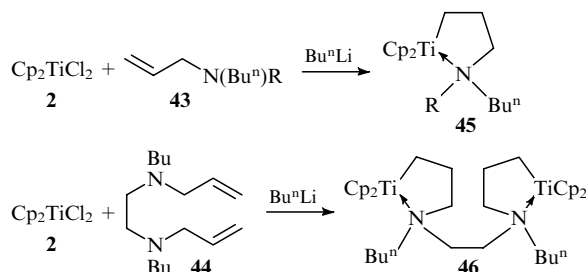


M = Na, Li.

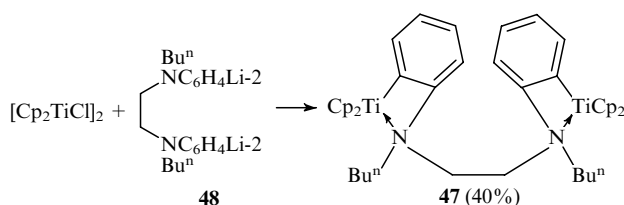
Compound	Cp ¹	Cp ²	R	Ref.
a	C ₅ H ₅	C ₅ H ₅	Ph	54
b	MeC ₅ H ₄	MeC ₅ H ₄	Ph	113
c	C ₅ H ₅	C ₅ H ₅	SiMe ₃	57
d	Me ₂ Si(C ₅ H ₄) ₂		Ph	17, 114

Dicyclopentadienyltitanium(III) monoacetylenides are formed as side products upon treatment of titanocene dichloride (**2**) with an excess of acetylenides $\text{EC}\equiv\text{CR}$ (E = BrMg, Na, Li; R = Ph, Et, Prⁿ, Buⁿ, Bu^t, SiMe₃).⁵⁶ The formation of a dicyclopentadienyltitanium(III) derivative $\text{Cp}_2\text{Ti}(2\text{-MeOCH}_2\text{C}_6\text{H}_4)$ proceeds through preliminary reduction of Ti(IV) to Ti(III) in the reaction of titanocene dichloride (**2**) with an equimolar amount of bis(2-methoxymethylphenyl)magnesium in THF. This is the first Ti(III) derivative in which the titanium atom is coordinated by oxygen. A similar reaction with bis(2-*N,N*-dimethylamino-methylphenyl)magnesium¹¹⁵ affords the Ti(III) complex $\text{Cp}_2\text{Ti}(2\text{-Me}_2\text{NCH}_2\text{C}_6\text{H}_4)$. Reactions of Cp_2TiCl_2 with sterically hindered lithium alkyls devoid of β -hydrogen atoms, such as LiCHPh_2 or $\text{LiCH}(\text{SiMe}_3)_2$ yield the Ti(III) complexes Cp_2TiR [R = Ph_2CH , $(\text{Me}_3\text{Si})_2\text{CH}$]. Dicyclopentadienyltitanium(III) chloride was found to be the intermediate product of these reactions.¹¹⁶

Treatment of titanocene dichloride (**2**) with *n*-butyllithium yields Cp_2TiH which adds to allylamines **43** and **44** to give 1-titana-2-azacyclopentanes **45** and **46**.¹¹⁷



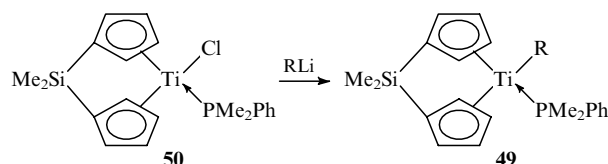
The binuclear complex **47** was prepared by the reaction of dicyclopentadienyltitanium(III) chloride with *N,N'*-bis(*o*-lithium-phenyl)-*N,N'*-di(*n*-butyl)ethylenediamine **48**.⁷⁴



The reaction of dicyclopentadienyltitanium(III) chloride with lithium tetramethylaluminate in toluene at 0°C was used to prepare the complex $\text{Cp}_2\text{Ti}(\mu\text{-Me})_2\text{AlMe}_2$ containing two bridging methyl groups.¹¹⁸ The titanocene derivatives $\text{Cp}_2\text{Ti}(\mu\text{-Cl})(\mu\text{-CH}_2)\text{AlMe}_2$ (see Ref. 119) and $\text{Cp}_2\text{Ti}(\mu\text{-CH}_2)_2\text{PPhR}$ (R = Me, Ph)¹²⁰ containing bridging methylene groups have also been synthesised.

The reaction of titanocene dichloride (**2**) with isopropylmagnesium chloride in a nitrogen atmosphere at temperatures below -78°C affords $[\text{Cp}_2\text{TiPr}]_2\text{N}_2$ with a coordinated nitrogen molecule.¹²¹ The complexes $[\text{Cp}_2\text{TiR}]_2\text{N}_2$ [R = CH_2Bu^t , CH_2SiMe_3 , 3-MeC₆H₄, 2,6-Me₂C₆H₃,¹²² $\text{C}(\text{Me})=\text{CHMe}$ (see Ref. 107)] were prepared from dicyclopentadienyltitanium(III) chloride and organomagnesium compounds under similar conditions.

The phosphine titanocene derivatives **49** containing σ -bound methyl- or trimethylsilylmethyl groups were synthesised by the reaction of the phosphine complexes **50** with organolithium compounds.¹²³



R = Me, Me_3SiCH_2 .

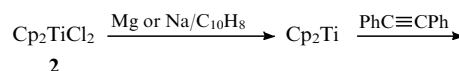
It was shown that the complexes $[\text{Cp}_2\text{TiR}_2]\text{M}$ (M = Li, Na; R = Me, Et, Prⁱ) stable only at low temperatures are formed upon treatment of titanocene dichloride (**2**) with an excess of organolithium or -sodium reagents at temperatures below -70°C .¹²⁴ The complex $[\eta^5\text{-(C}_5\text{HMe}_4)_2\text{Ti}(\eta^1\text{-C}\equiv\text{C}-\text{C}\equiv\text{CSiMe}_3)_2]^- [\text{Li}(\text{THF})_2]^+$ was isolated and characterised by X-ray diffraction analysis. This is the first complex in which the Li atom is located between the inner triple bonds of the ethynyl ligands.¹²⁵

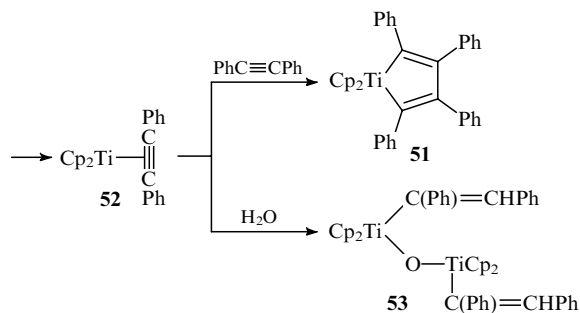
2. Synthesis of titanocene σ -derivatives using unsaturated organic compounds

Reactions resulting in metallacyclic titanocene complexes containing Ti–C σ -bonds can arbitrarily be divided into three groups:

1. Formation of a metallacycle by cross-linking of two unsaturated compounds including those π -coordinated by a metal atom;
2. Formation of a titanacycle by incorporation of an unsaturated compound into the Ti–C σ -bond;
3. Addition of molecules containing several multiple bonds to dicyclopentadienyltitanium derivatives.

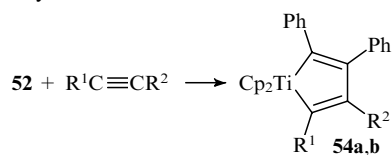
The first type of reactions include reduction of titanocene dichloride (**2**) with naphthalenesodium¹²⁶ or metallic magnesium^{127, 128} in the presence of diphenylacetylene resulting in 1,1-dicyclopentadienyl-2,3,4,5-tetraphenyl-1-titanacyclopentadiene (**51**).





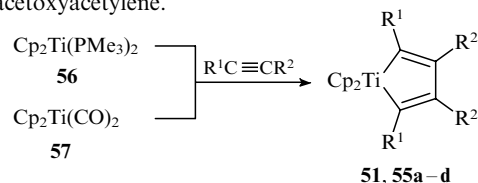
It is believed¹²⁹ that this reaction proceeds through the reduction of titanium(IV) to titanium(II) with subsequent formation of the tolan–titanocene π -complex **52**. Supporting evidence is provided by the fact that 1,1-dicyclopentadienyl-2,3,4,5-tetraphenyl-1-titanacyclopentadiene **51** is formed as a result of interaction of the complex **52** with tolan,¹²⁹ while treatment of the intermediate compound **52** with water gives the binuclear complex **53**.¹²⁷

Titanacyclopentadienes **54a,b** were synthesised by the reaction of the tolan–titanocene complex **52** with phenylacetylene or hex-3-yne.¹³⁰



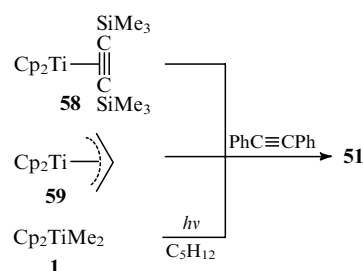
$R^1 = \text{Ph}$, $R^2 = \text{H}$ (**a**); $R^1 = R^2 = \text{Et}$ (**b**).

The dimerisation of alkynes and the formation of titanacyclopentadienes **51** and **55a–d** occur in the reaction of the diphosphine–titanocene complex **56** with acetylene, dimethylacetylene or methylacetylene or of the titanocenedicarbonyl **57** with tolan or diacetoxyacetylene.

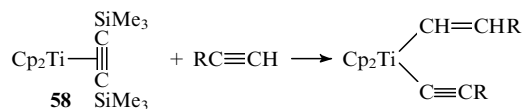


Compound	R^1	R^2	Ref.
55a	H	H	131–133
55b	Me	Me	134
55c	Me	H	133
55d	OC(O)Me	OC(O)Me	135
51	Ph	Ph	135

1,1-Dicyclopentadienyl-2,3,4,5-tetraphenyl-1-titanacyclopentadiene (**51**) was prepared by treatment of the titanocene complex with bis(trimethylsilyl)acetylene **58**¹³⁶ or of the π -allyl titanium(III) complex **59**¹³⁷ with an excess of tolan. The titanacycle **51** is also formed in a photochemical reaction of dimethyltitanocene (**1**) with tolan in pentane.^{138–140}

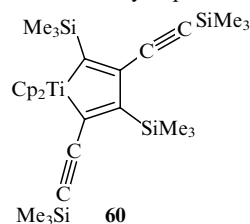


In contrast to the reaction of the bis(trimethylsilyl)acetylene–titanocene complex **58** with tolan, its reaction with mono-substituted alkynes yields alkenyltitanocene acetylenides.¹⁴¹

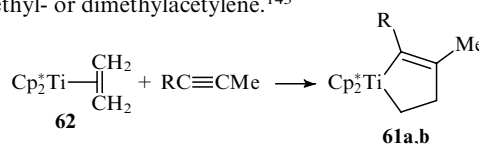


$R = \text{Ph}$, Me_3Si , $\text{Me}(\text{CH}_2)_3$.

The reaction of titanocene with bis(trimethylsilyl)butadiyne gives the titanacyclopentadiene derivative **60**.¹⁴²



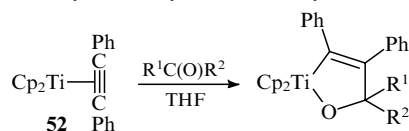
Cross-linking of ethylene and acetylene ligands and the formation of 1,1-bis(pentamethylcyclopentadienyl)-1-titanacyclopent-2-ene derivatives **61a,b** take place in the reaction of bis(pentamethylcyclopentadienyl)(ethylene)titanium (**62**) with methyl- or dimethylacetylene.¹⁴³



$R = \text{H}$ (**a**), Me (**b**).

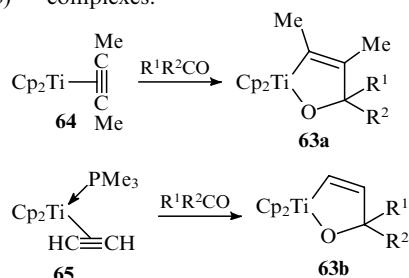
Compounds containing a titanacyclopentene fragment were prepared by reactions of (acetylene)(trimethylphosphine)di(cyclopentadienyl)titanium with ethylene¹⁴⁴ and by reactions of (diphenylacetylene)di(cyclopentadienyl)titanium with tricyclo[5.2.1.0^{2,8}]deca-2,5,8-triene.¹⁴⁵

Acetylene–titanocene complexes enter into heterocyclisation reactions with carbonyl compounds. Thus the tolan–titanocene complex **52** reacts with an equimolar amount of acetone^{146, 147} or benzaldehyde¹⁴⁷ to yield titanadihydrofuran metallacycles.



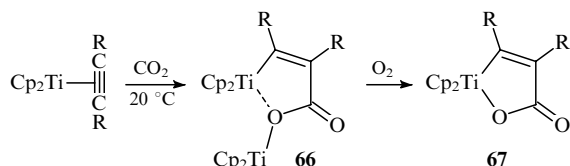
$R^1 = R^2 = \text{Me}$; $R^1 = \text{Ph}$, $R^2 = \text{H}$.

The titanadihydrofuran derivatives **63a,b** are formed by reactions of acetone or acetaldehyde with dimethylacetylene–titanocene (**64**)¹³⁴ or acetylene(trimethylphosphine)–titanocene (**65**)¹⁴⁴ complexes.



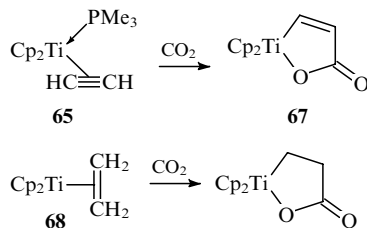
$R^1 = \text{H}$, $R^2 = \text{Me}$; $R^1 = R^2 = \text{Me}$.

The reaction of carbon dioxide with alkyne–titanocene π -complexes results in the binuclear σ -vinylcarboxylate complexes **66**. Their oxidation by atmospheric oxygen gives titanadihydrofuranones **67**.

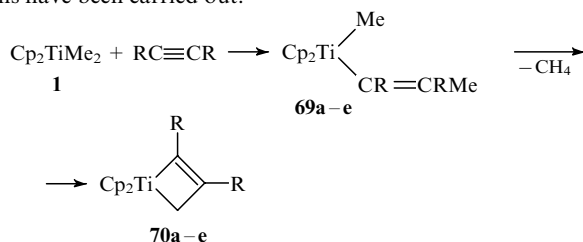


R = Ph,^{148–150} SiMe₃,^{149, 150} Me.¹³⁴

Titanadihydrofuranone (**67**) (R = H) was prepared by the reaction of carbon dioxide with the trimethylphosphinacetylene–titanocene complex **65**.¹⁴⁴ The reaction of the ethylene–titanocene complex **68** with CO₂ yields titanatetrahydrofuranone.¹⁴³

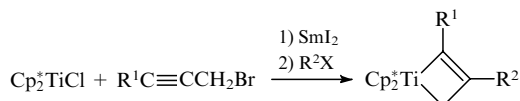


The reaction of dimethyltitanocene (**1**) with alkynes in boiling benzene in the dark is a typical reaction of the second type, which consists in the formation of titanacycles due to incorporation of unsaturated compounds into the Ti–C σ -bond. In the first step, methyl(vinyl)titanocene complexes **69a–e** are formed; in the case of R = Ph¹⁵¹ and C₆F₅ (see Ref. 152), these complexes were isolated in an individual state. In the second step, methane is abstracted from the complexes **69a–e** resulting in the titanacyclobutene derivatives **70a–e**.^{151, 153} In-depth studies of these reactions have been carried out.¹⁵⁴



R = Et (**a**), Prⁿ (**b**), Ph (**c**), Me₃Si (**d**), C₆F₅ (**e**).

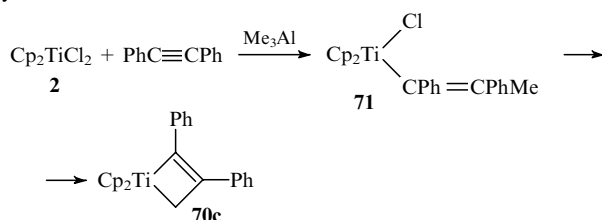
Titanacyclobutene derivatives were prepared by the reaction of bis(pentamethylcyclopentadienyl)titanium chloride with propargyl bromides in the presence of samarium diiodide with subsequent treatment of the reaction mixture with an equimolar amount of the corresponding halide.^{155, 156}



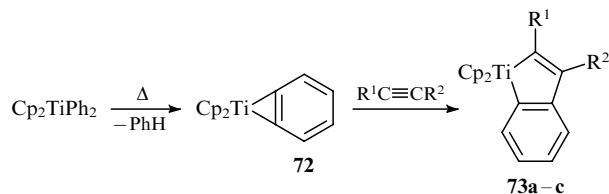
R¹ = H; R² = Bn; R¹ = Me, R² = MeC $\equiv$ CCH₂, Bn;

R¹ = Ph, R² = Bn, PhC $\equiv$ CCH₂; X = Hal.

Diphenyl-substituted titanacyclobutene **70c** was synthesised by the reaction of titanocene dichloride (**2**) with tolan and trimethylaluminium. This reaction proceeds *via* the intermediate vinyl derivative **71**.¹⁵⁶

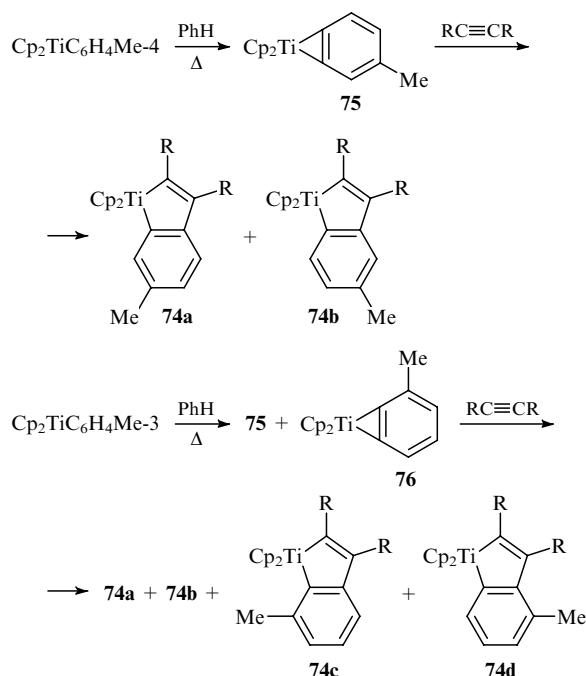


Thermal reactions of alkynes with diphenyltitanocene are also accompanied by insertion of alkyne into the Ti–C σ -bond. It is believed^{157, 158} that the phenylenetitanium complex **72** is formed in the first step as a result of splitting of the benzene molecule from diphenyltitanocene. Subsequent insertion of alkyne into one of the Ti–C σ -bonds results in titanaindenes **73a–c**.



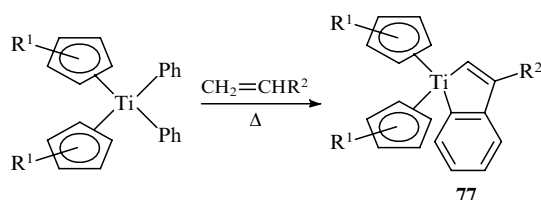
R¹ = R² = Ph (**a**), R¹ = R² = C₆F₅ (**b**), R¹ = SiMe₃, R² = Ph (**c**).

Analogous reactions yielding mixtures of substituted titanaindenes **74a–d** occur on heating of *m*- or *p*-tolyltitanocenes in the presence of alkynes.¹⁵⁹ The formation of a complex mixture of reaction products in the case of the *m*-tolyl derivative is explained by the fact that this compound yields a mixture of isomeric phenylenetitanium complexes **75** and **76** upon heating.¹⁵⁹



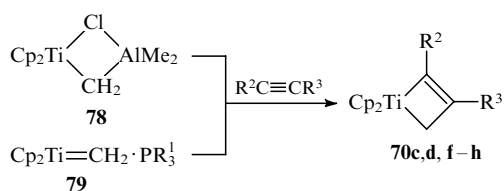
Titanaindene **73a** was prepared by reduction of titanocene dichloride (**2**) with magnesium in the presence of tolan and *o*-bromofluorobenzene.¹²⁸

Heating of diphenyltitanocene derivatives in the presence of alkenes results in titanaindenes **77**.¹⁶⁰



R¹ = H, Me; R² = H, Me, Buⁿ.

The 1,1-dicyclopentadienyl-1-titanacyclobut-2-ene derivatives **70c,d,f–h** were prepared by the reaction of alkynes with the titanium–aluminium complex **78** in the presence of pyridine^{161, 162} or with carbene–titanocene complexes **79**.^{163–165}

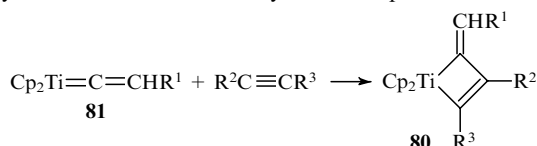


$\text{R}_3^1 = \text{Me}_3, \text{Me}_2\text{Ph}, \text{Et}_3$; $\text{R}^2 = \text{R}^3 = \text{Ph}$ (**70c**), SiMe_3 (**70d**);

$\text{R}^2 = \text{CMe}=\text{CH}_2$, $\text{R}^3 = \text{Et}$ (**70f**); $\text{R}^2 = \text{Et}$, $\text{R}^3 = \text{CMe}=\text{CH}_2$ (**70g**);

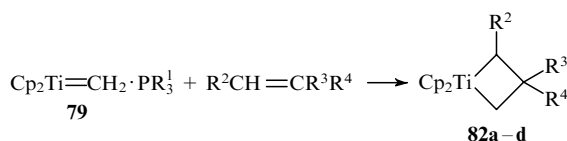
$\text{R}^2 = \text{CEt}=\text{CH}_2$, $\text{R}^3 = \text{Me}$ (**70h**).

Alkylidenetitanacyclobutenes **80** are formed in reactions of alkynes with the titanocenevinylidene complexes **81**.¹⁶⁶



$\text{R}^1 = \text{Ph}, \text{Pr}^n, n\text{-C}_5\text{H}_{11}$; $\text{R}^2 = \text{H}, \text{Pr}^n, n\text{-C}_5\text{H}_{11}, \text{Ph}$; $\text{R}^3 = \text{Pr}^n, \text{Ph}, \text{SiMe}_3$.

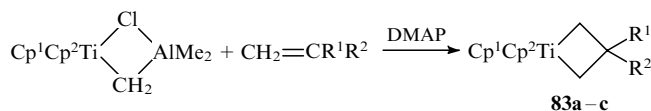
The titanacyclobutane derivatives **82a–d** result from reactions of trisubstituted alkenes with the carbene–titanocene complexes **79**.^{163–165} Titanacyclobutenes **83a–c** were prepared by the reaction of terminal alkenes with titanium–aluminum complexes in the presence of 4-dimethylaminopyridine (DMAP).^{91,167} The titanium–aluminum complex **78** yields the titanabicyclopentane derivative **84** in the reaction with 3,3-dimethylcyclopropene.¹⁶⁸



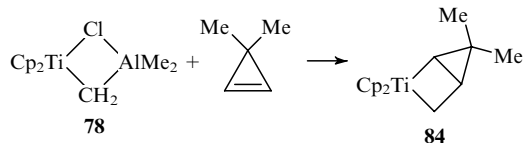
$\text{R}_3^1 = \text{Me}_3, \text{Me}_2\text{Ph}, \text{Et}_3$; $\text{R}^2 = \text{R}^3 = \text{H}$; $\text{R}^4 = \text{Bu}^n$ (**a**);

$\text{R}^2 = \text{R}^3 = \text{H}$, $\text{R}^4 = \text{Bu}^t$ (**b**), $\text{R}^2 = \text{H}$, $\text{R}^3 = \text{R}^4 = \text{Me}$ (**c**);

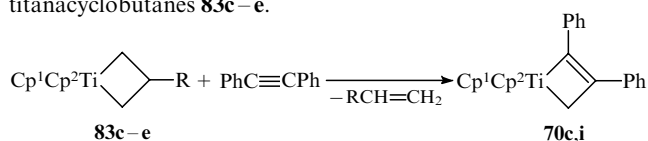
$\text{R}^2 = \text{R}^4 = \text{Me}$; $\text{R}^3 = \text{H}$ (**d**).



Compounds 83	Cp^1	Cp^2	R^1	R^2	Ref.
a	C_5H_5	C_5H_5	Me	Pr^i	167
b	$\text{C}_5\text{H}_4\text{Me}$	$\text{C}_5\text{H}_4\text{Me}$	Bu^t	H	91
c	C_5H_5	$\text{C}_5\text{H}_4\text{Me}$	Bu^t	H	91

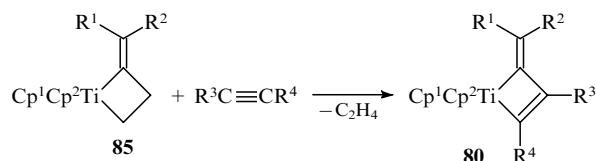


Titanacyclobutane derivatives react with alkynes to give titanacyclobutenes and the corresponding alkenes. Thus titanacyclobutenes **70c,i** were synthesised from diphenylacetylene and titanacyclobutenes **83c–e**.



Titanacyclobutenes	Cp^1	Cp^2	R	Titanacyclobutenes	Ref.
83e	C_5H_5	C_5H_5	Bu^t	70c	169, 170
83d	C_5H_5	C_5H_5	Pr^i	70c	169, 170
83c	C_5H_5	$\text{C}_5\text{H}_4\text{Me}$	Bu^t	70i	91

Alkylidenetitanacyclobutenes **85** react with alkynes at 70 °C in benzene or toluene to give alkylidenetitanacyclobutenes **80**.^{171,172}



$\text{Cp}^1 = \text{Cp}^2 = \text{C}_5\text{H}_5$; $\text{R}^1 = \text{R}^2 = \text{Me}$; $\text{R}^1 = \text{Me}$, $\text{R}^2 = \text{Pr}^i$;

$\text{R}^3 = \text{R}^4 = \text{Me}, \text{Et}$; $\text{Cp}^1 = \text{Cp}^2 = \text{C}_5\text{Me}_5$; $\text{R}^1 = \text{R}^2 = \text{H}$,

$\text{R}^3 = \text{R}^4 = \text{H}, \text{Me}, \text{Ph}, \text{SiMe}_3, \text{SiBu}_3$; $\text{R}^3 = \text{Pr}^n$, $\text{R}^4 = \text{H}$;

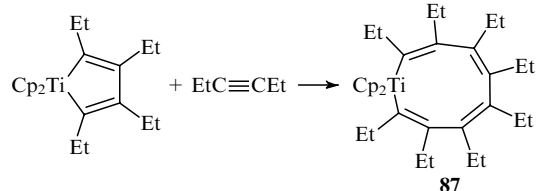
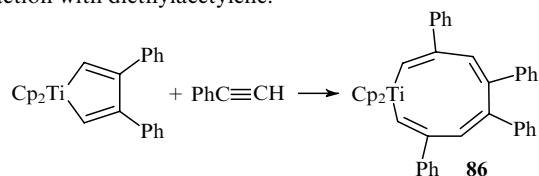
$\text{R}^3 = \text{Me}$, $\text{R}^4 = \text{Et}$; $\text{R}^3 = \text{Et}$, $\text{R}^4 = \text{Me}$; $\text{R}^3 = \text{Me}$, $\text{R}^4 = \text{MeC}\equiv\text{C}$;

$\text{R}^3 = \text{Ph}$, $\text{R}^4 = \text{PhC}\equiv\text{C}$; $\text{R}^3 = \text{Me}$, $\text{R}^4 = \text{Ph}$;

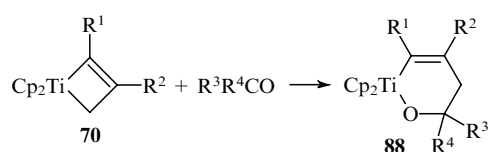
$\text{R}^3 = \text{Ph}$, $\text{R}^4 = \text{Me}$; $\text{R}^3 = \text{Ph}$, $\text{R}^4 = \text{SiMe}_3$.

Reactions of titanacyclobutane complexes with 1,1-dimethyl- and 1-isopropyl-1-methylallenes result in the formation of alkylidenetitanacyclobutene derivatives **80** ($\text{R}^1 = \text{R}^2 = \text{Me}$, $\text{R}^1 = \text{Me}$, $\text{R}^2 = \text{Pr}^i$; $\text{R}^3 = \text{R}^4 = \text{H}$).^{172,173}

Some reactions of titanacyclic complexes with unsaturated or carbonyl compounds are accompanied by expansion of the metallacycle. Thus 1,1-dicyclopentadienyl-3,4-diphenyl-1-titanacyclopentadiene reacts with phenylacetylene to give a nine-membered titanacycle **86**. 1,1-Dicyclopentadienyl-2,3,4,5-tetraethyl-1-titanacyclopentadiene forms a similar cyclic derivative **87** in a reaction with diethylacetylene.¹⁷⁴



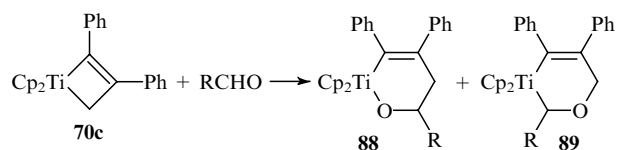
Insertion of aliphatic ketones into the Ti–C σ -bond of the titanacyclobutene derivatives **70** results in six-membered metallacycles **88**.¹⁷⁵



$\text{R}^1 = \text{R}^2 = \text{Ph}$; $\text{R}^3 = \text{R}^4 = \text{Me}$; $\text{R}^3 = \text{Me}$, $\text{R}^4 = \text{Ph}$, $\text{CH}_2 = \text{CH}$;

$\text{R}^3 = \text{Ph}$, $\text{R}^4 = \text{cyclo-C}_3\text{H}_5$; $\text{R}^1 = \text{Ph}$, $\text{R}^2 = \text{Me}$; $\text{R}^3 = \text{Me}$, $\text{R}^4 = \text{Me}, \text{Ph}$.

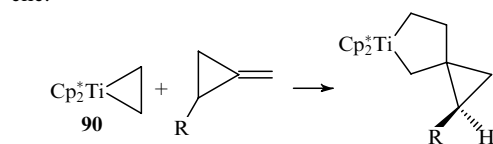
Reactions of 1,1-dicyclopentadienyl-1-titana-2,3-diphenylcyclobut-2-ene **70c** with aldehydes yield mixtures of isomeric titanadihydropyrans **88** and **89**.¹⁷⁵



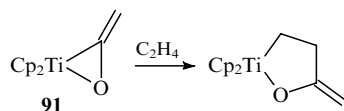
$\text{R} = \text{Me}, \text{Ph}, \text{Bn}$.

The expansion of the metallacycle also takes place in reactions of 1,1-bis(pentamethylcyclopentadienyl)-1-titanacyclopentane **90** with methylidenecyclopropane or 1-methylidene-2-phenylcyclo-

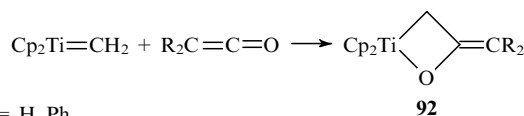
propane¹⁷⁶ and the ketene–titanocene complex **91** with ethylene.¹⁷⁷



R = H, Ph.

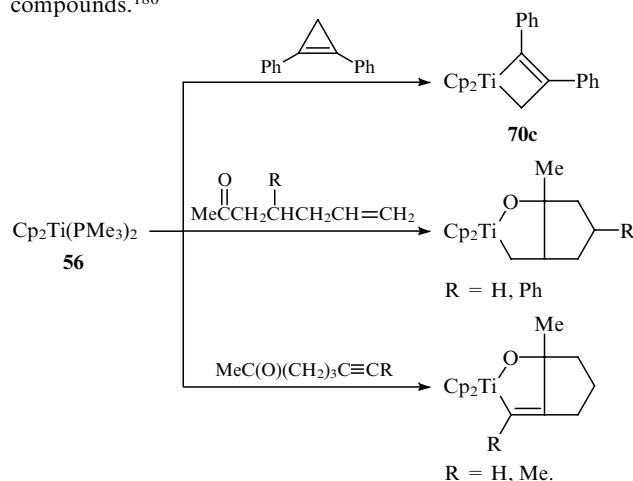


The metallacyclic compounds **92** were prepared by reactions of the carbene–titanocene complex with ketenes.¹⁷⁸

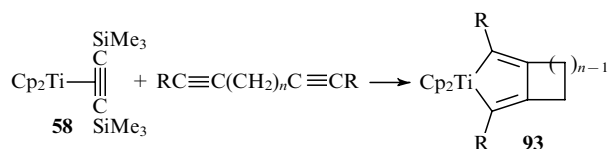


R = H, Ph.

Reactions of bis(trimethylphosphine)titanocene (**56**) with 1,2-diphenylcyclopropene,¹⁷⁹ δ -enones and δ -inones belong to the third type of reactions leading to the formation of titanacyclic compounds.¹⁸⁰

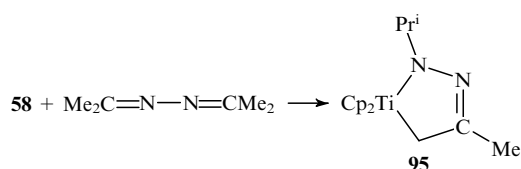
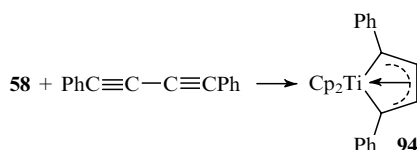


A reaction of the bis(trimethylsilyl)acetylene–titanocene complex **58** with diynes was used for the preparation of bicyclic titanacyclopentadiene derivatives **93**.¹⁸¹

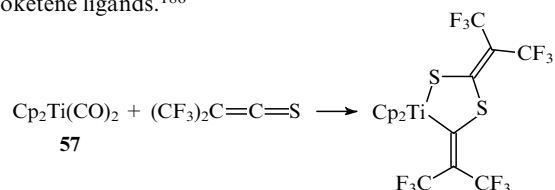


n = 2, R = Me, Bu; n = 4, R = Et.

The reaction of the bis(trimethylsilyl)acetylene–titanocene complex **58** with 1,4-diphenylbuta-1,3-diyne results in titanacyclocumulene **94**,¹⁸² while the reaction with acetone azine gives the 1-titana-2,3-diazacyclopent-3-ene derivative **95**.^{183, 184}



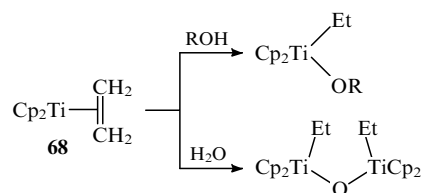
The reaction of di(carbonyl)di(cyclopentadienyl)titanium (**57**) with 1,1,3,3-tetramethyl-2-thiocarbonylcyclohexane gives a monomeric alkylidenetitanathiirane containing a η^2 -(C–S)-bound thioetone ligand.¹⁸⁵ The reaction of di(carbonyl)di(cyclopentadienyl)titanium (**57**) with bis(trifluoromethyl)thioetone yields a titanacycle in which the titanium atom is bound to two thioetone ligands.¹⁸⁶



3. Miscellaneous methods for the synthesis of titanocene σ -derivatives

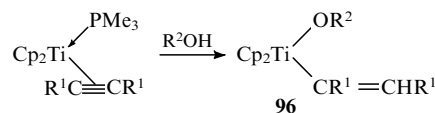
In some cases, addition of various substrates to π -bound organic ligands of titanocene derivatives results in the formation of Ti–C σ -bonds.

Treatment of di(η^5 -cyclopentadienyl)(η^2 -ethylene)titanium (**68**) with alcohols, phenols^{187, 188} and water¹⁸⁸ gave mono- and binuclear derivatives of ethyltitanocene.



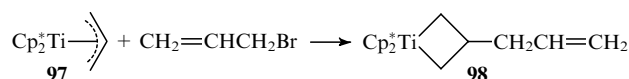
R = Me, Et, Ph.

The reactions of acetylene titanocene complexes with alcohols or phenols yielded σ -alkenyl complexes **96**.^{187, 188}

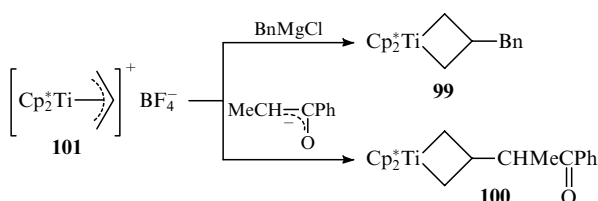


R¹ = Ph, Me; R² = Me, Et, Ph.

Bis(η^5 -pentamethylcyclopentadienyl)(η^3 -allyl)titanium (**97**) reacts with allyl bromide to give the titanacyclobutane complex **98**.¹⁸⁹

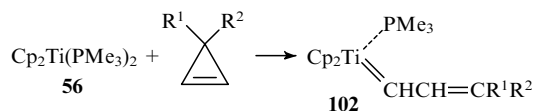


Reactions of the cationic π -allyl complex **101** with benzylmagnesium chloride or propiophenone enolate lead to the titanacyclobutane derivatives **99** and **100**.¹⁹⁰



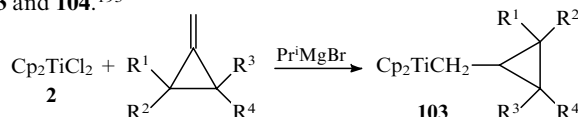
Bis(pentamethylcyclopentadienyl)titanium hydride reacts with alkenes to give the σ -alkyl derivatives $\text{Cp}_2^*\text{TiCH}_2\text{CH}_2\text{R}$ ($\text{R} = \text{H}, \text{Me}$).¹⁰⁸

Reactions of bis(trimethylphosphine)titanocene (**56**) with an equimolar amount of 3,3-disubstituted cyclopropanes afford the titanocene(vinylcarbene) complexes **102**.¹⁹¹ The complex **102** ($\text{R}^1 = \text{R}^2 = \text{Ph}$) was prepared together with the complex $\text{Cp}_2\text{Ti}(\text{PMe}_3)_2 = \text{C} = \text{C} = \text{CPh}_2$ by treatment of titanocene dichloride with two equivalents of butyllithium in the presence of trimethylphosphine and 3,3-diphenylcyclopropane.¹⁹²

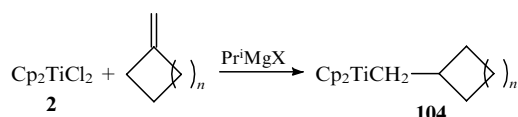


$\text{R}^1 = \text{R}^2 = \text{Me}, \text{Ph}$; $\text{R}^1 = \text{Me}, \text{R}^2 = \text{Ph}$.

Reduction of titanocene dichloride (**2**) by isopropylmagnesium halides in the presence of methylidenecyclopropanes, methylenecyclobutane or methylenecyclopentane results in the di(cyclopentadienyl)(cycloalkylmethyl)titanium(III) complexes **103** and **104**.¹⁹³



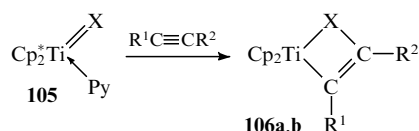
$\text{R}^1, \text{R}^2, \text{R}^3, \text{R}^4 = \text{H}, \text{Me}$.



$n = 1, 2$; $\text{X} = \text{Cl}, \text{Br}$.

Titanium enolates of the formula $\text{Cp}_2^*\text{TiMe}(\text{OCR}^1 = \text{CR}^2\text{R}^3)$ were prepared by heating bis(pentamethylcyclopentadienyl)dimethyltitanium(IV) in the presence of epoxides, *e.g.*, cyclohexene oxide, *cis*- and *trans*-but-2-ene oxides.¹⁹⁴

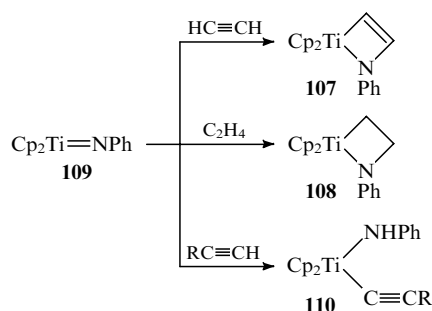
The titanocene sulfide and titanocene oxide complexes **105** enter into [2+2]-cycloaddition reactions with alkynes to give titanaoxa- (**106a**) and titanathiacyclobutenes (**106b**).^{195, 196}



106a: $\text{X} = \text{O}$; $\text{R}^1 = \text{H}$; $\text{R}^2 = \text{Me}, \text{Bu}^t, \text{Ph}, 4\text{-MeC}_6\text{H}_4$; $\text{R}^1 = \text{R}^2 = \text{Ph}$;

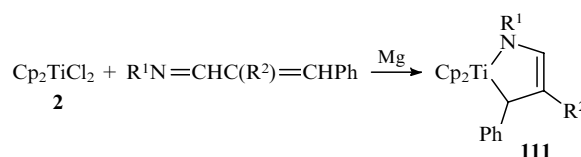
106b: $\text{X} = \text{S}$; $\text{R}^1 = \text{R}^2 = \text{H}$; $\text{R}^1 = \text{H}, \text{R}^2 = \text{Ph}, \text{Me}_3\text{Si}$.

The azatitanacycles **107** and **108** are prepared by the reaction of the complex **109** with acetylene or ethylene, respectively. Reactions of the complex **109** with phenyl- or trimethylsilylacetylene yield acetylenides **110**.¹⁹⁷



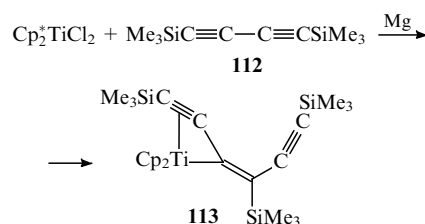
$\text{R} = \text{Ph}, \text{Me}_3\text{Si}$.

Some titanocene derivatives containing Ti—C σ -bonds were prepared by the reduction of titanocene dichloride (**2**) in the presence of unsaturated compounds. Thus its reduction by magnesium in the presence of Schiff's bases prepared from α, β -unsaturated aldehydes yields titanazacyclopentenes **111**.¹⁹⁸



$\text{R}^1 = \text{Bu}^t, 4\text{-MeC}_6\text{H}_4, \text{R}^2 = \text{H}$; $\text{R}^1 = \text{cyclo-C}_6\text{H}_{11}, \text{R}^2 = \text{Me}$.

Reduction of bis(pentamethylcyclopentadienyl)titanium dichloride by magnesium in the presence of 1,4-bis(trimethylsilyl)buta-1,3-diene (**112**) results in the η^3 -enyne complex **113**.¹⁹⁹



Reduction of bis(trimethylsilyltetramethylcyclopentadienyl)-titanium dichloride by magnesium in THF in the presence of bis(trimethylsilyl)acetylene gives $\eta^5: \eta^1\text{-}[\text{C}_5\text{Me}_4\text{Si-Me}_2\text{CH}_2]$. $[\eta^5\text{-C}_5\text{Me}_4(\text{SiMe}_3)]\text{Ti(III)}$.²⁰⁰

Reactions of ylides $\text{Me}_{3-n}(\text{Me}_2\text{N})_n\text{P}=\text{CH}_2$ ($n = 1, 2$) with titanocene dichloride yield complexes $\text{Cp}_2^*\text{TiCl}(\text{CH}=\text{PR}^1\text{R}^2)$, where $\text{R}^1 = \text{NMe}_2, \text{R}^2 = \text{Me}$; $\text{R}^1 = \text{Me}, \text{R}^2 = \text{NMe}_2$.²⁰¹

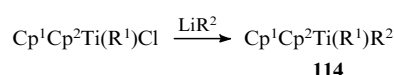
Reactions of the titanocene(dicarbonyl) **57** with alkyl iodides gave the acyl complexes $\text{Cp}_2\text{Ti}[\text{C}(\text{O})\text{R}]$, where $\text{R} = \text{Me}, \text{Et}, \text{Pr}^i, \text{Bu}^n$ (see Refs 202, 203). Acyl titanocene halide derivatives are also formed upon treatment of the titanocene(dicarbonyl) **57** by organic acid chlorides^{202, 203} or by treatment of alkyl(titanocene) halides with carbon monoxide.²⁰⁴

III. Reactions of titanocene derivatives containing Ti—C σ -bonds

Reactions of titanocene derivatives containing Ti—C σ -bonds are little studied. The published data on the reactivities of these compounds are conventionally divided into two groups, *viz.*, reactions involving Ti—C σ -bonds and those with retention of these bonds.

1. Reactions with retention of Ti—C σ -bonds

Reactions of halide derivatives of titanocene σ -complexes with organometallic derivatives of non-transition metals belong to the most typical reactions of this type. Thus reaction of alkyl- or aryltitanocene chlorides with organolithium compounds was used for the preparation of the complexes **114**, which contain two different σ -bound organic radicals.

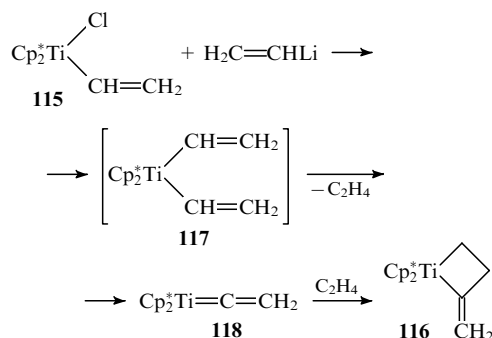


Cp^1	Cp^2	R^1	R^2	Ref.
C_5H_5	C_5H_5	Me	Ph	205
C_5H_5	C_5H_5	Me	4-MeOC ₆ H ₄	205
C_5H_5	C_5H_5	Me	4-MeC ₆ H ₄	205
C_5H_5	C_5H_5	2-thienyl	Me	206
C_5H_5	C_5H_5	2-thienyl	Ph	206
C_5H_5	C_5H_2	2-thienyl	$\text{C}\equiv\text{CPh}$	206
C_5H_5	C_5H_5	CH_2SiMe_3	$\text{C}\equiv\text{CX}^a$	207
C_5Me_5	$\text{C}_5\text{Me}_4(\text{CH}_2)_2\text{NMe}_2$	$\text{CH}=\text{CH}_2$	Me	13

Cp ¹	Cp ²	R ¹	R ²	Ref.
C ₅ H ₅	Bu ^t C ₅ H ₄	C ₆ F ₅	CH ₂ CH=CH ₂	208
C ₅ Me ₅	C ₅ Me ₅	CH=CH ₂	Me	209

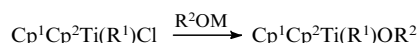
^a X = SiMe₃, 3,5-(Me₂NCH₂)₂C₆H₃, 4-NCC₆H₄, 4-C₅H₄N, Fc, 4-I-3,5-(Me₂NCH₂)₂C₆H₂.

In some cases, synthesis of this type of compound is complicated by side reactions. Thus the attempts to prepare non-symmetrical ethyltitanocene derivatives by the reaction of bis(pentamethylcyclopentadienyl)ethyltitanium chloride with methylolithium, benzylpotassium or vinylolithium yielded only the ethylene complex Cp₂Ti(η²-C₂H₄) concomitantly with the liberation of the corresponding hydrocarbon. Treatment of bis(pentamethylcyclopentadienyl)vinyltitanium chloride **115** with benzylpotassium or dimethylphosphinomethylolithium gave the complex (η⁵-C₅Me₅)(C₅Me₄CH₂)Ti–CH=CH₂.²⁰⁹ The reaction of the complex **115** with vinylolithium yields 1,1-bis(pentamethylcyclopentadienyl)-1-titana-2-methylidenecyclobutane (**116**).²⁰⁹ Presumably, bis(pentamethylcyclopentadienyl)divinyltitanium (**117**), which is formed in the first step of this reaction, is decomposed to give the derivative **118**. The latter adds the ethylene molecule at the Ti=C bond to give the final product **116**.

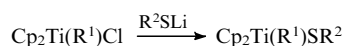


Apparently, reactions of phenyltitanocene chloride with butyl-, vinyl- or benzylolithium afford the intermediates Cp₂Ti(Ph)R (R = Buⁿ, CH=CH₂, Bn) which are further converted into phenyldicyclopentadienyltitanium(III).²⁰⁹

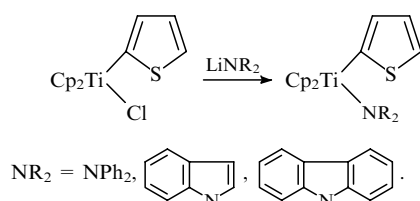
Treatment of alkyl- or aryltitanocene chlorides with alkali metals alcohols^{90, 96, 210–213} or thiolates^{87, 214} or with lithium amides²¹⁵ results in the replacement of chlorine atoms.



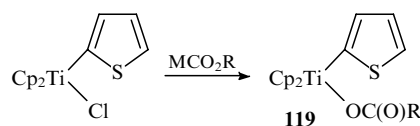
M = Na, Li; Cp¹ = Cp² = C₅H₅; R¹ = C₆F₅, R² = Me, Et; R¹ = Me, R² = CH=CH₂; R¹ = 2-thienyl, R² = 2,4,6-(NO₂)₃C₆H₂, 3,4-(NO₂)₂C₆H₃; Cp¹ = C₅H₅, Cp² = C₅H₄CH(Me)Ph, R¹ = C₆F₅, R² = 2-MeC₆H₄; R¹ = R² = Me.



R¹ = Me, R² = 4-NH₂C₆H₄; R¹ = 2-thienyl, R² = Bn, 2-thienyl.



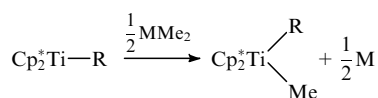
Reactions of 2-thienyltitanocene chloride with potassium 2,4-dichlorophenoxyacetate, mercury(I) benzoate or silver trifluoroacetate were used for the preparation of the corresponding 2-thienyltitanocene acylates (**119**).²¹⁶



M = K, R = 2,4-Cl₂C₆H₃OCH₂; M = Hg, R = Ph; M = Ag, R = CF₃.

The reaction of pentafluorophenyltitanocene chloride with sodium hydroxide occurs with the retention of the Ti–C σ -bond and results in the substitution of the hydroxy group for the chlorine atom.²¹¹

Some transformations of dicyclopentadienyltitanium(III) derivatives under the action of various oxidants, which may even include dimethylzinc, dimethylcadmium and PbCl₂, occur with the retention of the Ti–C σ -bond. Thus reaction of ethyl-, phenyl- or vinylbis(pentamethylcyclopentadienyl)titanium with dimethylzinc^{217, 218} or dimethylcadmium²¹⁷ afforded methyltitanocene derivatives along with metallic zinc or cadmium.

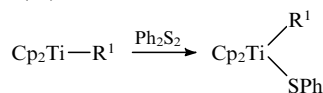


R = Et, Ph, CH=CH₂; M = Zn, Cd.

The methylbis(pentamethylcyclopentadienyl)titanium derivatives Cp₂^{*}Ti(Me)X, where X = Cl, OMe, N = CHBu^t, are also formed in the oxidation of the corresponding Cp₂^{*}TiX derivatives by dimethylzinc or -cadmium.^{217, 218} It is noted²¹⁷ that dimethylmercury does not enter into such reactions.

Alkyl- or acyldicyclopentadienyltitanium(IV) chlorides were prepared by oxidation of σ -alkyl- or σ -acyldicyclopentadienyltitanium(III) derivatives by lead dichloride.^{109, 219}

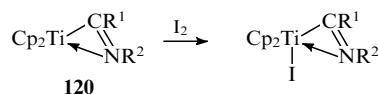
Treatment of dicyclopentadienyltitanium(III) derivatives with diphenyl disulfide is also accompanied by the oxidation of Ti(III) to Ti(IV) with the retention of the Ti–C σ -bond.^{102, 103, 107}



R¹ = C(O)CMe=CHMe; 2,6-Me₂C₆H₃N=CR²,

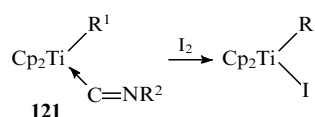
R² = Me, Et, Buⁿ.

In some cases, reaction of dicyclopentadienyltitanium(III) σ -derivatives, *e.g.*, complexes **120** and **121**, with iodine also occurs with the retention of the Ti–C σ -bond resulting in titanium(IV) derivatives.^{103, 220}



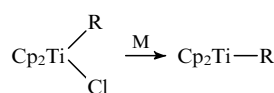
R¹ = Me, R² = 2,6-Me₂C₆H₃; R¹ = Ph, 2-MeC₆H₄,

R² = 2-MeC₆H₄, 2,6-Me₂C₆H₃.



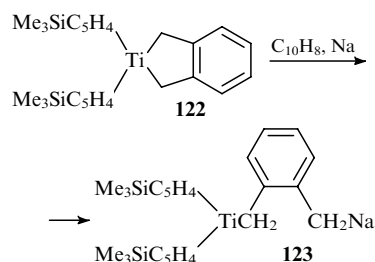
R¹ = Ph, 2-MeC₆H₄; R² = 2-MeC₆H₄, 2,6-Me₂C₆H₃.

Sometimes, reduction of titanocene σ -derivatives occurs with the retention of the metal–carbon σ -bond. Thus the reaction of alkyltitanocene chlorides with zinc or magnesium yields titanium(III) complexes.^{40, 104}

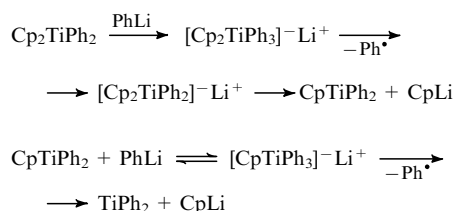


M = Zn, Mg; R = C₆F₅, Me, CH₂SiMe₃, CH₂PPh₂.

Reaction of titanaindan **122** with naphthalenesodium occurs with the opening of the metallacycle and the formation of the complex **123**.²²¹



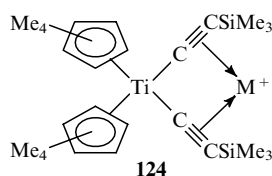
In some cases, the role of reducing agents for titanocene σ -derivatives is played by organolithium compounds. Thus the reaction of di(cyclopentadienyl)diphenyltitanium(IV) with phenyllithium in ether results in the reduction of Ti(IV) to Ti(III) and the formation of diphenyl(cyclopentadienyl)titanium(III) and diphenyltitanium(II). Diphenyl(cyclopentadienyl)titanium(III) is formed first. An excess of phenyllithium causes the decomposition of the Ti(III) complex, the diphenyltitanium being the final product.^{222, 223}



Reactions with retention of the Ti–C σ -bond include the formation of complex bimetallic compounds based on titanocene σ -derivatives. Thus reactions of diphenyltitanocene with diphenylzinc or triethylaluminium yield the binuclear complexes $(\text{C}_5\text{H}_4)_4\text{Ti}_2\text{Ph}_2\text{Zn}$ (see Ref. 224) and $[\text{Cp}(\text{C}_5\text{H}_4)\text{TiHAlEt}_2]_2$ in which Ti and Al atoms are linked through a bridging hydride ligand (see Ref. 225).

It is of note that the derivatives of the type $\text{Cp}_2\text{TiX}_2\text{AlR}_2$ (X = Cl, I, Br; R = Alk, Ar) are the most well-studied titanium–aluminium complexes;²²⁶ however, they do not contain Ti–C σ -bonds and are therefore not considered in this review.

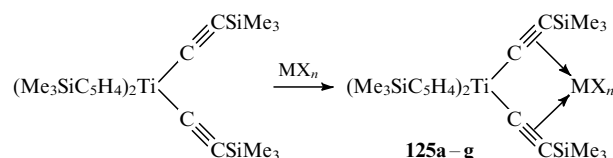
The bimetallic Ti(III) complexes in which the alkali metal ion was incorporated between the acetylenide fragments (tweezer complexes) were synthesised from titanocene acetylenides and its derivatives containing substituents in the cyclopentadienyl ligands. Thus the complexes **124** were prepared by the reaction of $(\eta^5\text{-C}_5\text{HMe}_4)_2\text{Ti}(\eta^1\text{-C}\equiv\text{CSiMe}_3)_2$ with alkali metals in toluene.^{63, 227}



M = Li, Na, K.

A similar complex $[(\eta^5\text{-C}_5\text{HMe}_4)_2\text{Ti}(\eta^1\text{-C}\equiv\text{CC}\equiv\text{CSiMe}_3)]^- [\text{Li}(\text{THF})_2]^+$ (see Ref. 125) was prepared by treatment of bis-(tetramethylcyclopentadienyl)(4-trimethylsilylbuta-1,3-dienyl)titanium in THF with an excess of 1-lithio-4-(trimethylsilyl)buta-1,3-diyne.

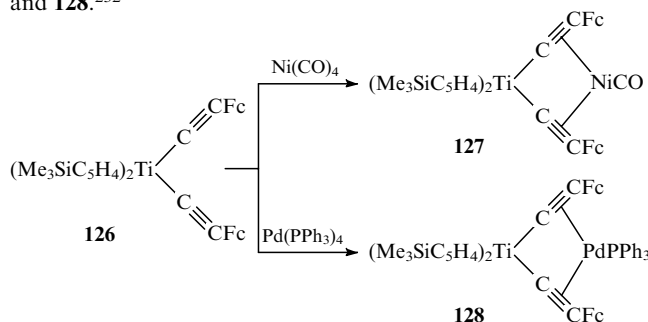
Bis(alkynyl)titanocenes are very good chelating ligands owing to their ability to form bimetallic complexes with copper(I), iron(II) and silver salts. Thus reactions of bis(trimethylsilylcyclopentadienyl)bis(trimethylsilylethynyl)titanium with CuCl , FeCl_2 and various silver salts yield the complexes **125a–g**.



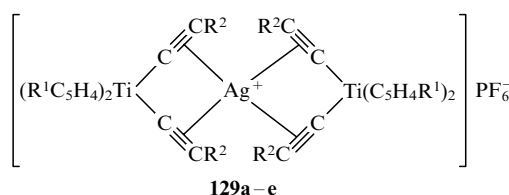
Compounds 125	M	X	<i>n</i>	Ref.
a	Cu	Cl	1	228, 229
b	Fe	Cl	2	228, 230
c	Ag	Cl	1	230
d	Ag	CN	1	230
e	Ag	SCN	1	230
f	Ag	NO ₂	1	230
g	Ag	ClO ₄	1	230

In the reaction of the complex **125a** with lithium acetylenides, the chlorine atom is replaced by the ethynyl group to give complexes of the general formula $(\eta^5\text{-C}_5\text{H}_4\text{SiMe}_3)_2\text{Ti}(\eta^1\text{-C}\equiv\text{CSiMe}_3)_2\text{CuC}\equiv\text{CR}$, where R = SiMe₃, Bu^t, Ph.²²⁹ The structurally similar copper and silver complexes $(\eta^5\text{-C}_5\text{H}_4\text{SiMe}_3)_2\text{Ti}(\eta^1\text{-C}\equiv\text{CSiMe}_3)_2\text{MR}$, where M = Cu, Ag and R = 2,4,6-Me₃C₆H₂, have been synthesised.²³¹

Bis(trimethylsilylcyclopentadienyl)bis(ferrocenylethynyl)titanium (**126**) reacts with nickel tetracarbonyl or tetrakis(triphenylphosphine)palladium to give the complexes **127**⁶⁹ and **128**.²³²

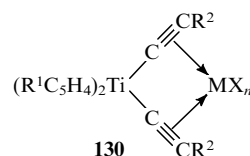


Reaction of the complex **126** with silver hexafluorophosphate yields the complexes **129a–c** in which the silver ion is bound to the four triple bonds of the acetylenic groups.²³³ Compounds **129d,e** were prepared analogously.



R¹ = H, R² = Fc (**a**); R¹ = Me₃Si, R² = Fc (**b**);
R¹ = H, R² = (C≡C)₂Fc (**c**); R¹ = Me₃Si, R² = Ph (**d**);
R¹ = Me₃Si, R² = Rc.

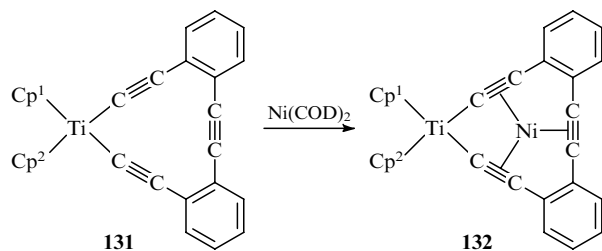
Bis(trimethylsilylcyclopentadienyl)(trimethylsilylethynyl)titanium and bis(trimethylsilylcyclopentadienyl)(hexa-1,3-diynyl)titanium chlorides form the complexes $[(\text{C}_5\text{H}_4\text{SiMe}_3)_2\text{Ti}(\text{R})\text{Cl}]$. CuBr [R = C≡CSiMe₃,²³⁴ C≡C–C≡CEt (see Ref. 61)] with copper(I) bromide. The complexes **130** were synthesised from



R¹ = Me₂NCH₂CH₂, R² = Me₃Si, MX_n = AgCl;
R¹ = Ph₂P, Ph₂P(O), Ph₂P(S); R² = Bu^t, MX_n = CuCl, Mo(CO)₄;
R¹ = Me₃Si, R² = Ph, MX_n = CoCO.

dialkynyltitanocene derivatives containing various substituents in the cyclopentadienyl ligands.^{65, 235}

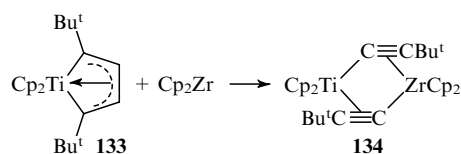
The reaction of the triyne titanacycles **131** with bis(cyclooctadiene)nickel $\text{Ni}(\text{COD})_2$ yields the binuclear complexes **132**.⁶⁰



$\text{Cp}^1 = \text{Cp}^2 = \text{C}_5\text{H}_5, \text{C}_5\text{Me}_5$.

Dicyclopentadienylbis(diphenylphosphinomethyl)titanium and bis(dicyclopentadienyldiphenylphosphinomethyl)titanium oxide form the complexes $[\text{Cp}_2\text{Ti}(\text{CH}_2\text{PPh}_2)_2\text{Rh}(\text{CO})\text{Cl}]_2$ (see Ref. 40) and $\text{O}[\text{Cp}_2\text{TiCH}_2\text{PPh}_2]_2\text{Rh}(\text{CO})\text{Cl}$ ²³⁶ with dicarbonylrhodium chloride. The cationic complex $[\text{Cp}_2\text{Ti}(\text{CH}_2\text{PPh}_2)_2\text{Rh}(\text{COD})]^+[\text{BPh}_4]^-$ was prepared by treatment of dicyclopentadienylbis(diphenylphosphinomethyl)titanium with the rhodium complexes $[\text{L}_2\text{Rh}(\text{COD})]^+[\text{BPh}_4]^-$, where $\text{L} = \text{Ph}_3\text{P}, \text{COD}$.²³⁷

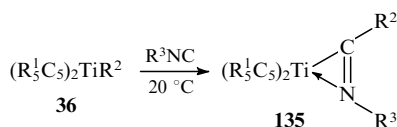
The reaction of titanacumulene (**133**) with dicyclopentadienylzirconium occurs with the cleavage of the central $\text{C}=\text{C}$ bond and results in the formation of the heterodimetallic titanocene–zirconocene complex **134** with a σ, π -alkynyl bridge.¹⁴²



2. Insertion into Ti–C σ -bonds

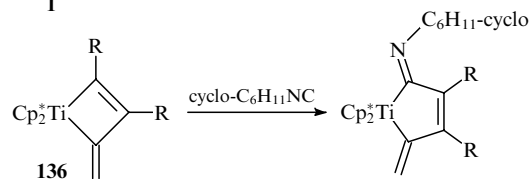
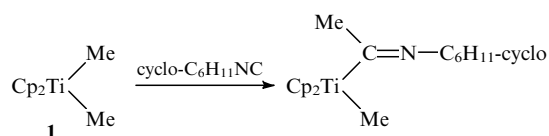
Transformations of titanocene derivatives occurring with insertion of various fragments into Ti–C σ -bonds have been described.

Thus isocyanides are inserted into the Ti–C σ -bonds of alkyl- or aryltitanocenes **36** to give the titanacycles **135** at 20 °C. At the same time, at -78 °C the reaction of the complexes **36** with isocyanides yields exclusively the adducts $\text{Cp}_2\text{TiR}^1\text{-R}^2\text{NC}$.

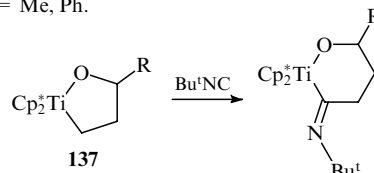


R^1	R^2	R^3	Ref.
H	Et	2,6-Me ₂ C ₆ H ₃	102
H	Bu	2,6-Me ₂ C ₆ H ₃	102
H	Me	2,6-Me ₂ C ₆ H ₃	102, 103
Me	Me	2,6-Me ₂ C ₆ H ₃	109
H	Ph	2-MeC ₆ H ₄	220
H	Ph	2,6-Me ₂ C ₆ H ₃	220
H	2-MeC ₆ H ₄	2-MeC ₆ H ₄	220
H	2-MeC ₆ H ₄	2,6-Me ₂ C ₆ H ₃	220

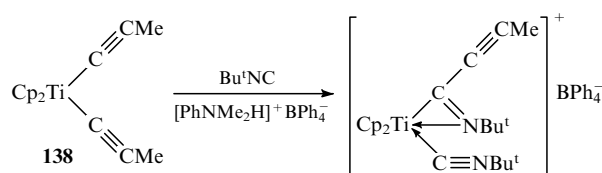
Insertion into the Ti–C σ -bond takes place in the reaction of cyclohexyl isocyanide with dimethyltitanocene (**1**)²³⁸ or the methylidenetitanacyclobutene complexes **136**¹⁶⁹ as well as in reactions of *tert*-butyl isocyanide with 1-oxa-5-titanacyclopentanes **137**²³⁹ or bis(methylethynyl)titanocene **138** in the presence of dimethylanilinium tetraphenylborate.²⁴⁰



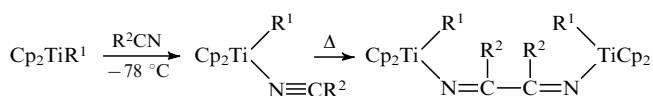
$\text{R} = \text{Me}, \text{Ph}$.



$\text{R} = \text{Me}, \text{Et}, \text{Pr}^i$.

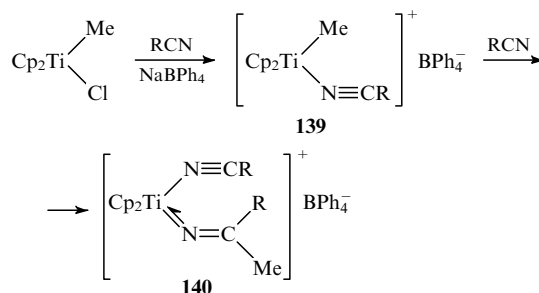


As in the case of isocyanides, reactions of alkyltitanocenes with nitriles at low temperatures give the adducts $\text{Cp}_2\text{TiR}^1\text{-R}^2\text{CN}$ ($\text{R}^1 = \text{Ph}, 2\text{-MeC}_6\text{H}_4, \text{Bn}, \text{C}_6\text{F}_5$; $\text{R}^2 = \text{Me}, \text{Bu}^t, \text{Ph}, 2\text{-MeC}_6\text{H}_4, 2,6\text{-Me}_2\text{C}_6\text{H}_3$).²⁴¹ An increase in the temperature leads to dimerisation of the nitrile ligand.²⁴²



$\text{R}^1 = \text{Ph}, 2\text{-MeC}_6\text{H}_4, \text{Bn}, \text{C}_6\text{F}_5$; $\text{R}^2 = \text{Ph}, \text{Me}, 2\text{-MeC}_6\text{H}_4$.

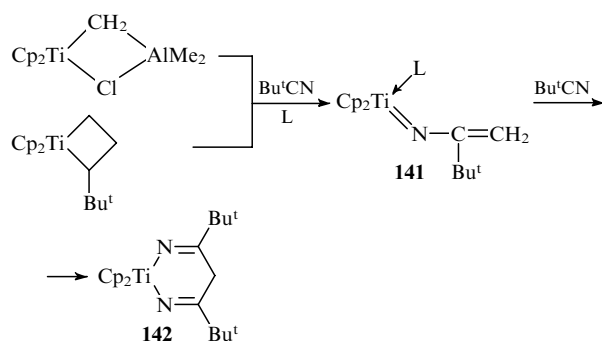
Treatment of methyltitanocene chloride with equimolar amounts of nitriles in the presence of sodium tetraphenylborate gives the complexes **139** which further yield the azaalkylidene derivatives **140** due to the insertion of the nitrile molecule into the Ti–C bond.^{243, 244}



$\text{R} = \text{Me}, \text{Pr}, \text{Ph}, \text{Bu}^t$.

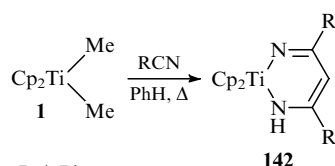
In this reaction, trimethylsilyl cyanide is isomerised into the corresponding isocyanide, which forms an η^2 -iminoacyl complex $[\text{Cp}_2\text{Ti}(\text{CMe} = \text{NSiMe}_3)(\text{C} \equiv \text{NSiMe}_3)]^+ \text{BPh}_4^-$ with methyltitanocene chloride (see Ref. 244).

Reactions of the titanaluminium complex $\text{Cp}_2\text{Ti}(\mu\text{-Cl})_2(\mu\text{-CH}_2)\text{AlMe}_2$ or 2-*tert*-butyl-1,1-bis(cyclopentadienyl)-1-titanacyclobutane with *tert*-butyl cyanide in the presence of trimethylphosphine or 4-(*N,N*-dimethylamino)pyridine gives first the vinylimide complexes **141**, which react with an excess of nitrile to yield the 2,6-diaza-1-titanacyclohexa-2,5-diene derivative **142**.^{245, 246}



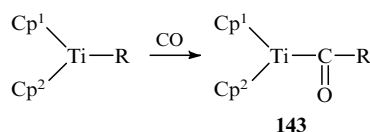
L = PMe₃, 4-Me₂NC₅H₄N.

2,6-Diazatitanacyclohexa-2,4-dienes **142** (R = Bu^t, Ph) are formed upon refluxing of *tert*-butyl or phenyl cyanide with dimethyltitanocene (**1**) in benzene.¹⁵¹



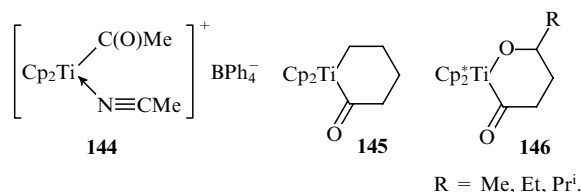
R = Bu^t, Ph.

The direction of reactions of titanocene σ -derivatives with carbon monoxide depends on the reaction conditions and the structure of the organometallic compound. Thus treatment of alkyl-, aryl- and vinylcyclopentadienyltitanium(III) derivatives as well as ethyl- or methyltitanocene chlorides with carbon monoxide leads to the insertion into the Ti–C σ -bond eventually resulting in the acyltitanocene complexes **143**.^{109, 204, 247, 248}



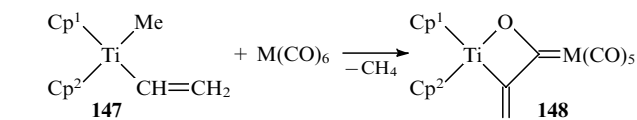
Cp ¹	Cp ²	R	T / °C	Ref.
C ₅ H ₅	C ₅ Me ₅	Me	–70	106
C ₅ H ₅	C ₅ Me ₅	Et	–70	106
C ₅ H ₅	C ₅ Me ₅	Me	0	247
C ₅ H ₅	C ₅ Me ₅	n-C ₅ H ₁₁	0	247
C ₅ H ₅	C ₅ H ₅	C(Me)=CHMe	20	106, 248
C ₅ H ₅	C ₅ H ₅	2-MeC ₆ H ₄	20	106, 248

The products of CO insertion into the Ti–C bond (**144–146**) were prepared by treating acetonitrile(methyl)titanocene tetraphenylborate²⁴³ or the corresponding titanacyclopentane and titanaoxacyclopentane derivatives^{77, 239} with carbon monoxide.



R = Me, Et, Prⁱ.

Reactions of chromium and tungsten hexacarbonyls with the methyl(vinyl)titanocene derivative **147** occur as the insertion of CO into the Ti–C σ -bond and the formation of the bimetallic complexes **148**.¹³

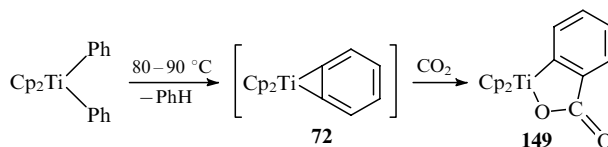


Cp¹ = C₅Me₄(CH₂)₂NMe₂, Cp² = C₅Me₅; M = Cr, W.

In contrast to alkylcyclopentadienyltitanium(III) derivatives, pentafluorophenyltitanocene reacts with carbon monoxide (25 °C, 1 atm) with the formation of the carbonyl complex Cp₂Ti(CO)C₆F₅.²⁴⁷ Photochemical reactions of dimethyl- or diphenyltitanocene with carbon monoxide^{25, 140} or treatment of dibenzyltitanocene^{204, 249} and titanaindan derivatives **18a, b**⁷⁰ in benzene with carbon monoxide gave the titanocenedicarbonyl Cp₂Ti(CO)₂. It was noted that the reaction of carbon monoxide with dibenzyltitanocene in pentane is sometimes associated with the intermediate formation of the benzylacyl complex Cp₂Ti(COBn)Bn.²⁴⁹

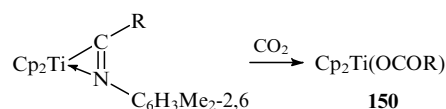
Reactions of some titanocene derivatives with carbon dioxide also occur by insertion into the metal–carbon σ -bond. Thus the photochemical reaction of dimethyltitanocene with carbon dioxide in pentane (16 °C, 20 h) results in methyltitanocene acetate Cp₂Ti(Me)[OC(O)Me].²⁵⁰ Passage of carbon dioxide through a solution of dimethyltitanocene in toluene at 80 °C leads to the insertion of CO₂ simultaneously into two Ti–C σ -bonds resulting in the titanocene diacetate Cp₂Ti(OC(O)Me)₂.²⁵¹

Treatment of diphenyltitanocene with carbon dioxide in xylene at 80–90 °C gives the titanacyclic compound **149**.^{251, 252}



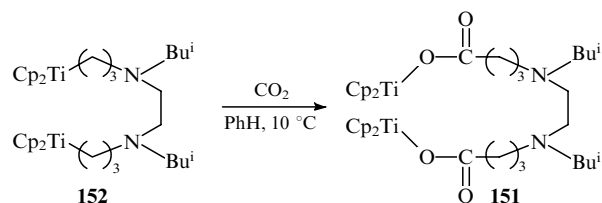
It is believed that compound **149** is formed as a result of insertion of carbon dioxide into the phenylenetitanium complex **72** formed upon splitting of the benzene molecule from diphenyltitanocene.

Reactions of η^2 -iminoacyl complexes with carbon dioxide occur by insertion of CO₂ into the Ti–Alk bond and yield dicyclopentadienyltitanium(III) acylates **150**.¹⁰²

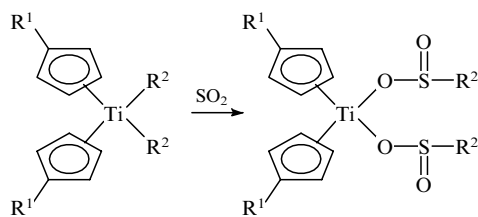


R = Me, Et, Buⁿ.

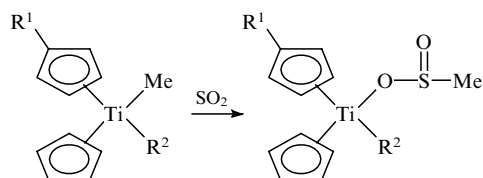
The product of insertion into the Ti–C σ -bond **151** was obtained in the reaction of the binuclear complex **152** with CO₂.²⁵³



The insertion into the Ti–C σ -bond and the formation of *O*-sulfates take place in the treatment of dimethyl-, diphenyl- or bis(2-thienyl)titanocenes^{254–256} and methylchloro- or methyl-(pentafluorophenyl)titanocenes^{254, 257, 258} with sulfur dioxide.



$R^1 = \text{H}, R^2 = \text{Me, Ph, 2-thienyl}; R^1 = R^2 = \text{Me}.$

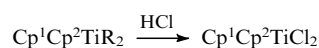


$R^1 = \text{CH(Me)Ph}, R^2 = \text{C}_6\text{F}_5; R^1 = \text{H}, R^2 = \text{Cl, C}_6\text{F}_5.$

The reaction of carbon disulfide with vinylindicyclopentadienyltitanium(III) gives the paramagnetic insertion product $\text{Cp}_2\text{Ti}[\text{SC(S)CMe}=\text{CHMe}]$.¹⁰⁷

3. Cleavage of Ti–C σ -bonds

Whereas the π -bond between the cyclopentadienyl ligand and the titanium atom is stable in acidic media, the Ti–C σ -bonds are easily cleaved by acids. Thus dialkyl- and diaryltitanocene derivatives react with an excess of hydrogen chloride to give the corresponding titanocene dichlorides.



Cp^1	Cp^2	R	Ref.
C_5H_5	C_5H_5	Ph	259
C_5H_5	C_5H_5	Me	260
C_5H_5	C_5H_5	Fc	49
		Me	260
$\text{C}_5\text{H}_4\text{Me}$	$\text{C}_5\text{H}_4\text{Me}$	$\text{C}\equiv\text{CR}^a$	56
$\text{C}_5\text{H}_4\text{SiMe}_3$	$\text{C}_5\text{H}_4\text{SiMe}_3$	$\text{C}\equiv\text{CR}^a$	56

^a R = Et, Prⁿ, Buⁿ, Bu^t, Me₃Si, Ph.

Titanocene dichloride is prepared by treatment of titanacycles, such as 1,1-dicyclopentadienyl-1-titanacyclopentane,⁷⁸ 1,1-dicyclopentadienyl-1-titanafluorene,⁷³ titanacyclopentadienes **54a,b**,¹³⁰ or titanabicyclopentane **84**,¹⁶⁸ with an excess of hydrogen chloride.

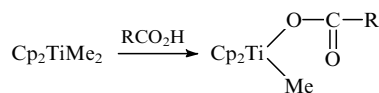
The complexes $\text{Cp}^1\text{Cp}^2\text{TiCl}_2$ containing two different π -bound cyclopentadienyl ligands were prepared by the reaction of hydrogen chloride with the titanocene derivatives $\text{Cp}_2^1\text{Ti}(\text{Cp}^2)\text{Cl}$ in which the two cyclopentadienyl ligands were linked by π -bonds and one cyclopentadienyl ligand, by σ -bonds.^{261, 262}

Reactions of dialkyl- or diaryltitanocenes with equimolar amounts of hydrogen chloride result in the cleavage of only one Ti–C σ -bond and yield alkyl- or aryltitanocene chlorides $\text{Cp}^1\text{Cp}^2\text{Ti}(\text{R})\text{Cl}$ and $\text{Cp}_2^1\text{Ti}(\text{R})\text{Cl}$, where $\text{Cp}^1 = \text{C}_5\text{H}_5$, $\text{Cp}^2 = \text{C}_5\text{Me}_4\text{H}$; R = Me, Ph, 4-MeC₆H₄;⁷ $\text{Cp}^1 = \text{Cp}^2 = \text{C}_5\text{H}_5$, R = 2-thienyl,²¹⁴ 3,4,5-trichloro-2-thienyl.⁴³ The cationic complex $[\text{Cp}_2\text{TiMe}]^+\text{BF}_4^-$ was prepared by the reaction of dimethyltitanocene with an equimolar amount of fluoroboric acid.²⁶³

In contrast to the majority of titanocene σ -derivatives, bis(*o*-carboranylmethyl)- and bis(pentafluorophenyl)titanocenes are relatively stable in acidic media and are converted into titanocene dichloride only after prolonged boiling with hydrochloric acid.^{24, 45} The retention of the σ -bond between the titanium

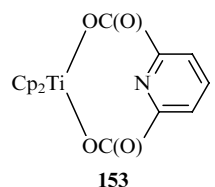
atom and the perfluorophenyl ligand was also observed in the treatment of methylsulfinates and perfluorophenyltitanocene alcohols $\text{Cp}(\text{C}_5\text{H}_4\text{CHMePh})\text{Ti}(\text{C}_6\text{F}_5)(\text{O}_2\text{SMe})$ (see Ref. 257) and $\text{Cp}(\text{C}_5\text{H}_4\text{CHMePh})\text{Ti}(\text{C}_6\text{F}_5)\text{OR}$ (R = Me, 2-MeC₆H₄) with hydrogen chloride.⁹⁶

The cleavage of Ti–C σ -bonds takes place upon treatment of alkyl- or aryltitanocenes with organic acids. Thus dimethyltitanocene reacts with equimolar amounts of acetic,²⁰⁵ benzoic or 2-phenylpropionic acids²⁶⁴ with cleavage of one of methyl groups eventually resulting in the corresponding methyltitanocene acylates.

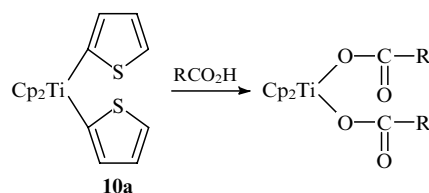


R = Me, Ph, CH(Me)Ph.

Treatment of dimethyltitanocene with an excess of phenylpropionic or trifluoromethanesulfonic acid results in the replacement of two σ -bound methyl groups by acid residues.^{265, 266} The reaction of pyridine-2,6-dicarboxylic acid with dimethyltitanocene yields the complex **153**.²⁶⁰

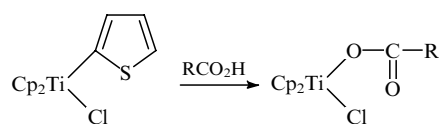


The formation of titanocene diacylates takes place in the reaction of bis(2-thienyl)titanocene **10a** with 3,5-dinitrobenzoic, perfluorobenzoic and trifluoro-, trichloro- and tribromoacetic acids.⁴²



R = 3,5-(NO₂)₂C₆H₃, C₆F₅, CF₃, CCl₃, CBr₃.

The reaction of methyltitanocene chloride with benzoic or phenylacetic acids afforded mixtures of titanocene dichloride with the corresponding titanocene diacylates $\text{Cp}_2\text{Ti}[\text{OC}(\text{O})\text{R}]_2$; their formation is due to symmetrisation of the intermediate chlorotitanocene acylates $\text{Cp}_2\text{TiCl}[\text{OC}(\text{O})\text{R}]$.²⁶⁷ The formation of a Cp_2TiMe_2 , $\text{Cp}_2\text{TiMe}[\text{OC}(\text{O})\text{CF}_3]$ and $\text{Cp}_2\text{Ti}[\text{OC}(\text{O})\text{CF}_3]_2$ mixture is also observed upon treatment of 1,1,3,3-tetracyclopentadienyl-1,3-dititanacyclobutane with trifluoroacetic acid.¹⁶⁷ Reactions of (2-thienyl)titanocene chloride with trichloro- and tribromoacetic, perfluorobenzoic or 2-nitrobenzoic acids gave the corresponding chlorotitanocene acylates.²¹⁶



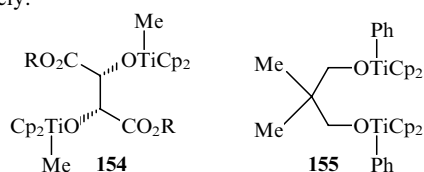
R = CCl₃, CBr₃, C₆F₅, 2-NO₂C₆H₄.

It is of note that treatment of some methyltitanocene alcohols $\text{Cp}_2\text{TiMe}(\text{OR}^1)$ (R¹ is benzyl, menthyl, bornyl) with benzoic or diphenylacetic acids results in the cleavage of the alkoxide ligand (rather than the methyl ligand) and affords the methyltitanocene acylates $\text{Cp}_2\text{Ti}(\text{Me})\text{OC}(\text{O})\text{R}^2$, where R² = Ph, CHPh₂.²⁶⁷

Ti–C σ -bonds are cleaved upon the action of hydrogen chloride on alkyl- or aryl[dicyclopentadienyltitanium(III)] and their complexes with molecular nitrogen or

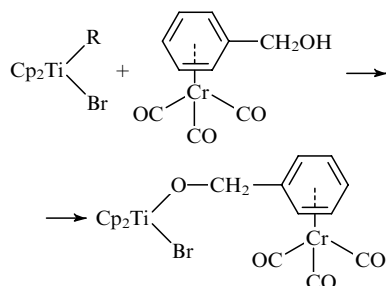
nitriles.^{103, 105, 112, 241, 268} The titanocene monochloride formed at low temperatures (-78°C) is oxidised to titanocene dichloride at 20°C .

The Ti–C bond is also cleaved under the action of some alcohols and phenols on titanocene derivatives. Thus reactions of dimethyltitanocene with an equimolar amount of alcohols bearing bulky radicals gave the methyltitanocene alcoholates $\text{Cp}_2\text{Ti}(\text{Me})\text{OR}$ [R is benzyl, menthyl, bornyl,²⁶⁷ $\text{CHMeC}_8\text{H}_{17}$, CMePh_2 , CHPr^nPh , CHPhBn , $\text{CH}_2\text{CH}=\text{CHPr}^n$ (see Ref. 264)]. Titanocene trifluoromethanesulfonate alcoholates $\text{Cp}_2\text{Ti}(\text{O}_3\text{SCF}_3)(\text{OR})$, where R = Me, Me_3Si , $\text{Me}_2\text{Bu}^t\text{Si}$, are formed upon treatment of methyltitanocene trifluoromethanesulfonate with the corresponding alcohols.²⁶⁵ Reactions of dimethyltitanocene with (+)-(2*R*,3*R*)-dimethyl and (+)-(2*R*,3*R*)-dibutyl tartrates²⁶⁹ and reactions of diphenyltitanocene with 2,2-dimethylpropane-1,3-diol²⁷⁰ yielded the binuclear complexes **154** and **155**, respectively.

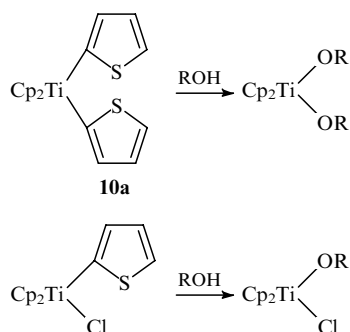


R = Me, Bu^n .

A bimetallic complex was also formed when chromotricarbonyl(hydroxymethyl)benzene was used.²⁷¹

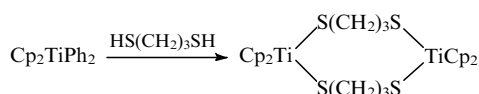


The reaction of bis(2-thienyl)titanocene (**10a**) or (2-thienyl)titanocene chloride with picric acid, 4-hydroxybiphenyl or 3,4-dimethylphenol afforded the corresponding titanocene diphenolates and chlorotitanocene phenolates.²¹³



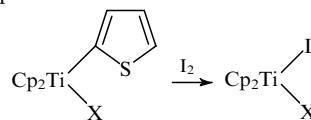
R = 2,4,6-(NO_2) $_3\text{C}_6\text{H}_2$, 4- PhC_6H_4 , 3,4- $\text{Me}_2\text{C}_6\text{H}_3$.

The cleavage of the Ti–C σ -bond by propane-1,3-dithiol has been described.²⁷²



Treatment of dialkyl- or diaryltitanocene derivatives with halogens results in the cleavage of the metal–carbon σ -bonds to give the corresponding titanocene dihalides Cp_2TiX_2 (X = Cl, Br, I).^{31, 42, 56, 73, 78, 79, 273, 274} It was shown that the reaction of

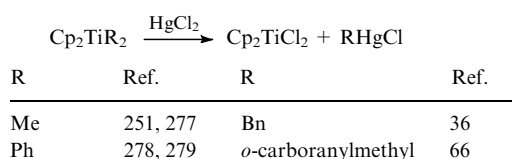
(2-thienyl)titanocene derivatives with iodine proceeds in a step-wise manner; the σ -bound thienyl group is split off in the first step.^{275, 276}



X = 3,4- $\text{Me}_2\text{C}_6\text{H}_3\text{O}$, PhS, Ph_2N , Cl, 2-thienyl.

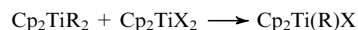
Treatment of alkyl- or aryldicyclopentadienyltitanium(III) derivatives with an excess of halogens occurs as the cleavage of the Ti–C σ -bond and the oxidation of the titanium atom leading to the formation of titanocene dihalides.^{105, 112, 268}

Substitution of chlorine atoms for σ -bound alkyl or aryl ligands takes place in the reaction of dialkyl- or diaryltitanocenes with mercury dichloride.



The cleavage of σ -bound pentafluorophenyl ligands in bis-(pentafluorophenyl)titanocene under the action of TiCl_4 (see Ref. 255) or BCl_3 was observed.³⁵ The cleavage of Ti–C σ -bonds and the formation of titanocene dichloride takes place upon treatment of dicyclopentadienyl-2,4-bis(trimethylsilyl-ethynyl)-3,5-bis(trimethylsilyl)titanacyclopenta-2,4-diene with S_2Cl_2 ,²⁸⁰ as well as upon treatment of $\text{Cp}_2\text{Ti}[\text{C}\equiv\text{CFc}]_2$ with nickel chloride.⁶²

Exchange reactions of methyl and phenyl groups for halogen atoms upon treatment of dimethyl- or diphenyltitanocene with titanocene dihalides have been studied.²⁵¹



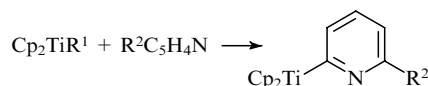
R = Me, Ph; X = F, Cl, Br, I.

It was found that reaction rates decrease in the following order: $\text{I} > \text{Br} > \text{F} > \text{Cl}$ for dimethyltitanocene and $\text{I} > \text{Cl} > \text{Br} > \text{F}$ for diphenyltitanocene.

Heating of dimethyl- or diphenyltitanocene with chloroform or carbon tetrachloride is also accompanied by the cleavage of Ti–C σ -bonds resulting in titanocene dichloride.^{277, 279} Heating of diphenyltitanocene with benzyl chloride yields a titanocene dichloride–(cyclopentadienyl)titanium trichloride mixture.²⁸¹ 1,1-Dicyclopentadienyl-1-titanacyclobutane reacts with benzyl or allyl chloride to give alkyltitanocene chlorides $\text{Cp}_2\text{Ti}(\text{CH}_2\text{R})\text{Cl}$ (R = Bn, All).²⁸²

Cleavage of Ti–C σ -bonds takes place upon treatment of diphenyltitanocene with benzoyl peroxide.^{283–285} When this reaction is carried out in isopropyl alcohol, titanocene dibenzoate $\text{Cp}_2\text{Ti}(\text{O}_2\text{CPh})_2$ is formed as the major product. The dicyclopentadienyltitanium fragment is destroyed in ether or benzene to give the cyclopentadienyltitanium dibenzoate $\text{CpTi}(\text{O}_2\text{CPh})_2$. In contrast to reactions of diphenyltitanocene with benzoyl peroxide, treatment with 3- or 4-nitrobenzoyl peroxides is not accompanied by the cleavage of the titanocene fragment and the corresponding titanocene bis(nitrobenzoates) are formed.²⁸⁶

The Ti–C σ -bonds of methyl- or butyltitanocenes are split off under the action of pyridine derivatives.²⁸⁷



$\text{R}^1 = \text{Me, Bu}$; $\text{R}^2 = 2\text{-Me, 2-Ph, 2-CH}=\text{CH}_2$.

Reactions of thienyltitanocene chloride with acetylacetone, benzoylacetone or dibenzoylmethane gave the corresponding chlorotitanocene β -diketonates.²⁸⁸



$R^1 = R^2 = \text{Me}$, Ph; $R^1 = \text{Ph}$, $R^2 = \text{Me}$.

* * *

The data presented demonstrate high reactivities of titanocene derivatives containing Ti–C σ -bonds. The ease and selectivity of reactions involving these bonds, the possibility of titanium to exist in different oxidation states and the formation of complex bimetallic compounds suggest that titanocene σ -derivatives are promising reagents for fine organic and organometallic syntheses.

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Chemical aspects of implantation of high-energy ions into polymeric materials

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Abstract. Data on the study of the influence of accelerated ion beams on polymeric materials are generalised. The mechanisms of chemical processes occurring in a polymer matrix upon ion implantation and resulting in crucial changes in the electrical conductivity, microhardness, hydrophilicity and other characteristics of the irradiated polymer surface are discussed. Main fields of applications of ion-implanted polymeric materials are considered. The bibliography includes 188 references.

I. Introduction

Long-term ion bombardment of a polymer causes important transformations of the material, accompanied by the formation of specific modifications of amorphous hydrogenated carbon which exhibits conducting properties. Ion irradiation is also responsible for an increase in the conductivity of initially dielectric polymers (*e.g.*, polyimide and polyethylene) by 10 to 15 and even 18 orders of magnitude. Studies carried out in the last decade allowed one to gain a deeper insight into the mechanisms of ion bombardment induced processes in polymeric materials and showed that varying the main parameters of ion irradiation (energy and mass of implanted ions, implantation dose, ionic current) has a significant effect on the formation of a carbonaceous phase in the implanted layer. These studies also revealed the possibility of effective control of not only conducting and optical, but also tribological, hydrophilic and hydrophobic properties of the irradiated polymer surface.

Salient features of ion implantation into polymeric targets have been reviewed.^{1–6} However, the emphasis was placed on systematisation of the data on the nature of the conducting properties of ion-implanted polymers. This review (i) concerns the character and mechanisms of chemical reactions occurring in the polymer matrix during ion irradiation to high fluences and (ii) analyses the role of these processes in the formation of the properties of ion-implanted layers formed at the surface of polymeric materials.

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II. Peculiarities of the interaction of high-energy ions with polymeric target

Specific effects of ion irradiation on polymeric samples are first of all due to very high density of energy transferred to the irradiated target. Energy loss of incident ions in polymer matrices can be as high as tens and even hundreds of electron-volts per 1 Å of track length. Energy deposition occurs within a very small volume along the ion track and takes a very short time ($\sim 10^{-13}$ s).⁷ Taking into account the fact that the bond dissociation energies in polymers do not exceed 10 eV (*e.g.*, 4.3 eV for the C–H and 9.3 eV for the C=N bond), the energy deposited by the stopping projectile is high enough to break a large number of chemical bonds within the track volume even in the case of implantation of ions with medium energies (from tens to hundreds of kiloelectron-volts). This, in turn, creates prerequisites for essential transformations in the irradiated polymer during ion bombardment.

The character of chemical processes induced in the polymer matrix by ion implantation is strongly affected by two fundamentally different mechanisms of energy transfer from the incident ions to the polymer, namely, by inelastic (electronic excitations) and elastic (nuclear) collisions.⁷ The former mechanism leads to excitation and ionisation of polymer molecules and (also as a result of fast subsequent neutralisation) to the formation of a large number of mobile radical species (first of all, H[•] radicals) and macroradicals. Nuclear collisions are accompanied by massive rupture of chemical bonds due to displacement of atomic nuclei and by transfer of rather high energy to the polymer matrix in the form of phonons.⁷ Once the deposited energy is sufficiently high, the displaced atoms can, in turn, create their own track cascades.^{1,7} The contribution of each mechanism to the overall energy loss of an incident ion is characterised by its stopping power, S_n (for 'nuclear') and S_e (for 'electronic' energy loss), which represents the change in the ion energy caused by its interaction with the polymer matrix per unit path length. The S_n and S_e values depend on the energy and mass of incident ions. High-energy light ions deposit their energy mostly by electronic excitations, while heavy ions lose their energy nearly completely by nuclear collisions.^{7,8} As the ion slows down, the contribution of each mechanism to the overall energy loss substantially changes (*e.g.*, a feature of the implantation of light-element ions is an increase in the relative weight of 'nuclear' energy loss at the end of the ion track^{7,8}).

Thus, stopping of ions is accompanied by deposition of rather high energy within the ion tracks and is followed by the formation of radicals, secondary ions and electrons. A certain fraction of

electrons (the so-called δ -electrons) have energies high enough to escape the primary ion track.^{7,9} The tracks of δ -electrons (secondary tracks) form a region called 'penumbra'¹⁰ in which the excitation and ionisation of the polymeric material also occurs. For ions with energies of the order of 100 keV to 1 MeV per nucleon, the radius of the primary track lies between 5 and 10 Å¹¹ while the penumbra radius can reach 50 to 100 Å (this estimate was obtained for water which differs only slightly in stopping power from most polymers).^{10,11} Compared to the ion track, the density of energy deposited in the penumbra is an order of magnitude lower^{1,9-11} and the processes occurring in this region can be considered as pure radiation processes. Energy deposition occurs mainly within the track core which is thus heated to very high temperatures. Heating is due to electrons confined within the track by a strong electric field¹² perpendicular to the track axis and to direct transfer of vibrational energy to polymer by nuclear collisions.⁷ The 'thermal spike' model allows estimation of temperature within a cylindrical track as a function of the radial distance (r) and time (t) elapsed after passage of an ion as follows:¹³⁻¹⁶

$$T(r, t) = \frac{T_0}{1 + 4\delta t/r_0^2} \exp \left[-\frac{(r/r_0)^2}{1 + 4\delta t/r_0^2} \right],$$

$$T_0 = \frac{S}{\pi \rho C_V r_0^2},$$

where T_0 is the initial temperature (at the instant the thermal spike is created), δ is the thermal diffusivity of the condensed medium in which the ion slows down, r_0 is the radius of the ion track, S is the overall stopping power for the incident ion, ρ is the density of the polymer and C_V is the heat capacity of the polymer. The T_0 values corresponding to the implantation of ions with energies ranging from 0.1 to 1 MeV into various polymers can be as high as $\sim 10^4$ K, while quenching of the track down to the temperature of a polymeric target under ion irradiation [$\sim 100-150$ °C (see Refs 17 and 18)] takes $10^{-9}-10^{-10}$ s. This formula provides only a rough estimate of the parameters of the thermal pulse produced upon passage of a high-energy ion; nevertheless, it allows one to estimate the main parameters (including the time parameters) of the thermal effects accompanying ion implantation. It should be noted that the experimental estimate of the temperature of the electron cloud created during ionisation of the atoms within the ion track can be obtained from analysis of the C (KVV) spectrum of the Auger electrons generated in the ion bombarded amorphous carbon (this is closely related to the conditions in heavily implanted polymeric materials); the theoretical estimate of the T_0 value is in reasonable agreement with the experimental results of these experiments.¹⁹

Build up of the dose of implanted ions leads to basic changes in the character of ion-induced processes. Initially, a pristine polymer is ion bombarded until accumulation of a certain dose D_f corresponding to complete coverage of the surface of the polymer sample with ion tracks. Further implantation occurs into the polymer exposed to ion irradiation. In this case, the processes in the polymeric target represent a specific kind of pulse thermoradiolysis since the products of radiochemical reactions formed within and in the vicinity of the track region and those accumulated in the polymer matrix during previous irradiation are involved in the thermally induced reactions occurring in the thermal spike.

III. Chemical processes occurring during ion bombardment of polymers

Studies of the effect of ion irradiation on various polymeric materials showed that implantation to high doses leads to carbonisation of the surface of the polymer sample and to the formation of specific surface forms of amorphous hydrogenated carbon.²⁰⁻²⁴ Carbonisation occurs efficiently if the energy loss per

unit track length (or the linear energy transfer, LET) of incident ions exceeds a particular threshold value (15 to 20 eV Å⁻¹ for aliphatic polymers¹). Accumulation of carbon in the implanted layer is accompanied by evolution of a large amount of dihydrogen (usually, the major gaseous product of ion implantation), low-molecular-mass hydrocarbons (first of all, acetylene) and CO and CO₂ in the case of oxygen-containing polymers (Table 1).^{1,24-28}

Table 1. Relative yields of molecular products formed during irradiation of polymer surface with 200 keV He⁺ ions.^{1,24}

Molecular species (fragment)	Polyethylene	Polystyrene	Polyimide
H ₂	1 ^a	1 ^b	1
CH ₄	0.02	0.01	—
C ₂ H ₂	0.11	0.53	0.05
C ₃ H ₅	0.01	0.004	—
C ₆ H ₆	—	0.013	—
CO			2
CO ₂			1

Note. All values were normalised to the yield of dihydrogen.

^a The absolute yield is 4.8 hydrogen molecules per 100 eV adsorbed by the polymeric target.¹

^b The absolute yield is 1.15 hydrogen molecules per 100 eV adsorbed by the polymeric target.¹

The amount of gaseous products formed in ion-induced, radiochemical pyrolytic processes exponentially decreases as the surface of a polymeric target is covered by ion tracks:^{1,5}

$$Q = Q_0 \exp(-\varepsilon D),$$

where Q_0 and Q are the initial and current yields of the detected gaseous product, respectively; ε is the cross-section of the reaction accompanied by gas evolution (based on the ε value, one can estimate the reaction volume in which ion-induced thermoradiolysis occurs); and D is the implantation dose. Clearly, the ε^{-1} value allows estimation of D_f for a polymer irradiated under particular implantation regime.^{1,5} For ions with energies of the order of hundreds of kiloelectron-volts, the cross-sections of ion-induced reactions accompanied by gas evolution are $\sim 10^{-14}-10^{-15}$ cm² (see Refs 1, 5, 29). Since the radiation processes accompanied by evolution of dihydrogen also occur within the penumbra, the cross-section of the reaction of H₂ liberation is somewhat larger than those of the reactions of formation of hydrocarbons (CO and CO₂) released immediately in the intra-track region.³⁰

The fact that radiochemical processes in the penumbra allow cross-linking of polymer chains is of great importance. For instance, the yield of cross-linking for electron beam irradiated polyethylene (this regime is analogous to the action of δ -electrons) is 3 to 5 times higher than the chain scission yield.³¹ In this case, radiation-induced cross-linking of the polymer occurs even at low fluences, which are two orders of magnitude lower than D_f for medium-range energy ions.^{5,32} This must strongly affect the course of ion-induced pyrolytic processes. This conclusion is, in particular, supported by the fact that, in contrast to pristine polyethylene, thermal degradation of radiochemically cross-linked polyethylene leads to the formation of a solid carbonaceous phase with pronounced semiconductor properties rather than a mixture of liquid hydrocarbons.³³

Radiolysis products are involved in the intra-track pyrolytic processes or are accumulated within the implanted layer to be consumed at later stages of ion irradiation. High-temperature pyrolysis in the track and its immediate vicinity is accompanied by scission of polymer chains. This provides the possibility of cyclisation of radiochemically generated unsaturated linear chain fragments by the intramolecular Diels–Alder mechanism (aromatic hydrocarbons are much more stable than linear unsaturated hydrocarbons).

turated hydrocarbons at temperatures above 800 °C). As the track is cooled down, the newly formed aromatic fragments and analogous fragments present in the pristine polymer and released upon thermoradiolysis are linked together, thus being stabilised due to extension of the conjugation system.³

According to data from mass-spectrometric analysis, the exhaust gases evolved during ion implantation include hydrogen and hydrocarbons with different molecular masses.^{1,24,34} Usually, the most abundant product is acetylene which is the most stable acyclic unsaturated hydrocarbon at high temperatures. Large amounts of saturated hydrocarbons (methane, ethane) are produced by ion irradiation of polypropylene and polybutylene.³⁴ Despite the fact that the exhaust rate of the gases evolved can be as high as hundreds of metres per second,¹⁶ most of them have no time to leave the heating zone during the dispersal time of the thermal spike. Evidently, a fraction of these hydrocarbons can react before escaping the track region; however, the contribution of such processes to the formation of the end products of thermoradiolysis is still to be clarified.

In deeper stages of ion implantation, polynuclear compounds (in essence, they represent primary carbon-containing cluster structures) and other thermoradiolysis products (unsaturated compounds, stable macroradicals) formed in the track region are involved in the growth of carbon clusters. For both aliphatic and aromatic polymers irradiated by ions with medium energies (hundreds of kiloelectron-volts) carbonisation of their surfaces nearly goes to completion at implantation doses of 5×10^{15} to 10^{16} cm^{-2} and subsequent ion bombardment causes only slight changes in the composition of the implanted layer.^{35,36} Noteworthy is that no full carbonisation of the polymer surface occurs. For instance, implantation of polyethylene with 150 keV F^+ ions ($S_e/S_n \approx 5$) leads to an increase in the concentration of carbon in the implanted layer from 33% (in the pristine polymer) to 40%.³⁵

The extent of dehydrogenation of ion irradiated polymers rapidly increases with increasing energy transferred from the incident ions by nuclear collisions. In particular, saturation of carbon concentration in the implanted layer is reached at 65% for implantation of polyethylene with 150 keV As^+ ions ($S_e/S_n \approx 0.3$).³⁵ If the electronic stopping mechanism dominates, dehydrogenation is of low efficiency. This can be rationalised by delocalisation of excitations over sufficiently large carbon clusters. Direct cleavage of chemical bonds upon nuclear collisions is more efficient to provide deep dehydrogenation of the polymer matrix. The extent of carbonisation that can be reached in this case is first of all controlled by the trapping of hydrogen radicals by broken carbon bonds. A profound dehydrogenation (concentration of bound hydrogen less than 10%) can be achieved with electronic deposition mechanism when ions with energies of several tens of MeV are implanted in a polymer target.²¹ In this case, the formation of broken bonds, due to migration of excitations, is concentrated at the edges of growing carbon clusters and carbonaceous phase produced by high-fluence implantation exhibits the Raman spectrum similar to that of ion-implanted graphite.²¹

Implantation of high-energy ions can provide prerequisites for intra-track formation of fullerenes C_{60} and C_{70} . This is supported by the results of mass-spectrometric analysis of gaseous products evolved during implantation of poly(vinylidene chloride) with ions with energies of the order of several tens of megaelectron-volts³⁷ and by the data of chromatographic analysis of the products extracted from the ion-implanted layer on the surface of polyimide irradiated with 5 MeV Li^+ ions.^{38,39} Taking into account modern concepts of the mechanism of fullerene formation in plasma (vapour phase),^{40–45} one can assume that the synthesis of bulky carbon structures involves coalescence of polycyclic radicals (e.g., combining of six perdehydronaphthalene radicals to yield the C_{60} molecule⁴⁵). This must be favoured by shrinking of the reaction volume upon track 'collapse'.⁴⁴ Fullerene formation can also occur *via* polyynes⁴³ (products of deep dehydrogenation of polymers or intra-track conversion of

acetylene) which lose their stability as the molecular chain is lengthened. This reaction is to be exothermic, since the enthalpy of formation of polyynes (27 kcal mol^{-1} per carbon atom⁴⁶) is much larger than that of fullerene ($9.08 \text{ kcal mol}^{-1}$, see Ref. 47). Accumulation of alkynyl groups in the polymer matrices irradiated with high-energy ions⁴⁸ suggests the possibility of polyyne formation during ion implantation.

The composition of the polymer matrix can strongly affect the composition of the products of ion-induced thermoradiolysis. This can be best exemplified by halogenated polyolefins. Ion irradiation of perfluorinated polyolefins results in lower unsaturated perfluorocarbons (C_2F_4 , C_2F_6) as major gaseous products since the energy of the C–F bond is higher than those of the C–H and C–C bonds.²⁴ Because of this, detectable carbonisation of ion irradiated polytetrafluoroethylene (PTFE) can be reached only at very high doses⁴⁹ while the implantation is accompanied by erosion of the polymer sample⁵⁰ (up to perforation²⁴). Ion bombardment of partially halogenated aliphatic polymers causes radical-induced dehydrohalogenation^{1,18,23,27} accompanied by dehydrogenation and evolution of acetylene (Table 2). Accumulation of double bonds in the polymer matrix accelerates dehydrohalogenation and the newly formed polyenes are involved in the formation of the carbonaceous phase. It is believed that efficient ion-induced carbonisation of poly(vinyl chloride)^{1,18} is favoured by the fact that thermolysis of this polymer can occur at low temperatures ($\sim 200^\circ\text{C}$, see Ref. 51).

Table 2. Relative yields of molecular products formed during irradiation of polytetrafluoroethylene²⁴ and Tefzel (copolymer of ethylene and tetrafluoroethylene)²³ with 200 keV Si^+ ions.

Product	PTFE	Tefzel
H_2	—	4.34
C_2H_2	—	0.87
HF	—	3.91
C_2F_4	1	1
C_2F_6	2.05 ^a	0.35 ^a

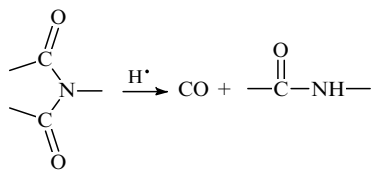
Note. All values were normalised to the yield of C_2F_4 .

^a Determined from the yield of the CF_3^+ fragment detected in the mass spectrum.

Ion-induced thermoradiolysis of organosilicon polymers leads to gradual accumulation of $\{\text{SiO}_4\}$ clusters at the irradiated surface due to the lack of efficient mechanisms of silicon sublimation. The loss of most of methyl groups in polymethylsiloxane as the result of bombardment with 5 keV Ar^+ leads to the formation of carbon–silicate composite, the composition of which varies from $\text{Si}_{1.3}\text{CO}_{2.0}$ at the surface to $\text{Si}_{1.5}\text{CO}_{2.5}$ in the depth, with silicon atoms in this composite being directly bound to oxygen ones.⁵² Noteworthy is that implantation of a copolymer of polydimethylsilane and methylphenylsilane, $[\sim \text{Si}(\text{CH}_3)_2 - \text{SiPhCH}_3]_n$, with 2 MeV Ar^+ ions leads to the formation of silicon carbide as a result of cleavage of the Si–Si and C–H bonds and by elimination of methyl side groups.⁵³

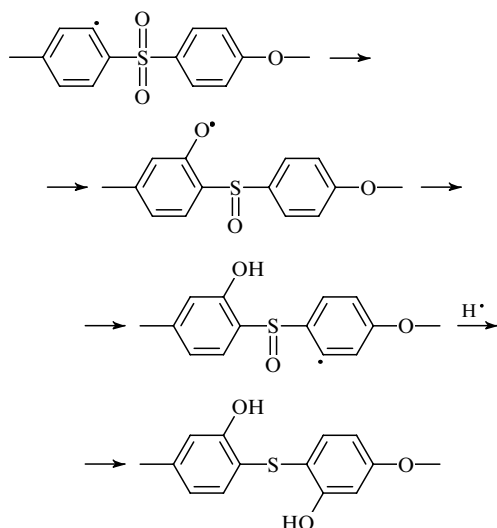
Depending on the mechanism of energy deposition by incident ions to the polymer matrix, strongly different thermoradiolysis can be induced. The distinctions are due to the fact that nuclear collisions involve direct nonselective (in essence, random) breakage of chemical bonds, whereas an electronic excitation can migrate over a rather long distance during the lifetime of the excited state ($\sim 10^{-12} \text{ s}$) (according to calculations for an aliphatic chain,⁵⁴ the mean path length of electronic excitation can amount to 100 monomer units) and therefore energy deposition by 'electronic' stopping implies scission of the weakest bonds. This makes possible selective initiation of chemical reactions in the polymer matrix, especially in the case of ion irradiation of heterochain polymers.

Implantation of polyimide with 90 keV N^+ ions or 150 keV Ne^+ ions ($S_e/S_n > 6.5$) leads to cleavage of bonds between aromatic rings⁵⁵ and to transformation of imido groups into amido groups without fragmentation.^{56, 57}



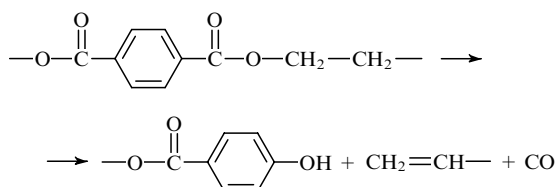
This process occurs simultaneously with dehydrogenation of polyimide and causes the loss of some carbonyl groups⁵⁸ accompanied by the evolution of CO (major gaseous product formed during ion irradiation of polyimide).²⁴

A feature of the irradiation of aromatic poly(ether sulfone) under analogous conditions ($S_e \gg S_n$) is the fast transformation of sulfone groups into sulfoxide ones and then, at high fluences, into sulfide groups in the reactions involving mobile radical species $H^\cdot$.^{6, 59}



During ion irradiation of aliphatic polysulfones the reduction of sulfone groups and their elimination in the form of sulfur dioxide occur in comparable yields.⁶⁰

The formation of hydroxy groups in the polymer matrix was revealed in the study of low-dose ion implantation of poly(ethylene terephthalate) (PETP) under conditions where the electronic stopping prevails.⁶¹



This allows rapid accumulation of unsaturated groups in the ion-implanted layer on the PETP surface [these groups are accumulated in PETP faster than in, e.g., poly(butylene terephthalate)⁶²]. Ion-induced processes occurring during bombardment of PETP by high-energy ions (with energies of the order of several tens of megaelectron-volts and, correspondingly, with large S_e values) proceed by the same mechanism.⁶³ Implantation of this material with ions with energies of the order of several hundreds of megaelectron-volts leads to profound dehydrogenation of the irradiated polymer, accompanied by accumulation of alkynyl groups in the ion-implanted layer.⁴⁸ Peculiar to polystyrene and polyimide implanted in this regime is the formation of

groups containing triple bonds [e.g., isocyanate ($-\text{N}=\text{C}=\text{O}$) and cyanate ($-\text{O}-\text{C}\equiv\text{N}$) end groups for polyimide].⁴⁸

Thus, if energy transfer to the polymeric target is mainly by electronic excitations, the bridging bonds are broken and functional groups undergo transformations (as a rule, towards the reduction of heteroatoms), whereas aromatic fragments remain intact and can be involved in the formation of polycyclic fused structures. Heterocycles with asymmetrical delocalised π -electron systems are much less stable. For instance, experiments on electron beam irradiation of poly(2-vinylpyridine) (in this case, energy is deposited in the polymeric target solely by electronic excitations) showed that the pyridine ring rapidly breaks down with the formation of amino groups⁶⁴ in contrast to the aromatic rings in polyimide that are stable under these conditions.^{6, 64}

A consequence of the increased contribution of a collision term to the overall energy loss of the stopping ions is the change in the character of processes occurring in the polymeric target. In particular, destruction of highly stable aromatic rings is made possible. For instance, irradiation of aromatic poly(ether sulfone) with 50 keV As^+ ions ($S_n/S_e = 5.6$) causes not only the transformation of sulfone groups, but also the release of acetylene and the formation of 1,4-substituted butadiene.⁶⁵ Similarly, implantation of polyimide with ions that lose their energy mostly by nuclear collisions is accompanied by breakage of aromatic rings and formation of acetylene²⁴ and by nonselective degradation of imido groups resulting in the formation of various products (Fig. 1).^{6, 66–68} Similar products were also detected during *in vacuo* thermal decomposition of polyimide.⁶⁷ However, their concentrations are substantially different from those in the ion-implanted layer (see Fig. 1) because these products are formed in two different ways, *viz.*, in the course of several concurrent radical processes (ion implantation) and in consecutive chemical transformations of the polymer matrix (thermal decomposition).

The overall picture of the processes occurring during ion-induced thermoradiolysis of heteroatom-containing polymers can be described as follows. Until build up of a certain implantation dose corresponding to D_f (a single track regime) the polymer matrix undergoes dehydrogenation and some other unambiguously identifiable chemical transformations. The pathways of

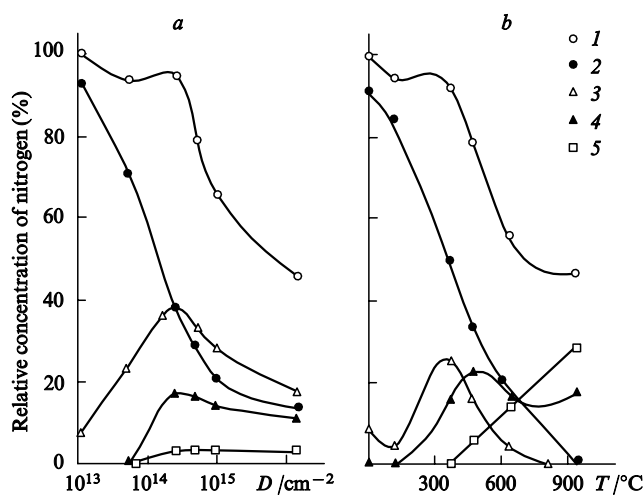
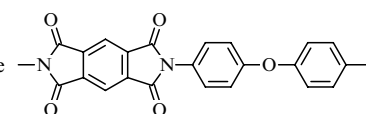


Figure 1. Changes in relative concentration of nitrogen-containing

groups in polyimide  during

implantation with 5 keV Ar^+ ions (a) and thermal decomposition (b) (according to XPS data).^{6, 67}

Total nitrogen content (1), imide groups (2), $-\text{C}=\text{N}-$ groups (3), pyridine groups (4) and tertiary amines (5).

these processes are first of all determined by the ratio of energy transfer from the implanted ions by electronic excitations and by nuclear collisions. Within this implantation dose, the overall concentration of heteroatoms in the ion-implanted layer (nitrogen atoms in irradiated polyimide^{6,67} or sulfur atoms in irradiated polysulfone^{6,59}) can remain virtually constant (Figs. 1 and 2) while the energy of the implanted ions is expended for structural rearrangement of the polymer.⁶ Aromatic fragments released in this stage are fused to form 'pre-carbon' structures. These processes can occur involving the heteroatoms incorporated into the pyridine, pyran and thiopyran rings. Because of this, a large fraction of heteroatoms (first of all, sulfur and nitrogen) is retained in the implanted layer in chemically bound form even at high implantation doses.⁶

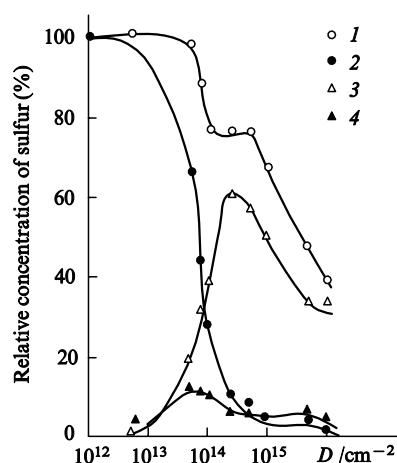


Figure 2. Changes in relative concentration of sulfur-containing groups in poly(ether sulfone) during implantation with 150 keV Ar⁺ ions.⁶ Total sulfur content (1); sulfone (2), sulfide (3) and sulfoxide (4) groups.

IV. Peculiarities of the morphology and properties of ion-implanted layer

Electron microscopy studies of ion-implanted polymers revealed the formation of carbon aggregates of a size up to several tens of nanometres in polymeric targets implanted with high doses.²³ Using the small-angle neutron scattering technique, it was established that these aggregates are comprised of small carbon clusters.⁶⁹ In particular, it was found that high-dose irradiation of PETP films with 50 MeV B⁺ ions leads to the formation of nanoclusters of size 6 to 7 nm separated by ~13 nm and united into spherulites of diameter up to 50 nm in the implanted layer.⁶⁹ This is consistent with the results obtained by optical spectroscopy, according to which the build up of implantation dose is accompanied by a shift in the edge of the optical absorption band of the irradiated polymer towards the long-wavelength region due to extension of the conjugated system in the growing carbon clusters. The magnitude of the shift indicates that the size of the clusters formed during implantation with medium energy ions is at most several nanometres.^{70–72} Using an approach developed for amorphous carbon,⁷³ the mean size of a carbon cluster grown in the implanted layer can be estimated as follows:

$$E_g = 2|\beta|N^{-0.5},$$

where E_g is the optical gap, β is the resonance integral (according to EHT calculations, $\beta = 2.9$ eV) and N is the number of rings in the compact two-dimensional carbon cluster (fragment of graphite sheet). As the implantation dose D increases, the E_g value exponentially decreases^{71,72}

$$E_g = E_{g0} + A \exp(-\eta D),$$

where E_{g0} is the energy gap corresponding to the largest clusters that can grow under the given implantation regime, η is the cross-section of the growth reaction of carbon clusters and A is a constant. The growth rate of the carbon nanophase and the η value depend first of all on the nature of the polymer,⁷¹ while the E_{g0} value is mainly determined by the mass and energy of ions implanted.^{3,72} Implantation of light ions with energies ranging from 100 to 300 keV into polyolefins and polystyrene saturates the E_g values at 0.6 eV,^{70–72} which corresponds to clusters with a mean size of 2.7 nm (~75 rings). Peculiar to the irradiation of polyamide-6 under analogous conditions is the formation of smaller clusters ($N \sim 60$, $E_g = 0.76$ eV, see Ref. 72). The fact that there exists a limiting size of carbon clusters for a given implantation regime can be rationalised^{3,72} by delocalisation of the energy of incident ions over the carbon network and by expenditure of this energy for cleavage and formation of carbon bonds accompanied by trapping of the H[•] radicals. Not counting subtle details, this produces no significant variations in the medium-range order of the implanted layer. In this case, an increase in the implantation dose causes gradual growth of small carbon clusters up to the limiting size.⁷⁰ For polyamide-6, the formation of smaller carbon clusters is a result of the incorporation of a heterocyclic nitrogen atom into the growing cluster (due to, e.g., the formation of pyridine rings).⁷² The outermost heteroatoms cannot play the role of nucleation sites of the carbon clusters and their presence in the clusters reduces the size of extended regions of the π -electron conjugation system and, as a consequence, the effective size of carbon clusters determined from electronic spectra.^{3,72}

An increase in the size and concentration of carbon clusters in the ion-implanted layer with the implantation dose is accompanied by an increase in the concentration of paramagnetic centres (radicals stabilised by delocalisation of their π -electrons over the π -electron system of the carbon nanophase).^{25,65,74,75} There is a correlation between the increase in the ESR signal during implantation and completion of dehydrogenation of the polymer matrix.^{17,29} At high implantation doses where the possibilities of further carbonisation are exhausted the prerequisites are created for compensation of the terminated carbon bonds by their recombination that results in the decrease of spin concentration.^{17,29,65,74,76,77} This effect can be readily traced for polyimide,²⁹ polyacrylonitrile⁷⁴ and other polymers containing a large number of groups that can be efficiently fused during thermoradiolysis. Aliphatic polymers are characterised by a much lower yield of carbon clusters compared to polymers with conjugated bonds. In this case, the spin concentration plotted as a function of implantation dose exhibits no extremum (Fig. 3) even at high fluences (10^{17} cm⁻²).^{75,78} As the dose increases, the ESR line becomes narrower due to extension of the π -electron conjugated system in the ion-implanted layer.^{29,74,78} Studies of temperature dependence of the ESR linewidth and of the effect of oxygen pressure on the ESR spectrum revealed the formation of quasi-two-dimensional degenerate electron gas in the carbonaceous layer on the surface of heavily implanted polymers ($D > 2 \times 10^{16}$ cm⁻² for polyethylene and polyimide irradiated with 100 keV B⁺ ions).^{75,78,79}

A salient feature of the morphology of the ion-implanted layer is the presence of nanopores that are formed along the trajectories of projectiles. Pore mouths can be clearly seen in, e.g., atomic force microscopy images of the PETP surface irradiated with low doses of heavy high-energy ions.⁸⁰ Implantation of low-energy (100–200 keV) ions is also accompanied by the formation of a developed pore system. This is indicated by the possibility of spontaneous incorporation of molecular iodine from the vapour phase^{81,82} and Pb²⁺, Fe³⁺, K⁺ and Cl⁻ ions (see Refs 83–85) and some bulky molecules (a carborane complex of cobalt,⁸⁶ amino acids⁸⁷) from aqueous solutions into the implanted layer and by the possibility of extension of the oxidation of radical

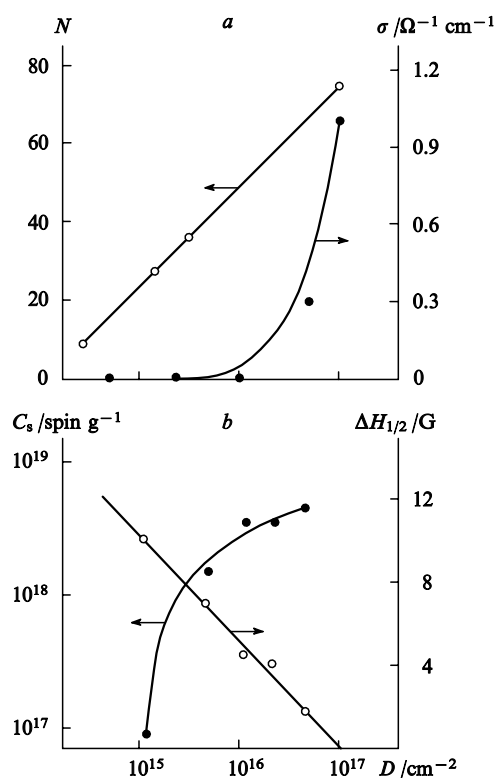


Figure 3. Dependences of the average number of carbon rings (N) in carbon cluster and of the dc conductivity (σ) (a), concentration of unpaired spins (C_s) and ESR linewidth (b) on the implantation dose for polyethylene irradiated with 100 keV B^+ ions.⁷⁵

centres across the whole width of the implanted layer.^{35, 88–90} Sometimes, changes in the polymer density along the track of the implanted ion are insufficient to ensure the pore formation. In this case, slow oxygen diffusion *via* ion-induced defects occurs along the so-called latent tracks (the regions in which locally reduced density appeared in the polymer matrix during passage of an ion). For ion irradiated polypropylene, the oxidation front propagates in the implanted layer with a velocity which does not exceed $4 \times 10^{-5} \text{ nm s}^{-1}$ and complete oxidation takes several weeks,³⁵ whereas the oxidation of polyethylene irradiated under the same regime is completed virtually immediately after the vacuum–open air transition.³⁵ According to IR spectroscopy data, oxygen fixation in the ion-implanted layer is accompanied by the formation of carbonyl^{88, 91} and hydroxy groups.⁹²

Trapped oxygen is accumulated in the domains with high density of the broken carbon bonds formed during implantation; therefore, the character of oxygen distribution in the irradiated polymer contains information on the structure of the implanted layer.^{3, 35, 89, 93} Rutherford backscattering spectroscopy studies showed that the concentration of trapped oxygen in the irradiated polyethylene monotonically increases during ion irradiation⁹⁰ and reaches a maximum value at fluences of $(1–5) \times 10^{14} \text{ cm}^{-2}$ for heavy ions^{35, 93} and at $5 \times 10^{15} \text{ cm}^{-2}$ for light ions.⁸⁸ The total amount of oxygen assimilated within the implanted layer can be rather large (the concentration of oxygen in polyethylene irradiated with 150 keV F^+ ions at a fluence of $5 \times 10^{15} \text{ cm}^{-2}$ is 0.24 per carbon atom⁸⁸). Using the depth profiles of oxygen trapped in the implanted layer, it was found that the role played by the ‘electronic’ and ‘nuclear’ stopping mechanisms in the generation of dangling carbon bonds is dependent on the implantation dose.^{88, 93} If a pristine or slightly dehydrogenated polymer is ion irradiated, the formation of free valences in the growing carbonaceous phase is first of all a result of ‘electronic’ energy loss. If a partially carbonised polymer is implanted, the carbon bonds are

mainly broken by nuclear collisions, whereas the energy transferred to the irradiated polymeric target by electronic excitations dissipates in carbon structures or is expended for their rearrangement. Therefore, even for irradiation with heavy ions characterised by large S_n/S_e ratios the oxygen depth profile reconstructed from the Rutherford backscattering spectra corresponds to the ‘electronic’ loss distribution at low fluences ($\sim 10^{14} \text{ cm}^{-2}$) and to the ‘nuclear’ loss distribution at higher fluences.^{3, 88, 93}

At high fluences, a well-developed carbonaceous phase can form by linking individual carbon clusters. In this case, the concentration of oxygen scavengers substantially reduces and the concentration of oxygen in the implanted layer and the yield of carbonyl groups per implanted ion rapidly decrease as fluence increases.⁹³ The minimum concentration of trapped oxygen in the implanted layer corresponds to maximum enrichment of this layer with carbon as a result of ion-induced thermoradiolysis.⁸⁹ It should be noted that in polyethylene and polyamide-6 heavily implanted with medium-range energy (100–200 keV) light (*e.g.*, B^+ , see Refs 94 and 95) and heavy (*e.g.*, Sb^+ and As^+ , see Refs 3, 89, 93) ions the spatial region of maximum carbonisation is beneath the polymer surface.^{75, 95, 96} This can be illustrated by the depth profile of the relative concentration of carbon in the near-surface layer and by the presence of an additional maximum of the concentration of trapped oxygen on the surface of irradiated samples (in this case, the oxygen depth profile exhibits two peaks, see Fig. 4). The ‘buried’ carbonaceous layer is separated from the surface by a layer of non-carbonised, radiation damaged polymer.^{75, 94, 96} This effect can be rationalised by higher heat release at the track ends of implanted ions and by lateral spread of the thermoradiolysis zone within the collision cascade region.³

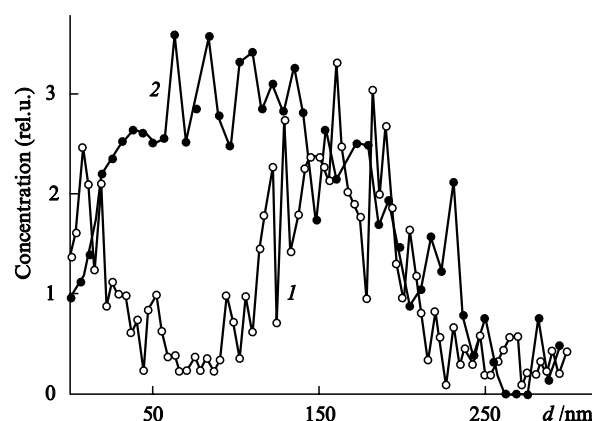


Figure 4. Depth profiles for trapped oxygen (1) and for an increase in the carbon concentration (2) in polyethylene irradiated with 150 keV As^+ ions at a fluence of $5 \times 10^{16} \text{ cm}^{-2}$ (according to Ref. 89).

Rutherford backscattering studies of the implant distribution (for implantation with heavy ions) and neutron depth profiles (for implantation with light ions) showed that sometimes high penetrability of the implanted layer allows the implant to diffuse out of the irradiated polymer. The pore system produced by the tracks of implanted ions provides conditions for specific gas transport reactions. In these situations the implant is either not detected^{97, 98} or the experimental depth profile differs from the corresponding calculated depth profile to such a high extent^{99, 100} that this can be explained by neither changes in the polymer density due to carbonisation and ion-induced erosion of the surface of the sample nor by backscattering of ions at high fluences. These effects are observed if the implant is incapable of bonding to the polymer matrix or if the interaction between the implant and matrix results in volatile products (here, heating of the polymeric target to moderate temperatures is sufficient for complete sublimation of the implant). This is characteristic of, *e.g.*, implanta-

tion of noble gas ions^{97,98} and F^+ ions in polyolefins.⁸⁸ In the latter case, volatile fluorocarbons are formed. Volatile compounds are also formed during implantation of PTFE with Sb^+ ions, which is accompanied by sublimation of antimony fluorides.⁴⁹ However, if the flux of implanted ions is rather low, the noble gas ions are retained in the polymeric target (e.g., Xe^+ ions in poly(ether sulfone),²¹ Kr^+ ions in polyimide¹⁰¹), but they diffuse out of the ion-implanted layer with time.¹⁰²

In the case of implantation of polymeric targets cooled down to 90 K, the depth profile of noble gas ions (in particular, xenon¹⁰³) matches the corresponding calculated depth profile to an accuracy of 10%.

Diffusion of low-molecular-mass compounds formed in the interaction of thermalised implanted ions with the polymer matrix (including the interaction on storage) can have a significant effect on the spatial distribution of the implant. For instance, phosphorus implanted into a molecular film based on a dianthrylidene derivative of γ -substituted pyrone diffuses towards the surface of the irradiated sample (probably, in the form of phosphines). The interaction with dioxygen causes phosphorus fixation in the form of corresponding oxides.¹⁰⁴ As a result, the phosphorus depth profile in the implanted layer appears to be bimodal. The first maximum corresponds to medium projected range of the implanted ions while the second maximum is at the surface of the sample.¹⁰⁴ High mobility is also characteristic of implanted lithium (the form in which lithium is transferred is unknown). A fraction of lithium ions diffuses towards the surface of irradiated polymers.^{105,106} Substantial redistribution of boron implanted into various polymers is illustrated by Fig. 5. According to XPS data, the boron escaped from the polymer bulk is oxidised.¹⁰⁸ The formation of volatile alkylboron compounds during implantation of boron ions has been suggested;³ this is indicated by the fact that, according to cryochemical atomic-beam experiments,¹⁰⁹ elemental boron readily reacts with hydrocarbons. The interaction with dioxygen and atmospheric moisture results in volatile oxidised alkylboron compounds and alkylboric acids. This is responsible for the possibility of thermally induced desorption of implanted boron¹¹⁰ and for complete disappearance of boron from the implanted layer upon long-term storage.⁹⁷

Obtaining mobile implant at low fluences implies that the stopping ions transfer to the polymer a rather high energy (15–20 eV $\text{\AA}^{-1}$, see Ref. 105) which is sufficient for occurrence of efficient thermoradiolysis and provides a necessary decrease in the density of the material of the polymeric target within the track region of implanted ions. Under these conditions, diffusion occurs

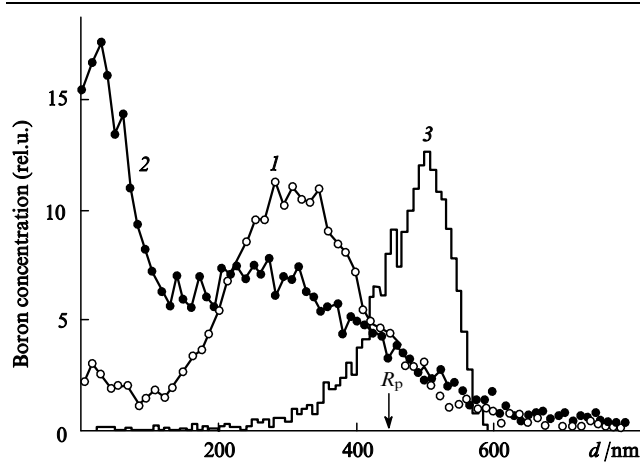


Figure 5. Boron depth profiles for polyethylene (1) and polyamide (2) irradiated with 100 keV B^+ ions ($D = 5 \times 10^{16} \text{ cm}^{-2}$, see Refs 3 and 93) and calculated depth profile for boron implanted into polyethylene (3) (results of Monte Carlo simulation using the TRIM code¹⁰⁷). R_p is the theoretical projected range of the implanted ion.

nearly completely along ion tracks.¹⁰⁶ On the other hand, the formation of developed carbonaceous phase in heavily irradiated polymer samples creates a barrier to diffusion of the implant towards the surface.¹¹¹

The reduction conditions which are created in the surface layer during the bombardment of a polymeric target by metal ions favours the formation of metal nanophase.¹¹² This process was studied taking polymethylphenylsiloxane and epoxy resins implanted with Ag^+ , Fe^+ and Co^+ ions as examples (see Refs 113–118). It was found that the morphology of the newly formed metal nanophase is to a great extent controlled by the viscosity of the polymer matrix. Ion implantation of polymers in the viscous-flow state is accompanied by the formation of spherical nanoparticles with narrow size distribution, while transition of the polymer matrix to the glassy state leads to the formation of facet metal structures in the implanted layer.¹¹⁴ Spherical metal nanoparticles are also formed in polyimide implanted with 150 keV copper, zinc and silver ions in high doses [$D = (1-5) \times 10^{17} \text{ cm}^{-2}$],^{119,120} whereas the implantation of polyimide with W^+ ions causes the formation of a tungsten carbide nanophase.¹²¹

A consequence of essential structural changes in the polymer matrix, caused by ion bombardment is a substantial change in the polarity of the polymer surface (Fig. 6). This can be due to both degradation of initial (if they exist) and formation of new polar groups. The latter can be formed either immediately during implantation (for heteroatom-containing polymers) or as a result of the oxidation of radical centres due to contact with dioxygen. For instance, transformation of an imide group into an amido group during low-dose implantation of 90 keV N^+ ions into polyimide leads to a more than twofold decrease in the polar component of the surface free energy.⁵⁶ A decrease in the surface polarity was also observed in the course of ion irradiation (Sb^+ , 150 keV) of polyamide-6,⁴⁹ whereas ion irradiation of PETP (N^+ , 90 keV) accompanied by transformation of ester groups into hydroxy groups leads to an insignificant (by 30%) increase in the surface polarity.⁶¹ These rearrangements of the polymer surface occur at low irradiation doses. Polarity of heavily implanted samples first of all depends on the presence of carbonyl groups formed involving uncompensated bonds of carbon atoms at the boundaries of the carbonaceous phase. For aliphatic polymers (polyethylene, polypropylene) the formation of carbonyl groups is the main factor responsible for a substantial increase in the polarity of the polymer surface at any dose.^{49,88} An increase in the surface polarity of polysiloxanes after ion implantation is due to the formation of nanodispersed SiO_2 phase inclusions in the implanted layer.⁵²

The sorption properties of irradiated polymers are affected by the developed system of nanopores in the implanted layer and by ion-exchange character of the sorption sites inside the pores (the

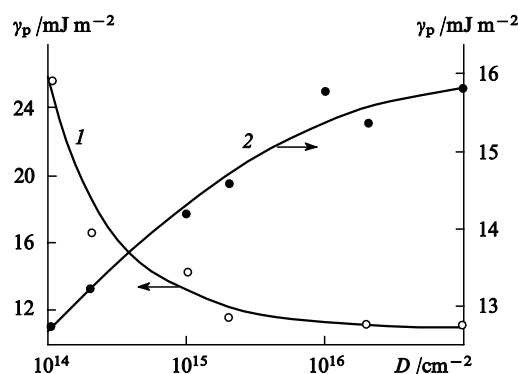


Figure 6. Polar component of the surface free energy (γ_p) of polyimide (1) and PETP (2) films irradiated with 90 keV N^+ ions plotted as a function of the implanted dose (according to Refs 56 and 61).

adsorption capacity of irradiated polyethylene and polypropylene with respect to cations is 2 to 5 times higher than with respect to anions^{84, 85}).

Carbon-containing species formed during ion implantation reinforce the polymer surface. In some instances the microhardness of the irradiated surface can be substantially increased (up to 50 to 70 times^{122–126}). These effects were observed for various polymers, namely, polyimide,^{28, 123, 126} polystyrene,^{122, 123} polyethylene,^{92, 127} PETP,²⁸ polycarbonate $\{[\sim\text{OC}_6\text{H}_4\text{C}(\text{CH}_3)_2-\text{C}_6\text{H}_4\text{OCO}\sim]_n\}$,¹²⁸ partially fluorinated polyethylene,²³ poly(ether ether ketone) $\{[\sim\text{OC}_6\text{H}_4\text{OC}_6\text{H}_4\text{COC}_6\text{H}_4\sim]_n\}$ ¹²⁹ and some other polymers irradiated with different (mostly light and not too heavy) ions with energies ranging from 100 keV to 1 MeV. The microhardness of carbonaceous products is first of all determined by the character of interconnectivity within the carbon cluster aggregates.²⁰ High microhardness requires that the incident ions deposit their energy mainly by electronic excitations (this provides the formation of carbon clusters) and the energy loss by nuclear collisions be relatively small. Though nuclear collisions are responsible for the formation of random links between the clusters, a general trend is towards an increase in the microhardness with an increase in the relative weight of energy loss by electronic excitations (Fig. 7).^{122, 130} However, since the displacement energy of an sp^3 -hybridised carbon atom (80 eV for diamond) is much higher than that of an sp^2 -hybridised carbon atom (30 eV for graphite),⁵ one can expect that nuclear collisions lead to gradual accumulation of domains with predominant sp^3 -hybridisation of carbon atoms and increased microhardness of the ion-implanted layer.

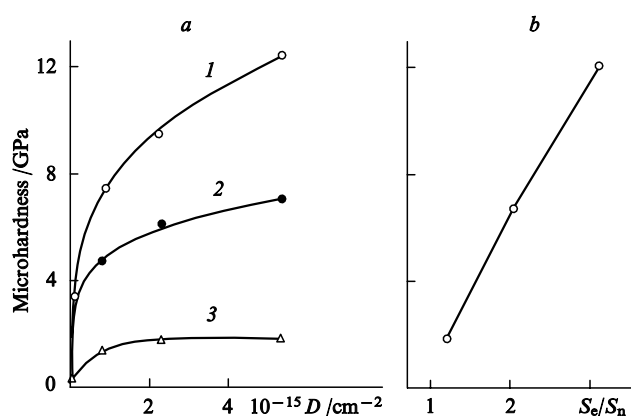


Figure 7. Microhardness of a polystyrene surface irradiated with Ar⁺ ions plotted as a function of irradiation dose (a) and of the relative weight of energy transferred from the incident ion to polymer by electronic excitations and nuclear collisions (b).¹²²
Ion energy /keV: 1000 (1), 500 (2) and 200 (3).

One of the most important consequences of ion implantation is the onset of conductivity of initially dielectric polymers. It is of great importance that the conductivity of irradiated polymers is due to the formation of carbon-containing structures in the implanted layer rather than ion doping. Therefore the conductivity, which is proportional to the optical absorption of the carbonaceous phase,¹³¹ only indirectly depends on the nature of implanted ions, being mainly determined by the energy loss during the stopping of ions.^{1, 17, 21, 129} Since the conducting phase in the ion-implanted layer is formed by discrete carbon clusters and their associates, the onset of conductivity in an irradiated polymer upon build up of implantation dose has a threshold character (see Fig. 3) and the transition from dielectric to conductor can be considered as percolation transition.^{5, 17, 29, 132} The dependence of the dc conductivity, σ , on the implantation dose is given by the formula:^{1, 17, 29, 132}

$$\sigma \sim (D - D_c)^t,$$

where D_c is the critical dose corresponding to the percolation threshold.

Thermoradiolysis in the implanted layer occurs under conditions of gradual coverage of the surface of polymeric target with ion tracks. Nevertheless, the formation of an infinite conducting cluster is, as a rule, observed at implantation doses corresponding to a smaller fraction of the surface covered with ion tracks compared to those predicted by the two-dimensional percolation problem. For instance, the percolation threshold for polyimide irradiated with 500 keV N⁺ ions corresponds to a coverage factor of 0.3 (see Ref. 29), whereas theory predicts that percolation in an ideal two-dimensional system must occur at a critical coverage of ~ 0.45 . This suggests some ordering in the carbonaceous phase and is also supported by large values of the exponent t in the above-mentioned formula for the polymers that are prone to form carbon clusters [polyimide,²⁹ polyacrylonitrile,¹⁷ poly(2,6-dimethylphenylene oxide),¹⁷ molecular films based on perylene derivatives¹⁸]. In this case, the t values estimated from the slope of the linear dependence $\log \sigma \sim \log(D - D_c)$ can be as high as 4–5 if energy deposition during implantation occurs mainly by nuclear collisions and even as high as 7–8 if the electronic stopping prevails. On the other hand, for poorly carbonised polyethylene irradiated with 100 keV B⁺ ions the percolation threshold corresponds to $D_c = 1.5 \times 10^{15} \text{ cm}^{-2}$ (i.e., in this case, $D_c > D_f$) and the exponent t in the above-mentioned formula does not exceed a value of 2.^{75, 133}

As the irradiation dose increases, a system of conducting ‘islands’ separated by potential barriers is formed within the implanted layer.^{1, 18, 134} The nanostructured carbonaceous phase formed in the immediate vicinity of the percolation threshold acquires semiconductor properties.¹³⁵ Studies of temperature dependence of the conductivity of some irradiated polymers [polyethylene, poly(ether ether ketone),^{21, 136} etc.] showed that the formation of developed carbonaceous phase at high implantation doses causes transition from one-dimensional to three-dimensional conductivity. A similar phenomenon was observed for polyimide heavily implanted with 90 keV N⁺ ions⁵⁶ and for polyamide-6 irradiated with 150 keV Sb⁺ ions.⁴⁹ For polymers which are prone to undergo carbonisation during irradiation [e.g., poly(*p*-phenylenebenzobisoxazole), poly(*p*-phenylenebenzobisthiazole), poly(benzimidazobenzophenanthroline)], the conductivity of the ion-implanted layer formed at high implantation dose (Kr⁺, 200 keV, $D = 4 \times 10^{16} \text{ cm}^{-2}$) is close to the metal conductivity.^{137, 138}

At implantation doses close to D_c , the conductivity of implanted polyethylene can be increased by 3 orders of magnitude by diffusion doping with molecular iodine.⁸⁰ However, the doping effect is unstable and ion-implanted polyethylene takes the initial value of the electrical resistance much faster than changes in the concentration of the trapped iodine diffusing out of the implanted layer occur.¹³⁹ It should be noted that it is difficult for molecular iodine vapours to penetrate the implanted layer in heavily irradiated polymers due to destruction of the system of track channels caused by the formation of the carbon nanophase.^{81, 139} Doping of irradiated polyethylene with FeCl₃⁸⁴ and treatment of ion-implanted polyimide with molecular chlorine lead to an increase in the conductivity by two orders of magnitude (despite the fact that addition of chlorine to some unsaturated bonds occurs simultaneously in the latter case).¹⁴⁰

The conductivity of the implanted layer is strongly dependent on the peculiarities of the morphology of the carbonaceous phase (the size of carbon clusters, character of their linking in aggregates, the presence of heteroatoms). As a result, the electrical resistance of different polymers that were ion implanted under the same conditions can differ by several orders of magnitude, e.g., the specific resistance of polyethylene and polyimide irradiated with 1 MeV Xe⁺ ions ($D = 10^{16} \text{ cm}^{-2}$), is 6.8×10^{-3} and $30 \Omega \text{ cm}$, respectively (see Ref. 55). The conductivity of the implanted layer

is also determined by the implantation regime and, in particular, by the energy of the implanted ions, by the presence (or absence) of forced cooling of the polymer sample (polyimide films irradiated in the absence of forced cooling have lower electrical resistance than those irradiated in the presence of forced cooling¹⁴¹), film thickness (thick films exhibit lower conductivity due to efficient cooling of the implanted layer during irradiation²⁵). Nevertheless, a general trend is towards an increase in the conductivity of irradiated polymers with increasing energy of implanted ions. The highest conductivity is observed if energy deposition by incident ions occurs mostly by an 'electronic' mechanism.^{21, 65, 123, 130, 142}

V. Prospects for practical applications of ion-implanted polymers

Initially, interest in studies of the effect of ion irradiation on polymers was due to fabrication of resists (both negative and positive) for lithographic processes with submicron resolution. Detailed reviews concerning the cross-linking–chain scission effects observed at very low implantation doses (10^{11} – 10^{12} cm⁻²) and responsible for changes in the solubility of irradiated polymers have been reported.^{1, 143} On the other hand, the possibility of initiation of essentially different radiolytic and thermoradiolytic processes (cross-linking–fragmentation of polymer chains at low implantation doses, transformations of functional groups at implantation doses comparable with D_f and carbonisation of polymers at high implantation doses) by ion irradiation allows control of the sorption, tribological, optical and conducting properties of the polymer surface. This opens up new fields of practical applications of polymeric materials.

Implantation of PETP with heavy high-energy ions is accompanied by the formation of latent tracks in the polymer. This makes possible perforation of polymer films 10–20 µm thick by hydrolytic etching and fabrication of membranes with a controllable number of identical pores.^{144–146} The pore diameter can be varied over a wide range (0.01–5 µm) by varying the duration of etching. Studies of the character of energy loss of α -particles in perforated PETP films obtained using this procedure allowed one to trace the changes in the shape of membrane channels in different stages of etching.¹⁴⁷ It was found that the channels have rather long cylindrical sections (up to 2/3 of the overall thickness of the polymer film) that are transformed into conical pore mouths.¹⁴⁷ Cylindrical channels with smooth walls can also be formed by etching ion irradiated polyimide in the presence of hydrogen peroxide¹⁴⁸ and hypochlorites.¹⁴⁹ On the other hand, typical of many polymers [e.g., poly(methyl methacrylate),¹⁴⁸ polycarbonate,¹⁴⁶ etc.] is the formation of channels with irregular shape and broad size distribution. High uniformity of etching channels in PETP is due to some features of latent track structure.^{146, 150, 151} The track core, which is at most several nanometers in radius, represents a degraded, rapidly soluble polymer containing a large number of isolated pores¹⁵² and surrounded by a shell of radiochemically cross-linked polymer.^{80, 146, 150} The shell diameter is 50 to 60 nm for implantation of xenon ions (1 MeV per nucleon) and is much larger than the penumbra diameter.^{80, 150} This can be explained by the formation of cross-links due to recombination of macroradicals formed in the interaction of polymer chains with knock-on hydrogen atoms¹⁴⁶ (including those formed as a result of hydrodynamic shock accompanying the passage of high-energy heavy ions¹⁵³). Probably, high spatial selectivity of etching is to some extent due to ordering of the polymer structure as a result of reorientation of the macromolecules along the ion tracks.⁶³ It should be noted that forced orientation of polymer molecules along the direction of ion flux can be observed not only during implantation of high-energy ions, but also in the case of ion irradiation with energies of the order of several kiloelectron-volts¹⁵⁴ at a fluence of $\sim 5 \times 10^{15}$ cm⁻².

The formation of surface pores, changes in the polar component of the surface free energy and the appearance of specific adsorption sites as a result of ion bombardment can have both

positive^{52, 155–162} and negative¹⁵⁶ effects on the efficiency of adsorption of living cells on the polymer surfaces (e.g., polystyrene,^{156, 158, 159} polyurethane,^{160, 161} polymethylsiloxane,⁵² collagen,^{156, 162} etc.). This opens up new possibilities of control of biocompatibility of polymeric materials. As a rule, cell adsorption efficiency nonmonotonically depends on the implantation dose (i.e., it is determined not only by the effects of changes in hydrophilicity) and reaches a maximum value at implantation doses that are somewhat lower than D_f .^{158, 160} It was also shown that changes in the dynamics of plasma protein adsorption on the surface of silicon rubber induced by irradiation with 150 keV H₂⁺, N₂⁺, Na⁺ and Ne⁺ ions leads to nearly complete suppression of thrombogenicity.¹⁶³

At low ion implantation doses, the refractive index, n , of a polymer increases with the polymer density. In some instances a relative increase in the refractive index can be substantial. In particular, poly(methyl methacrylate) is known to lose methoxy groups upon ion irradiation and undergo gradual transformation into an analogue of cross-linked polyethylene.¹⁶⁴ For this polymer, the $\Delta n/n$ ratio can be as high as 0.3 (see Refs 165 and 166) and the dependence of the refractive index on the implantation dose is nearly linear up to $D \approx 10^{15}$ cm⁻². At higher doses, the polymer becomes turbid due to carbonisation.¹⁶⁶ This allows the formation of light guides and other optical devices (couplers, interferometers) on the polymer surface.^{167–169} It is of great importance that the use of high-energy ions characterised by a shift of maximum energy loss towards the track end allows fabrication of 'buried' (including crossed) light guide structures at a depth from several to several tens of micrometres under the surface of a polymer sample (depending on the energy of implanted ions).^{167, 170}

Fabrication of nonlinear optical devices in the form of metal particles dispersed in a dielectric matrix¹⁷¹ by implantation of polymer with corresponding metal ions is a difficult task since the optical density of the polymeric host increases with the implantation dose. On the other hand, one can expect that the formation of a metal nanophase during ion irradiation of the polymers containing chemically bound metal ions will occur at low implantation doses.

As mentioned above, carbonisation of polymers at high implantation doses leads to a substantial increase in their microhardness,²⁸ which can be as high as 22 GPa¹²³ (cf. a value of less than 12 GPa for martensite steel) and is comparable with the hardness of diamond-like carbon films. The best results were obtained in the case of simultaneous implantation of ions with different mass and energy, i.e., characterised by different penetration depth and responsible for different degrees of carbonisation of polymers.²⁸ An increase in hardness of the surface of implanted polymers [polyimide,^{123, 126, 172} polystyrene,^{122, 123} polycarbonate,^{128, 173} pristine^{92, 127} and partially fluorinated polyethylene,²³ poly(2,6-dimethylphenylene oxide),¹⁷⁴ etc.] is accompanied by reduction of their electrical resistance¹²² and causes substantial improvement of wear resistance.^{122, 124} The latter parameter nonmonotonically depends on implantation dose since an increase in hardness of the implanted layer makes it more brittle and causes a gradual decrease in its adhesion to the polymeric support. The dramatic decrease in the friction coefficient upon ion irradiation observed for polycarbonate^{173, 175} and poly(2,6-dimethylphenylene oxide)¹⁷⁴ seems to be to a great extent due to an increase in hydrophilicity of the polymer surface, which favours the formation of a surface layer of chemisorbed water with good antifrictional properties.

The carbonised surface layer substantially improves the chemical stability of irradiated polymers towards organic solvents; however, this layer is porous and therefore provides no perfect protection of the polymeric support.¹⁷⁶ High-dose implantation of low-energy (25–40 keV) Si⁺, Al⁺, Y⁺, Y²⁺ and Y³⁺ ions leads to suppression of erosion of the surface of polyimide, PETP and some other polymers exposed to a flux of oxygen atoms (under conditions corresponding to Earth orbit space environment) due to the formation of a composite oxide-carbon coating.¹⁷⁷

Polymers irradiated to high doses represent an unusual electrode material, the surface properties of which can vary depending on the ratio of the concentrations of sp^2 - and sp^3 -hybridised carbon atoms in the implanted layer. Since the carbon clusters responsible for conductivity of the implanted layer are small, their oxidation under anodic polarisation observed in the absence of depolarisers is accompanied by irreversible loss of the electrochemical activity of irradiated polymers.⁷⁵ On the other hand, for initially conducting polymers (polyaniline,¹⁷⁸ polypyrrole,¹⁷⁹ polythiophene,¹⁸⁰ polybithiophene,¹⁸¹ polyethoxythiophene,¹⁸² polyethylenedioxythiophene¹⁸²) that lose their electrochemical activity as a result of degradation of the π -electron system at low implantation doses ($D < 10^{15} \text{ cm}^{-2}$)¹⁸⁰ the surface of the polymeric electrode exhibits recovery under anodic polarisation due to electrochemical oxidation of the carbonaceous phase.^{179, 181, 183} The possibility of ion-induced passivation of conducting polymers towards the processes of electrochemical polymerisation^{181, 183} and electrochemical deposition of metals^{179, 180, 182} allows one to change the surface profile of polymeric electrodes¹⁸¹ and to form metal patterns with micrometre resolution.^{179, 180, 182}

The possibility of varying the conducting properties of implanted polymers opens up new prospects for fabrication of microelectronic systems including the formation of conducting strips on the surface of polymeric materials,¹⁸⁴ fabrication of planar resistors with variable electrical resistance which can be varied over a wide range,² thermistors and bolometers.² Ion implantation can be used for development of more complex polymer-based electronic devices, namely, diodes and transistors. It is of great importance for fabrication of polymeric electronic devices (in particular, p - n -junctions^{185, 186} and conducting channels of field-effect transistors¹⁸⁷) that many of the initially conducting polymers with well-developed π -electron conjugation systems [e.g., poly(p -phenylenevinylene), polyacetylene]^{186, 187} exhibit resistance towards ion-induced dehydrogenation. Therefore, they can be doped by implantation of ions with medium-range energies ($\sim 30 \text{ keV}$). Under these conditions, purely chemical doping of p -type for implantation of iodine ions and of n -type for implantation of alkali metal ions can be accompanied by the effects associated with the formation of structural defects in the polymer matrix (e.g., as a result of electron capture from the π valence band of polyparaphenylene by the lower-lying sp^2 -electron energy levels corresponding to dangling bonds of carbon atoms¹⁸⁸). The possibility of fabrication of unusual electronic switching devices (analogues of field-effect transistors^{3, 75, 94, 96}) based on implanted, initially dielectric polymers (polyethylene, polyamide-6) with a 'buried' carbonaceous phase separated from the surface by a dielectric layer $\sim 10 \text{ nm}$ thick was also demonstrated. This layer can be made more uniform by electrochemical polymerisation of dielectric poly(o -phenylenediamine) in the pores of the implanted layer.⁷⁵ The spatial characteristics of this structure allow the 'buried' layer to act as a conducting channel of the field-effect transistor. The ac resistance of such a channel changed by more than four orders of magnitude upon applying an external electric field.^{3, 75, 94}

VI. Conclusion

The above-mentioned experimental results indicate that ion irradiation of polymers causes some specific phenomena that currently should be considered within the framework of a special division of high-energy chemistry. Ion-induced processes in polymeric targets represent a kind of pulse thermoradiolysis which occurs in the subnanosecond time scale and sometimes under conditions of massive ('non-thermodynamic') breakage of chemical bonds by nuclear collisions. The energy deposited by the incident ions in the polymer matrix is rather high; however, carbonisation of the polymer surface observed in this case cannot be reduced to simple 'graphitisation' of the polymer within the track of the stopping ion.

The formation of the carbonaceous phase on the polymer surface with an increase in the implantation dose involves some consecutive stages essentially differing in character of the corresponding ion-induced reactions. These stages include (1) dehydrogenation of a polymer (this occurs, as a rule, simultaneously with the radiation-induced cross-linking of the polymer) and transformation of functional groups, which results in the formation of 'pre-carbon' structures; (2) growth of carbon clusters, the limiting size of which is determined by the energy of implanted ions; (3) aggregation of carbon clusters and the formation of conjugated and non-conjugated bonds. The energy loss of high-energy ions affects the composition of the newly formed nanostructured carbonaceous phase more than the nature of the irradiated polymer. On the other hand, subtle variations of the short- and medium-range order of the carbonaceous nanophase, which determine such fundamental properties as conductivity and microhardness, depend on the mechanism of ion-induced thermoradiolysis and are very sensitive to the composition of the irradiated polymeric target. By and large, this type of influence of the polymer nature on the properties of ion implantation products can be considered as specific memory effect.

Figure 8 presents a diagram which qualitatively outlines main consequences of ion irradiation of polymers. By varying the irradiation dose one can control the rheological, sorption, conducting, electrochemical and optical properties of polymers and their microhardness, wear resistance and biocompatibility.

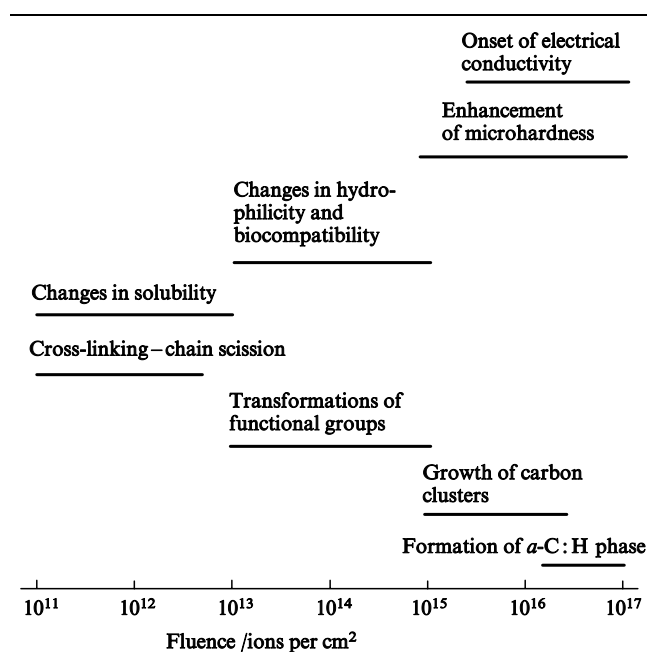


Figure 8. Principal transformations in the implanted layer and related changes in the physical and chemical properties of the polymer surface irradiated with different ion doses at energies between 0.1 and 1 MeV.

Thus, ion irradiation is a promising method of targeted modification of polymer surfaces. Build up of implantation doses causes processes of fundamentally different nature which can be controlled by varying the energy and masses of the implanted ions. All potentialities of this experimental technique and detailed mechanisms of physicochemical processes accompanying ion implantation of polymeric materials require further study.

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^d — *High Energy Chem. (Engl. Transl.)*

^e — *Dokl. Chem. (Engl. Transl.)*

^f — *Phys. Solid State (Engl. Transl.)*

^g — *Herald Russ. Acad. Sci. (Engl. Transl.)*

^h — *Colloid J. (Engl. Transl.)*

ⁱ — *J. Exp. Theor. Phys. Lett. (Engl. Transl.)*

The state-of-the-art and prospects for the development of rechargeable lithium batteries

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Abstract. The state-of-the-art of investigations into the development and perfection of the most promising class of chemical power sources, namely, rechargeable lithium batteries, is considered. The main problems of designing the batteries with a metallic lithium electrode are formulated and the use of alternative negative electrodes is substantiated. Special attention is paid to the studies dealing with the principles of the performance of lithium-ion batteries as well as the key directions for the perfection of these devices, which mainly concern the elaboration of new materials for lithium-ion batteries. A separate section is devoted to the consideration of polymeric electrolytes for lithium and lithium-ion batteries. The bibliography includes 390 references.

I. Introduction

A new type of chemical power source, namely, lithium cells with aprotic electrolytes appeared for the first time in the early 1970s and later gained wide acceptance.^{1,2} Thus, a long-standing idea of scientists, *viz.*, to build a chemical power source with the most active reductant, *i.e.*, an alkali metal, was materialised. The use of such a reductant allowed one to enhance both the operational voltage of a power source and its energy density.

In contrast to primary cells (one-shot cells) with lithium anodes, which were developed relatively quickly and successfully and are used now as the power sources in portable devices of every-day and special equipment, the history of the development of rechargeable lithium batteries has been very dramatic.^{3,4}

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II. The main problems in the development of rechargeable batteries with lithium anodes.

Primary cells designed for operation under ordinary conditions can be divided into two classes: cells with liquid and solid cathodes. For liquid cathodes-oxidants, thionyl chloride and sulfur dioxide, which simultaneously form the basis of the electrolytes, are used most often. Exhibiting high values of power and energy densities and operating in a wide range of temperatures, the cells with liquid oxidants represent, however, a fire hazard and are explosive and, hence, are used only in special equipment. For cells with solid cathodes, oxides of manganese, copper and certain other metals serve as the active cathodic materials, together with iron sulfide and fluorocarbons. Electrolytes in such cells represent solutions of certain lithium salts (perchlorate, hexafluoroarsenate, tetrafluoroborate, *etc.*) in organic nonaqueous aprotic solvents (propylene carbonate, dimethoxyethane, tetrahydrofuran, γ -butyrolactone and various mixtures). Depending on the cathodic material type, the working voltage of the cells can approach 3 V (for manganese dioxide and fluorocarbons) or 1.5 V (for copper oxide and iron sulfide); in the latter case, lithium cells and conventional cells based on the manganese dioxide–zinc system are interchangeable. It is the primary cells with aprotic electrolytes that are considered as the analogues of rechargeable (secondary) cells.

The reactions which proceed in primary cells with aprotic electrolytes are similar to those in secondary cells. In both types of cells, the discharge involves the same processes, *viz.*, the anodic dissolution of lithium and the cathodic insertion of lithium into the lattice of the positive electrode material. The charging in a secondary cell represents the reverse processes. The materials for positive electrodes on which the cathodic insertion and anodic extraction (in other words, cathodic intercalation and anodic deintercalation) of lithium proceed reversibly were found back in the late 1970s. Titanium and molybdenum disulfides can serve as examples of such compounds.

The main problem arisen concerns the choice of the negative electrode material. Its discharge, *i.e.*, cathodic deposition of lithium poses complications typical of electroplating practice. It is known that the lithium surface in aprotic electrolytes is coated with a thin passive film (its thickness does not exceed several nanometres) as a result of chemical reactions with the electrolyte components, namely, the organic solvent and anions. This film has the properties of a solid electrolyte with conduction in lithium

ions and adequately protects lithium from the reactions with the electrolyte (*i.e.*, prevents self-discharge).

On the cathode, the deposition of lithium results in the formation of dendrites and, in many cases, the film formed during charge–discharge cycles envelopes individual lithium microparticles preventing their electric contact with the support. Such a phenomenon called ‘encapsulation’ manifests itself in the fact that every charging step removes a part of lithium from the further operation. That is why, the secondary cells with metallic lithium electrodes should contain lithium in amounts exceeding (from 4- to 10-fold) its stoichiometric value; hence, the specific capacity decreases from the theoretical value of 3828 to 380–800 mA h g^{−1}. Moreover, the formation of dendrites increases the probability of short-circuiting and, hence, makes the cells inflammable and explosive.

Various methods for the treatment of the cathodic surface and a search for additives to the electrolyte that would prevent the dendrite formation during cathodic deposition of lithium yielded positive results. For example, it was shown that, being added to a propylene carbonate electrolyte, even trace amounts of hydrogen fluoride favour lithium deposition as a dense fine-grain continuous layer rather than in the form of dendrites.^{5,6} The beneficial effect achieved by treating the lithium surface with carbon dioxide (or, simply, by adding either CO₂ as such or substances evolving CO₂ into the electrolyte upon their reactions with lithium) has been repeatedly mentioned.^{7,8} It was suggested⁹ to modify the lithium surface by applying monomolecular layers of non-ionic surfactants, particularly, dimethyl ether of poly(ethylene glycol) and a dimethylsiloxane–propylene oxide copolymer. Electrolytes that prevent the dendrite formation even in the absence of additives were also found. For example, a solution of lithium hexafluoroarsenate in 1,3-dioxolane (this solution also contained tributylamine which prevents dioxolane polymerisation).^{10–12}

III. Practical developments in the field of metallic lithium cells.

Despite the fundamental obstacles in the development of secondary cells with metallic lithium electrodes, attempts were made to establish their commercial production. Thus in 1987, Moli Energy Ltd (Canada) started serial production of AA-size batteries (which corresponds to the Russian size of 316)[†] with positive electrodes made of molybdenum disulfide. The cells possessed the following characteristics: an initial voltage of 2.3 V, a capacity of 600 mA h for a discharge at a current of 0.2 A up to the final voltage of 1.3 V. In certain cases, the discharge to the final voltage of 1.1 V allowed one to reach a discharge capacity of 800 mA h. According to the reports by manufacturers, their cells had a cycle life of several hundred charge–discharge cycles; however, these results were disputed by some experts and consumers. In fact, a cycle life of 100 charge–discharge cycles could be claimed. In 1989, a modernised version of a secondary cell was developed which contained a positive electrode of molybdenum sulfide with a composition of Mo₆S₈. This cell had a higher discharge voltage (from 2.3 to 1.8 V) and a higher capacity (up to 1000 mA h) and allowed a high-current discharge (up to 1 A).

The characteristics of the secondary cells fabricated by Moli Energy Ltd could have been considered adequate even despite a considerable voltage decrease during the discharge and a short real cycle life, but the reliability of the cells proved to be

insufficient. In the summer of 1989, incidences of ignition of primary lithium cells were observed, as well as failures of the secondary cells produced by this firm, which made them stop the production.

At the Jet Propulsion Laboratory of the California Institute of Technology (USA), secondary cells with positive electrodes of titanium disulfide have been developed; however, no attempt has been made to organise their serial production mainly due to their low cycle life, namely, 100–200 charge–discharge cycles. The same situation was observed with the cells developed by Honeywell, Eveready Battery Co. Inc. (USA) and the United Design and Technology Bureau ‘Orion’ at the Novocherkassk Polytechnical Institute (Russia). Engineers of Matsushita Electric Industrial Co. (Japan) have developed AA-size rechargeable batteries of a higher quality using manganese dioxide as the active substance for positive electrodes. The batteries had a discharge voltage in a range from 3.2 to 2.0 V and a capacity of 800 mA h at the beginning of cycling and 600 and 450 mA h after 60 and 200 charge–discharge cycles, respectively.

At present, Tadiran (Israel) is engaged in the development of rechargeable batteries with metallic lithium electrodes; however, the prospects of their application are still vague. It was reported¹³ that, for AA-size cells, the gravimetric power density of 125–140 W h kg^{−1} and the volumetric power density of 280–315 W h dm^{−3} at a service life of 250 full depth charge–discharge cycles were achieved.¹³ [The depth of discharge (dod) or the cycling depth of a battery is the capacity fraction realised during the discharge from the total capacity designed into a rechargeable battery.] The reliability of these cells was not confirmed, but it was reported that explosions are ruled out even for substantial overcharges. However, in certain cases, the cells mildly leaked (without explosions) due to overheating.

IV. Materials alternative to metallic lithium

The attempts to solve the problems associated with the use of metallic lithium in negative electrodes involved substitution of lithium alloys for lithium. Lithium–aluminium alloys were assumed to be the most promising candidates. On such an electrode, the lithium concentration decreases during the discharge (lithium is etched out of alloys) and increases during the charge. The chemical activity of lithium in an alloy is somewhat lower as compared with that of metallic lithium; hence, the potential of an alloy-based electrode is more positive (by ~0.2–0.4 V) than the potential of an electrode of pure lithium. This results, on the one hand, in a decrease in the working voltage and, on the other hand, in a weakening of the alloy interaction with the solvent, *i.e.*, reduces the probability of self-discharge.

Disk-shaped rechargeable batteries of the VL 2020 model developed by Matsushita Electric Industrial Co. involved negative electrodes made of a lithium–aluminium alloy and positive electrodes of vanadium oxide. Such batteries were characterised by a rated capacity[‡] of 20 mA h being discharged from 3.2 to 2.0 V, their cycle life was ~1000 charge–discharge cycles for a 10% dod and ~450 cycles for a 20% dod. At the Jet Propulsion Laboratory of the California Institute of Technology (USA), specimens of cells were built with advanced characteristics: their cycle life reached 600 charge–discharge cycles at 50% dod.

Indeed, the small dod values typical of these batteries make their specific characteristics inferior as compared with secondary cells with lithium electrodes. A principal drawback of lithium–aluminium alloys consists in the fact that they change substantially their specific volumes during the cycling. A deep discharge can result in embrittlement and crumbling of the electrode. That is why, no further progress was observed in the field using lithium–aluminium alloys as the material for negative electrodes.

[†] In Russia, the sizes of cylindrical cells may be designated in accordance with three types of nomenclature: the GOST (State Standard) (three-digit numbers: 283, 286, 314, 316, 373, *etc.*), the recommendations by the International Electrotechnical Commission (R06, R03, R4, R6, R20, *etc.*) and the USA nomenclature (AAA, R, AA, D, *etc.*). Thus a cell with a diameter of 14.5 mm and a height of 50.5 mm may be designated as AA, 316 and R6; a cell of a diameter of 34.2 mm and a height of 61.5 mm may be designated as D, 373 and R20. Tables comparing different designations of cell sizes are available (*e.g.*, in Ref. 2, p. 216).

[‡] The rated capacity is a capacity realised in a 5 h discharge to a final voltage of 2.5 V.

Lithium alloys with heavy metals (such as the Wood's alloy) change their specific volumes during cycling to a lesser extent as compared with lithium–aluminium alloys. Matsushita Electric Industrial Co. has developed several versions of secondary cells with electrodes based on lithium alloys with heavy metals. Specific characteristics of these batteries were very low, and these alloys were considered to be of little promise.

V. Lithium-ion rechargeable batteries

1. General information

The publications reporting the secondary cells with negative electrodes of carbon materials developed in Japan marked a revolution in the field of rechargeable lithium batteries.^{14–17} Carbon was shown to be a very convenient matrix for intercalation of lithium. The specific volumes of many graphitised materials changed by no more than 10% upon insertion of sufficiently large amounts of lithium.¹⁸

The potential of carbon electrodes which contain moderate amounts of intercalated lithium can be 0.5–0.8 V more positive than the lithium electrode potential. To make the cell's voltage sufficiently high, Japanese researchers used cobalt oxide as the active material for positive electrodes. The potential of lithiated cobalt oxide was ~4 V vs. lithium electrode; the working voltage of the cell was 3 V.

During the discharge of this cell, lithium is deintercalated from the carbon material (on the negative electrode) and is intercalated into the oxide (on the positive electrode). The charge involves the reverse processes. Thus, the system contains no metallic (zero-valent) lithium, and its charge and discharge processes simply involve the transfer of lithium ions from one electrode to another. These rechargeable batteries were named lithium-ion,¹⁴ 'rocking-chair'¹⁹ and 'swing'²⁰ cells.

Figure 1 shows the scheme of performance of a lithium-ion battery. On the left, a negative graphite electrode is shown. Its structure is characterised by the presence of layers (conditionally shown as hexagonal fragments) between which lithium ions (black points) can be inserted. On the right, the positive electrode of lithium manganese spinel with a structure that can intercalate lithium ions is shown. Lithium salts in non-aqueous solvents are used as the electrolyte. During the charging of the cell, in the external circuit, an electronic current flows from the positive electrode to the negative one, whereas inside the cell, an ionic current flows also from the positive electrode to the negative one.

Since the appearance of first publications on the development of lithium ion batteries,^{14–17} active research into the intercalation of lithium into carbon and the other materials commonly used for the positive electrodes has started. To date, the publications on

this subject number in the hundreds and involve several reviews.^{19, 21–28}

2. Examples of lithium-ion batteries

In 1991, Moli Energy Ltd elaborated the specimen of lithium-ion batteries shaped as disks (coins).²⁹ A cell of the 1225 size⁸ had a capacity of ~7 mA h and a cycle life of ~300 charge–discharge cycles at a discharge current of 1 mA and a charge current of 0.5 mA.

Of Japanese firms, the leading position in the production of lithium-ion cells belongs to Sony which produces lithium-ion cells of various types, not only coin cells but also cylindrical ones of a spiral design and prismatic cells. Its annual production exceeds 10 million cells.³⁰ Sanyo Electric Co. holds the second position. Matsushita Electric Industrial Co. also has a large-scale production. In addition, six to eight other Japanese firms have just entered the market of lithium-ion batteries.

Since 1994, Sony has arranged the production of rechargeable batteries with sufficiently stable characteristics. The cells of AA size (according to Japanese nomenclature, US 14500) with a weight of 19 g, a rated capacity of 500 mA h at a voltage of 3.6 V are most representative. The manufacturer guarantees their performance in temperature ranges from –20 to +60 °C (discharge) and from 0 to +45 °C (charge). The energy density of these cells was ~95 W h kg^{–1} or 222 W h dm^{–3}. Cells of larger sizes had somewhat higher energy densities: *e.g.*, for cells of size 16 630 and 18 650 the energy densities were 105 and 126 W h kg^{–1} (or 250 and 290 W h dm^{–3}), respectively. Under the usual storage conditions, the self-discharge of the cells was ~10% in three months.²¹

The greatest rated capacity equal to 2800 mA h was demonstrated by a cylindrical cell of the size 26 650 weighing 83 g.

A discharge under a 1 h high-current mode reduced the capacity of Sony cells only insignificantly. The manufacturer guarantees cycle life of 500 charge–discharge cycles at only a 20% capacity fade.

In Japan, in addition to the development of lithium-ion cells of small sizes, attention has focused on elaboration of large-size rechargeable batteries, which can be used for both electrical vehicles and load distribution between autonomic nets. Since 1992, the studies have been carried out in accordance with the 'New Sunshine' program, which was intended to be accomplished in ~10 years with a total financing of ~\$140 mln (USA). This programme scheduled the development of two versions of rechargeable cells, *viz.*, batteries with medium energy densities (up to 140 W h kg^{–1}) designed for long-term service (the cycle life of 3500 charge–discharge cycles) and batteries intended for a short cycle life (500 charge–discharge cycles) but displaying enhanced energy densities (up to 180 W h kg^{–1}).^{31, 32}

In other countries, the industrial output of lithium-ion batteries ranks far below that in Japan; however, certain companies intend to substantially increase the production of these secondary cells.

In the USA, the engineers of Rayovac Corp. have developed specimens of both coin and cylindrical cells.²² Coin cells of the 1225 size were characterised by energy density of 35 W h kg^{–1} or 115 W h dm^{–3}. These characteristics rank substantially below those of the cylindrical cells produced by Sony, which is explained by the fact that the effectiveness of using the cell's mass and volume are different for small and large batteries (the share of casings and other structural elements in the cell's total weight is higher in coin cells as compared with cylindrical cells). The monthly self-discharge in these cells is ~5%, which is comparable with the characteristics of Japanese cells. Engineers of Rayovac

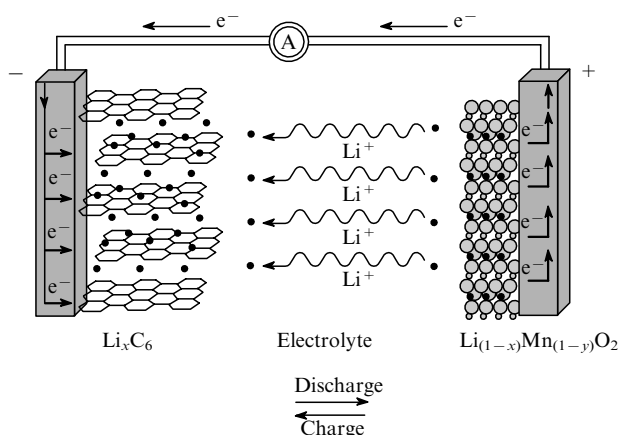


Figure 1. A scheme of performance of lithium-ion rechargeable batteries.

§ The designations of sizes of coin cells comprise the numbers that signify their diameters (in millimetres) and heights (thickness, in tenths of a millimetre). For instance, a cell of the 1225 size has a diameter of 12 mm and a thickness of 2.5 mm.

Corp. intend to organise the production of prismatic cells with an energy density approaching $\sim 130 \text{ W h kg}^{-1}$. Being designed for a long-term discharge (and charge) by small currents, the first version of these cells should demonstrate an enhanced capacity. The second version is designed to have a lower capacity and withstand high-current discharges and charges.

Bellcore (USA) has undertaken great efforts in the development of lithium-ion batteries.^{33,34} Their cell prototypes of the AA size with a capacity of 380 mA h (*i.e.*, lower as compared with similar batteries made by Sony) were, however, capable of discharging in a 20-min mode[¶] without substantial capacity loss ($< 20\%$).

Prismatic lithium-ion batteries developed by Yardney Corp. (USA)³⁵ exhibited capacities of 3 A h and energy densities of 87 W h kg^{-1} or 225 W h dm^{-3} .

SAFT (France) have completed the preliminary stage in the production of lithium-ion batteries to be used in both communication facilities and electric vehicles.^{36,37} The energy density of such a battery was $125\text{--}150 \text{ W h kg}^{-1}$ with discharge by low currents and $90\text{--}135 \text{ W h kg}^{-1}$ at a high-current discharge. In the latter case, the power density was $190\text{--}200 \text{ W h kg}^{-1}$. A decrease in the temperature to -30°C resulted in a $20\%\text{--}25\%$ decrease in the capacity, the cycle life was assessed to be ~ 400 charge–discharge cycles.

Large-size lithium-ion batteries (capacity from 40 to 100 A h) are being elaborated by engineers of VARTA (Germany).³⁸ The characteristics of the developed prototypes are still not too high: the energy density of a cell with a capacity of 100 A h was $50\text{--}70 \text{ W h kg}^{-1}$ for a 2 h discharge mode and $\sim 30 \text{ W h kg}^{-1}$ for a 30 min discharge mode. The capacity of the cells substantially decreased with cycling, which, apparently, is associated with the scale factor.

VI. The main problems in the development of lithium-ion batteries.

1. Materials for negative electrodes

The lithium-into-graphite intercalation compounds (layered graphite compounds) have been known for a long time (see, *e.g.*, Ref. 39). In the 1970–1980s, the reversible intercalation of lithium into graphite and certain other materials from lithium salt solutions in aprotic solvents was extensively studied.^{40–46} The very first studies on the reversible lithium intercalation have shown that lithium intercalation into carbon materials is a complex process with the mechanism and kinetics largely dependent on the choice of carbon material and the electrolyte. Whereas the effect itself was quite evident, however, the results of different authors on its mechanism appear to be extremely contradictory. Even now, an important question remains open as to which properties (structure, electronic structure, the presence of impurities, *etc.*) of carbon materials determine the intercalation and deintercalation processes.

Despite the uncertainty mentioned above, certain simple relationships and phenomena have been established unambiguously. Thus it was found that, upon the first contact of an aprotic electrolyte with a carbon material (irrespective of its structure), the latter acquires a potential in the range from 2.5 to 3.5 V *vs.* lithium electrode, the value being determined by the presence of compounds with certain chemical groups (first of all, oxygen-containing groups) in the electrolyte. At a cathodic polarisation, the potential shifts to negative values, and slow intercalation of lithium begins. Simultaneously, the electrolyte is reduced (both the solvent and different impurities), and this reaction proceeds much more easily (at less negative potentials) on the surface of carbon material as compared with the metallic lithium surface.

Being partially insoluble, the reduction products form a film of the carbon material surface. This film is similar in composition and properties to the passive film formed on the lithium surface. Thus, during the first charge, electricity is consumed in both lithium intercalation and passive-film formation. A completely formed film prevents direct contact between the electrolyte and carbon, thus virtually eliminating further reduction of the electrolyte.

The second undeniable fact is that the carbon material structure affects the mechanism of lithium intercalation. As a rule, intercalation of lithium into well pronounced graphite structures results in the formation of a thermodynamically stable compound, namely, LiC_6 . In this compound, the lithium activity is equal to unity, *i.e.*, the potential of such a compound is equal to that of a lithium electrode. The majority of authors represent intercalation–deintercalation by the following equation:



The dependence of the Li_xC_6 potential on the degree of intercalation x (*i.e.*, the charge curve of a graphite electrode) was shown to have several almost horizontal steps corresponding to the following compounds: LiC_6 , $\text{Li}_{0.5}\text{C}_6$, $\text{Li}_{0.33}\text{C}_6$, *etc.*⁴⁵ Intercalation of lithium into graphite structures occurs at negative potentials (the main part of lithium is intercalated at a potential more negative than 0.5 V), *i.e.*, the activity of lithium in such intercalates is sufficiently high. On the one hand, this is an advantage, because the cell voltage increases; however, on the other hand, this is a drawback, because the reduction of electrolytes on these intercalates proceeds more actively than on non-graphitised samples. Moreover, intercalation of lithium into graphite structures is often accompanied by co-intercalation of the solvent, which leads to swelling and exfoliation of graphite.

Intercalation of lithium into amorphous structures occurs at more positive potentials, as a rule, in the range from 0.9 to 0.0 V. In this case, x *vs.* potential plots represent smooth curves typical of uniform systems. Nongraphitised structures do not exfoliate during intercalation of lithium.

Numerous studies were devoted to elucidation of how the potential variation depends on the degree of intercalation x (thermodynamics of the intercalation process) (see, *e.g.*, Refs 18, 29, 45–48). It was shown that the dependence of the activity of intercalated lithium on its content has a complex form, its mechanism still being a subject of speculation.

Different scientists tried to find a correlation between the structure of carbon materials and their abilities to intercalate lithium reversibly. This correlation is still not established conclusively. Controversial assumptions have been drawn on this subject. For instance, it was supposed⁴⁹ that reversible intercalation is possible exclusively into materials with the well pronounced graphite-type crystal structure and is unfeasible for amorphous materials. In contrast, it was also proposed⁵⁰ that lithium is intercalated only into amorphous materials. Probably, the optimum materials should possess amorphous matrices with mesophase inclusions, *viz.*, nuclei of graphite crystals. These materials are represented by various cokes, pyrographite and pyrolysis (carbonisation) products of different polymers. This assumption was confirmed by the results of studying the possibility of lithium intercalation into the same substances preliminarily pyrolysed at different temperatures. The optimal pyrolysis temperature was found to correspond exactly to the formation of the hypothesised mesophase materials.^{51,52}

The research practice employs various carbon materials, whereas in the industry only certain specific materials which ensure adequate characteristics of negative electrodes for lithium-ion cells are used. Of the latter, a material produced by Osaka Gas Co. (Japan) which is called mesocarbon microbeads (MCMB) was employed most extensively. This material is the product of pitch carbonisation carried out under certain temperature conditions.^{53,54} It was assumed that fibrous materials are also promising for fabrication of anodes.^{55–59}

¶ A discharge with such a current that the total designed capacity is realised in 20 min.

Carbon materials (obtained by pyrolysis of certain organic substances, *e.g.*, poly(*p*-phenylene), phenol–formaldehyde resin, soluble phenol–formaldehyde resin and even sucrose) with the intercalation capacity exceeding 372 mA h g^{-1} , which corresponds to the LiC_6 limiting composition, have been described. Their real intercalation capacity could reach $600\text{--}700 \text{ mA h g}^{-1}$ (see Refs 60–71).

Naturally, elucidation of the reason for such an enhanced capacity became a challenge for scientists. It was found that lithium ions intercalated into graphite can occupy different sites in the graphite lattice, *viz.*, in interstitials (proper intercalation), at the edges and on surfaces of graphite crystals.⁷² These sites differ in the types of bonds formed between the lithium ions and carbon. In amorphous matrices, lithium appears to be dissolved and uniformly distributed. Materials of the MCMB type are considered as the mixtures of pure graphite and a certain amorphous (turbostratic) material.^{67,73} Furthermore, it was assumed that excessive lithium ions can be incorporated into nanosize microcavities.^{56,65,74} Strongly disordered structures contain isolated graphite sheets (a ‘house of cards’ structure) both sides of which can adsorb the incorporated lithium. Such an intercalation mechanism doubles the intercalation capacity. Moreover, a definite correlation has been found between the intercalation capacity and the content of residual hydrogen in the carbon material.^{75,76} The formation of hydrogen–lithium bonds was hypothesised.⁶⁵ Further studies have shown that the characteristics of disordered materials gradually deteriorate so that their enhanced intercalation capacity is observed only at the beginning of their operation. These studies are being continued, however, without any definite hopes for success.^{77–80}

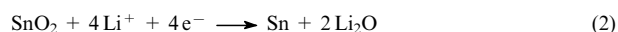
Passive films formed on the carbon material surface during the first cathodic charge have a great effect on intercalation–deintercalation processes. The problem of formation of passive films on carbonaceous materials has been extensively studied, being probably the central question in the development of lithium-ion cells. A vast number of studies were devoted to the elucidation of the formation mechanism, composition, structure and properties of these films. As was stressed above, the passive films on carbon material resemble those formed on the surface of pure lithium with respect to their composition and properties (see, *e.g.*, Refs 21, 81–89). They result from irreversible reduction of electrolyte components and serve as a natural barrier that prevents the further process. Thus, the carbon material surface catalyses the electrolyte reduction. The data on the kinetics of this process are contradictory.

Propylene carbonate is reduced most actively, hence, it is recommended not to use propylene carbonate-containing electrolytes in lithium-ion batteries. The electrolyte reduction during the first discharge consumes a charge which is comparable with the specific capacity of the material and represents the irreversible capacity of the negative electrode. To reduce this quantity, it is desirable to add different substances to the electrolyte, *e.g.*, carbon dioxide, crown ethers, sulfur dioxide, ethylene sulfite, nitrogen dioxide, vinylene carbonate, *etc.*^{83,90–96} Later, different procedures of surface treatment were proposed for carbon materials themselves, which includes deposition of certain protective coatings. For instance, it was proposed to oxidise^{65,97} the graphite material surface, silver-plate its particles⁹⁸ and vacuum spray fine tin films.⁹⁹ Coating of fine graphite particles with still finer nickel particles (in essence, coating of graphite with a porous nickel film) seems more practicable.¹⁰⁰ Such a treatment favours a decrease in the irreversible capacity from 310 to 40 mA h g^{-1} and a simultaneous increase in the reversible capacity. A similar result was achieved by applying a thin layer of non-graphitised carbon on the surface of graphite particles.^{101,102} Judging from the deposition method used, *viz.*, a fluidised bed treatment of graphite with a mixture of nitrogen and toluene vapour at 1000°C , the resulting coating represented pyrolytic carbon. It was shown¹⁰² that such a coating eliminates completely the irreversible capacity in such electrolytes as propylene carbonate (PC) and ethylene

carbonate (EC). Finally, an original proposal to precoat the surfaces of graphite materials with protective films which resemble the film usually formed during the first cathodic polarisation in the working electrolyte deserves mentioning. Such protective films can be formed using chemical (treatment with butyllithium)¹⁰³ and electrochemical¹⁰⁴ procedures.

It follows from above that in the elaboration of negative electrodes, attention is mainly focused on carbon materials; however, attempts have been made to study different substances. At one time, carbon compounds with nitrogen and boron were assumed to be promising.^{105–109} It was found that although their starting capacities (the capacity in the first cycles) are comparable with those of carbon materials, these decreased substantially during the cycling. The most promising results looked with carbon–silicon compositions.^{110–112}

In the late 1990s, the attention of many researchers has been attracted by the materials based on tin oxides.^{113–128} When negative electrodes made of such materials were used, lithium was intercalated into metallic tin formed during the initial cathodic polarisation of the electrode



rather than into the tin oxide.

Subsequent insertion of lithium into tin formally proceeds in the same fashion as its intercalation into carbon



but, for tin, the coefficient x can be sufficiently high, *i.e.*, reach 4.4 (for intercalation into graphite, $x = 1/6$). For $x = 4.4$, the theoretical specific capacity of a tin electrode is 991 mA h g^{-1} or $7234 \text{ mA h cm}^{-3}$. Such high values of specific capacity (especially the volumetric one) are responsible for the keen interest paid to these materials. Even being calculated with respect to the initial oxide SnO_2 rather than to tin (into which lithium is intercalated), the resulting values of specific capacity still remain sufficiently high, *viz.*, 781 mA h g^{-1} and $5428 \text{ mA h cm}^{-3}$. However, the use of tin oxides and other tin compounds entails a number of problems.

The common (and the main) drawback of all metal electrodes is the substantial change in their specific volumes upon lithium intercalation. During lithium intercalation, the specific volume of an alloy formed (or, more precisely, a binary system) substantially increases, which results in high internal stresses and, as a consequence, the electrode cracking. In turn, this results in the appearance of a high ohmic resistance at the boundaries of individual metal particles and a sharp polarisation rise. While, for primary cells, this factor cannot play any significant role, for a secondary cell (rechargeable battery), it is the determining factor. (It should be borne in mind that the specific volume changes induced by cycling were the reason for the failure of numerous attempts to create a negative electrode based on aluminium and certain alloys like the Wood alloy.)

Tin is a remarkable material because it can be obtained in a fine-grain form with a characteristic particle size of several nanometres using different technological procedures. Dispersion of tin occurs in particular owing to its formation in the lithium oxide matrix by Eqn (2). In several studies,^{115–190} this was considered to be the key factor.

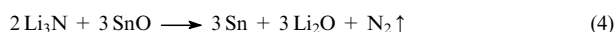
Yet another principle for the preparation of highly dispersed particles is the use of tin alloys and intermetallic compounds.^{121–130} However, in this method too, the stability of a finely dispersed phase of either tin or its intermetallic compound is favoured by the presence of another (inactive) phase. A relatively complex procedure of fabrication of negative electrodes based on tin, *viz.*, chemical deposition of tin into pores of a polymeric membrane has been proposed.¹²⁷ Such a membrane (a polycarbonate filter) has a system of monodispersed cylindrical pores with diameters of 50 nm . Prior to deposition of tin, the membrane was applied on a current collector made of foil. In the end, the membrane was burnt out to give a brush of tin hairs, which are

oxidised in air to give crystalline SnO_2 . The electrodes thus prepared exhibited highly stable characteristics and were capable of discharging by huge currents (a complete discharge in 1 min!).

A two-phase system consisting of mixed powders of tin and a tin–antimony intermetallic compound (SnSb) was suggested¹²⁸ for the fabrication of negative electrodes. The ultradispersed powders can be obtained by chemical reduction using borohydride. Being inserted into such a two-phase system, lithium occurs first in the intermetallic compound, the tin phase playing the role of a stabilising matrix. Following completion of this process, intercalation of lithium into tin begins. Thus, the tin ‘matrix’ is not inert (in contrast to Li_2O) but makes an additional contribution to the capacity. The use of these electrodes allowed a specific capacity of 360 mA h g^{-1} to be maintained for 200 charge–discharge cycles. It was proposed¹²⁶ to prepare a Ni_3Sn_2 intermetallic compound by a mechanochemical method, *viz.*, by processing nickel and tin powders in a ball mill. Electrodes based on such an intermetallic compound exhibited specific capacities up to 327 mA h g^{-1} or $2740 \text{ mA h cm}^{-3}$. The same method was proposed for fabricating an intermetallic compound of indium with antimony (InSb).¹²⁹ Despite their adequate characteristics, the electrodes made of this compound have several drawbacks, *viz.*, the high cost of indium and the toxicity of antimony. Later, copper was substituted for indium and tin was substituted for antimony.^{130, 131}

A Cu_6Sn_5 intermetallic compound was also shown to be quite plausible as a matrix for intercalation of lithium. In the potential range from 2.0 to 0.2 V, lithium intercalated successfully to give a $\text{Li}_{13}\text{Cu}_6\text{Sn}_5$ compound. True enough, such an intercalation was accompanied by a noticeable increase in the specific volume; however, this effect can be eliminated by decreasing the size of intermetallic compound particles. A proposal¹³² to prepare a microcomposite material from the Cu_6Sn_5 intermetallic compound and metallic copper was more successful. This material was prepared by the so-called mechanical alloying of an equi-atomic mixture of copper and tin powders in a high-speed planetary mill in an argon atmosphere. The electrodes made of this material withstand more than 80 charge–discharge cycles with a specific capacity of 200 mA h g^{-1} .

An interesting approach was suggested¹³³ for the preparation of a Sn–LiO_2 nanocomposite by a reaction of tin oxide with lithium nitride in a ball mill in an argon atmosphere. This reaction



was carried out for 5 days. However, in reward, this method produced a ready-for-use composite; hence, there was no need to spend the charge in the primary reduction of tin by reaction (2).

Amorphous oxides of silicon and tin $\text{SiO} \cdot \text{SnO}$ (see Ref. 134) are also considered as promising materials for negative electrodes. Powders of these oxides were also obtained in a planetary ball mill from the starting monoxides. Electrodes of these materials had the initial capacity of $\sim 600 \text{ mA h g}^{-1}$ which decreased to 350 mA h g^{-1} during the initial 20 charge–discharge cycles.

Recently, in addition to most popular tin-containing compounds, other materials were proposed for use as negative electrodes in lithium-ion batteries. The following examples may be mentioned: the KC_8 intercalation compound;¹³⁵ magnesium silicide Mg_2Si (the starting capacity of 1370 mA h g^{-1} which, however, smoothly decreased to 100 mA h g^{-1} in the initial 10 charge–discharge cycles);¹³⁶ a complex nitride $\text{Li}_{2.6}\text{Co}_{0.4}\text{N}$ (the starting capacity was 760 mA h g^{-1} and also decreased with time);¹³⁷ a sodium–molybdenum bronze of the $\text{Na}_{0.25}\text{MoO}_3$ composition which exhibited an intercalation capacity in lithium of 940 A h kg^{-1} (or $4000 \text{ mA h cm}^{-3}$).¹³⁸ However, the application field of lithium-ion batteries with electrodes of this bronze is rather narrow, because their potential changes within a very wide range, *viz.*, from 3 to 0.005 V during the discharge. It was proposed to use a material based on $\text{Li}_4\text{Ti}_5\text{O}_{12}$ (Refs 139, 140) and a lithium–zinc alloy¹⁴¹ for negative electrodes. The latter material can be obtained by controlled vapour codeposition of

individual metals, the vapour mixture being condensed on a titanium current collector cooled by dry ice. The microstructure formed makes it possible to carry out cycling at high current densities.

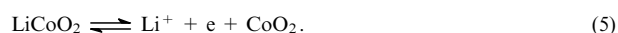
Lithium is known to form alloys with silicon up to the $\text{Li}_{4.4}\text{Si}$ composition, which corresponds to a theoretical specific capacity of 4000 mA h g^{-1} . However, intercalation of lithium into silicon is accompanied by great changes in the specific volume. A laser-induced method was applied for the preparation of silicon powder from silane.¹⁴² The particles measuring only $\sim 80 \text{ nm}$ did not destroy during cycling. Electrodes fabricated from a mixture of such a silicon powder with carbon black demonstrated the capacity values of 1700 mA h g^{-1} after the tenth cycle and 1300 mA h g^{-1} after the twentieth cycle.

Nanocomposites of silicon microparticles in a titanium nitride matrix were also used for negative electrodes.¹⁴³ In this case, lithium gets intercalated into silicon. For a 33% silicon content, the composite capacity reached 300 mA h g^{-1} and remained unchanged for 20 cycles (no data on long-term cycling is available). The Si/TiN nanocomposites were also fabricated in a high-speed ball mill.

Mention should be made of important problems of the technology of negative electrodes such as the difficulties in the development of binding materials and current collectors, the imperfect technology for the fabrication of the electrodes themselves that gives no way of providing their uniform (small) thickness, the questions associated with corrosion of electrodes, *etc.*

2. Materials for positive electrodes

The choice of the material for the positive electrode in rechargeable lithium-ion batteries is restricted to lithiated cobalt, nickel and manganese oxides. Electrodes based on lithiated cobalt oxide are characterised by the lowest polarisation and the highest specific capacity. The performance of a positive electrode is reduced to deintercalation of lithium during the cell discharge and intercalation of lithium during the charge



The operational characteristics of high-potential electrodes (*i.e.*, the electrodes with open-circuit potentials of $\sim 4 \text{ V}$ *vs.* lithium electrode, which maintains the discharge voltage at a level above 3 V) are approximately the same. The choice of the active substance for positive electrodes was arbitrary to a certain extent. Japanese scientists prefer cobalt oxides which are much more expensive than other materials; however, their industrial synthesis is relatively simple and reproducible.

In France and Canada, preference is given to cheaper nickel oxide. Lithiated nickel oxides operate at a less positive potential than cobalt oxide. This mitigates to a certain degree the requirements of the stability of the electrolyte to oxidation during charging. At the same time, the discharge curve of a nickel-oxide electrode is steeper, *i.e.*, the voltage variations during the discharge in a cell with nickel-oxide electrodes are greater as compared with cells equipped with electrodes of manganese and cobalt oxides. The USA industry mainly uses the materials based on manganese oxides (lithium–manganese spinels) which seem to be more attractive economically and environmentally safe (see, *e.g.*, Ref. 144).

Electrochemical characteristics of positive electrodes depend to a great extent on the technology used in their synthesis. Most publications were largely devoted to technological problems, and the questions of mechanisms of processes on these electrodes have received less attention. The technology of synthesis of lithiated oxides is based on the use of various high-temperature (sintering) and low-temperature (sol–gel, ion exchange, deposition from solutions) processes. Lithiated cobalt oxide was mainly prepared by a low-temperature technology,¹⁴⁵ whereas lithiated nickel oxide was fabricated by sintering.^{146, 147}

Numerous studies aimed at the perfection of positive electrodes for lithium-ion cells are largely limited to improvement of their

structures. This is achieved by both technological methods and the introduction of different modifiers.

For example, it was shown that lithium cobaltate with the $O2$ structure has a more pronounced layered structure (suitable for reversible intercalation of lithium) as compared with conventional lithium cobaltate with the $O3$ structure.¹⁴⁸ The modification with the $O2$ structure can be prepared, for instance, by ion exchange from a solution of sodium cobaltate ($\text{Na}_{2/3}\text{CoO}_2$) and lithium bromide in hexanol. Although the materials with the $O2$ and $O3$ structures hardly differ in many parameters, the former material is more cycling-stable. Yet another technology used in the preparation of lithium cobaltate with a good texture (preferential crystal orientation along a lithium intercalation direction) consists in radiofrequency magnetron sputtering of thin films on various conductive supports,¹⁴⁹ which also facilitates the reversible cycling, *i.e.*, increases the battery life. To obtain highly dispersed LiCoO_2 powders with enhanced reversibility degrees, an original method of supercritical aqueous synthesis was put forward.¹⁵⁰ For this purpose, the aqueous solutions of LiOH , $\text{Co}(\text{NO}_3)_2$ and H_2O_2 were fed under a pressure of 30 MPa to an electric furnace at 400 °C, where the synthesis was completed in 30 s.

A method of emulsion drying was used for the preparation of highly dispersed LiCoO_2 powders.¹⁵¹

As was mentioned above, a sufficiently high discharge potential of a positive electrode at which the lithiation occurs is one of the merits of lithium cobaltate. However, this property is simultaneously a drawback, because the charging of a positive electrode occurs at still higher positive potentials at which the electrolyte can be oxidised on the catalytically active surface of cobaltate (or on a carbon additive used for increasing the active-layer conductivity). To overcome this disadvantage, an original method for modifying the electrode surface by applying a very thin (no thicker than 0.1 μm) layer of diamond-like carbon by plasma spraying from ethylene has been proposed.¹⁵² The resulting electrodes could be cycled in the potential range from 3.0 to 4.2 V with a specific capacity above 200 mA h g^{-1} .

It is known that, being heated, lithium cobaltate decomposes to evolve oxygen. This reaction is especially fast for highly dispersed powders. To enhance the cycling stability of the lithium cobaltate structure, the latter was coated with a SnO_2 film using a sol-gel technology and then annealed.¹⁵³

A similar method was used for modifying a $\text{LiSr}_{0.002}\text{Ni}_{0.9}\text{Co}_{0.1}\text{O}_2$ mixed compound.¹⁵⁴ A powder of this compound was coated with a $\text{Mg}(\text{OH})_2$ layer and then annealed. The annealing resulted in the formation of a MgO coating which prevented electrolyte oxidation during the discharge, increased the discharge capacity from 145 to 160 mA h g^{-1} and enhanced the cycling stability (the capacity fade did not exceed 0.4 mA h g^{-1} per cycle).

A LiMn_2O_4 coating was applied on the LiCoO_2 powder to protect the electrolyte from oxidation during the charge and to enhance the thermal stability of lithium cobaltate.¹⁵⁵

The use of mixed oxides, particularly, cobalt and nickel oxides, substantially improves the characteristics of lithiated oxides. Although the materials for such compounds were proposed for this use long ago, they are still being refined.^{156–159} Complex mixed oxides are also of great interest. Thus in addition to $\text{LiSr}_{0.002}\text{Ni}_{0.9}\text{Co}_{0.1}\text{O}_2$ mentioned above, a material with the composition $\text{Li}_8(\text{Ni}_5\text{Co}_2\text{Mn})\text{O}_{16}$ remarkable for its sufficiently high specific capacity ($\sim 150 \text{ mA h g}^{-1}$) and cycling stability (a capacity fade was $\sim 0.4 \text{ mA h g}^{-1}$ per cycle) deserves mention.¹⁶⁰ This material can be obtained by fine synthesis from solutions of salts of the corresponding metals in methanol and tetrahydrofuran, which is followed by controlled annealing.

Materials of the compositions $\text{LiAl}_y\text{Co}_{1-y}\text{O}_2$ have also attracted attention of scientists.^{161, 162}

The promising mixed materials with a composition described by the general formula $\text{LiCo}_{1-y}\text{Fe}_y\text{O}_2$ should be also mentioned. The cost of lithium-ion batteries based on these materials could be substantially decreased by partial substitution of cheap iron for

extremely expensive cobalt.^{163, 164} First specimens contained low ($y < 0.1$) iron fractions; however, later, materials with $y = 0.24$ were developed. Unfortunately, the resulting materials were characterised by too fast a capacity fade during cycling.

The main drawback of lithium nickelates used as the materials for positive electrodes is the impossibility of complete deintercalation of lithium. As a rule, compounds Li_xNiO_2 are cycled only in the range of $0.5 < x < 1.0$. A deeper deintercalation results in irreversible structural changes. At the same time, it was found that a material with a violated stoichiometry with the composition $\text{Li}_x\text{Ni}_{1.02}\text{O}_2$ can be cycled reversibly in the whole range of x (*i.e.*, $0 < x < 1$).¹⁶⁵

An extension of the cycle range for nickelates can be also achieved by using mixed oxides. Lithiated nickel and cobalt mixed oxides (at a small content of the latter, see, *e.g.*, Refs 166–168) are gaining in acceptance. A mixed oxide material with a layered $O2$ structure and a composition described by the formula $\text{Li}_{2/3}(\text{Ni}_{1/3}\text{Mn}_{2/3})\text{O}_2$ has been proposed.¹⁶⁹ In the structural aspect, this material resembled the layered cobaltate modification¹⁴⁸ and was also obtained by ion exchange from a sodium bronze $\text{Na}_{2/3}(\text{Ni}_{1/3}\text{Mn}_{2/3})\text{O}_2$ [or, more generally, from $\text{Na}_{2/3}(\text{Ni}_y\text{Mn}_{1-y})\text{O}_2$]. The discharge capacity of this material was $\sim 180 \text{ mA h g}^{-1}$ but the discharge curve demonstrated two steps: at a potential of $\sim 3.9 \text{ V}$, which corresponded to electron transfer to the $3d$ level of nickel, and at 2.9 V where manganese changes its valence from +4 to +3.

A series of magnesium-modified lithium nickelates with the general composition $\text{Li}_{1+x}\text{NiMg}_y\text{O}_{2+2y}$ has been described.¹⁷⁰ An introduction of magnesium resulted in stabilisation of the nickelate structure, which, on the one hand, allows its deeper delithiation, *i.e.*, increases the specific capacity and, on the other hand, reduces the capacity fade during cycling. A material with $x = 0.15$ had a specific capacity of $\sim 145 \text{ mA h g}^{-1}$, which even increased a little during the first 30 cycles. Lithiated nickel–magnesium oxides with layered structures (and approximately the same characteristics) have been described.^{171, 172}

Lithiated nickel oxides are much cheaper than lithiated cobalt oxides; however, partial substitution of iron for nickel is believed to be economically warranted. Attempts^{173, 174} for such a substitution were made, which, however, were not too successful: only the materials with the $\text{Li}_x\text{Ni}_{1-y}\text{Fe}_y\text{O}_2$ composition, where $y < 0.1$, could be cycled reversibly.

Among lithiated manganese oxides, spinels with compositions similar to LiMn_2O_4 were used most often for fabrication of positive electrodes. Intercalation of lithium into such a material (*i.e.*, during a discharge of the lithium-ion battery) resulted in formation of compound $\text{Li}_{1+x}\text{Mn}_2\text{O}_4$. Such electrodes had a rated potential value of $\sim 3 \text{ V}$. In the lithium deintercalation (the formation of $\text{Li}_{1-x}\text{Mn}_2\text{O}_4$), the potential value approached $\sim 4 \text{ V}$. Various technologies for the preparation of spinels of different compositions (LiMn_2O_4 , $\text{Li}_2\text{Mn}_4\text{O}_9$, $\text{Li}_4\text{Mn}_5\text{O}_{12}$, *etc.*) were described.^{175–184} The best results were obtained using low-temperature ‘wet’ technologies which allow finely dispersed materials to be obtained,^{177, 183, 184} although plausible high-temperature versions are known.¹⁷⁹

In studying spinels, the main attention was paid to their lattice parameters. Intercalation of lithium into a spinel was accompanied by a decrease in the a_0 parameter of the cubic lattice^{180, 182, 185} and a linear decrease in the phase-transition temperature, which was attributed to disproportionation of the spinel and a loss of a certain amount of oxygen.

A substantial decrease in the capacity during cycling, especially at high temperatures, is a drawback of lithium–manganese spinels (as well as their low specific capacity as compared with cobaltates and nickelates). The reasons for deterioration of characteristics of spinel electrodes were discussed in Ref. 186. Fourier-transform IR spectroscopic studies¹⁸⁷ have shown that self-discharge of spinel electrodes is accompanied by simultaneous oxidation of the solvent on particles of a carbon conducting additive.

Recently, attention of researchers has been attracted to non-spinel metastable and disordered lithium–magnesium structures including their monoclinic and orthorhombic modifications.^{188–195} Good characteristics of these materials are associated particularly with the high defect densities at their grain boundaries and the small sizes of grains themselves (5–20 nm). Doping spinels with small amounts of other elements, such as aluminium^{192–195} and potassium was recommended¹⁹⁶ to obtain such structures. For example, a monoclinic modification of $\text{LiAl}_{0.25}\text{Mn}_{0.75}\text{O}_2$ had a capacity of 130–150 mA h g⁻¹, being cycled in a potential range from 2.0 to 4.4 V.¹⁹² A material of the composition $\text{LiAl}_{0.05}\text{Mn}_{0.95}\text{O}_2$ had a specific capacity of 150 mA h g⁻¹ for its orthorhombic modification and ~200 mA h g⁻¹ for the monoclinic modification.¹⁹⁴ Moreover, for these materials, the capacity faded by ~0.05% per cycle, whereas for common spinels this value exceeds ~0.5% per cycle.

Yet another way of enhancing the cycling stability of positive-electrode materials is the synthesis of amorphous (or amorphised) materials, *e.g.*, complex compounds such as $\text{Li}_{1.5}\text{Na}_{0.5}\text{MnO}_{2.85}\text{I}_{0.12}$ (see Refs 197–199). Its first 40 cycles not only showed no sign for the capacity fade but also resulted in its increase from 120 to 125 mA h g⁻¹. It was suggested²⁰⁰ to use an amorphous modification of manganese dioxide Li_xMnO_2 as a starting material that can be cycled to the depth of over 400 mA h g⁻¹, which corresponds to a change in x from 0 to 1.6. It is evident that the capacity of these electrodes should be lower but are quite acceptable (260 mA h g⁻¹ in a range from 4.0 to 2.5 V).

Yet another approach to the preparation of stable materials is the use of sol–gel technology. Its version using supercritical drying is the most interesting. For example, a technology was described²⁰¹ in which, first, a hydrogel was obtained from an aqueous solution of potassium permanganate and lithium fumarate, after which water was exchanged for acetone and then hexane. The hexanogel thus obtained was dried under conditions close to critical ones. In the process, the surface tension was eliminated, and an extremely fine-grain structure retained. An electrode made of this material with the composition $\text{Li}_{0.9}\text{MnO}_{2.5}$ had a capacity of ~440 mA h g⁻¹ at a discharge up to 2.9 V. It should be noted that such electrodes could be discharged by very high currents. Thus a discharge with a current of 270 mA g⁻¹ gave a capacity of 200 mA h g⁻¹ and a discharge at 100 mA g⁻¹, *i.e.*, in a 2.5C mode,[†] resulting in a capacity of 150 mA h g⁻¹ (the maximum load tested for these electrodes corresponded to the 7.5C mode, *i.e.*, a total discharge took 8 min). A material with the composition $\text{LiAl}_{0.24}\text{Mn}_{1.76}\text{O}_{3.98}\text{S}_{0.02}$ was obtained²⁰² using the sol–gel method. Having a well defined spinel structure, this material could be cycled without any noticeable capacity loss; its capacity was 230 mA h g⁻¹. A similar material (with sulfur partially substituted for oxygen) has been described.²⁰³ A $\text{LiAl}_x\text{Mn}_{2-y}\text{O}_{4-z}\text{F}_z$ material²⁰⁴ exhibited a high cycling stability; this was attributed to the presence of a small amount of fluorine in the oxygen sublattice.

In addition to lithium–manganese spinels doped with aluminium, materials with chromium atoms partly substituted for manganese were reported to show promise for using them in lithium-ion batteries.^{205–207}

A sample of lithium–manganese spinel with a well pronounced crystalline structure (with coarse crystals) was synthesised.²⁰⁸ This material exhibited cycling stability, although its capacity was not too high (less than 80 mA h g⁻¹).

As was noted above, cobaltate particles were coated with a thin layer of manganese oxides to protect electrolytes from oxidation and enhance the thermal resistance of electrode materials.¹⁵⁵ The same group of authors have proposed a ‘reverse’

version, *viz.*, deposition of lithium cobaltate on the particles of a lithium–manganese spinel.²⁰⁹ Such a coating was applied as a gel consisting of lithium and cobalt acetates, which was followed by annealing of the specimen. This procedure allowed the authors to reduce the capacity fade from 1.1 to 0.06 mA h g⁻¹ per cycle.

The use of certain cobalt–manganese mixed spinels provides a discharge at very high potential ratings, *viz.*, ~5 V. The use of such material poses very severe requirements to the electrolyte (which should not be oxidised at a potential of ~5.3 V). In principle, the possibility of enhancing the battery voltage is a challenge. ‘Five-volt’ materials are being elaborated for several years.^{210–212} To date, two of these materials have been described, *viz.*, $\text{Li}_2\text{CoMn}_3\text{O}_8$ and LiCoMnO_4 .

In addition to lithiated cobalt, nickel and manganese oxides, other materials were suggested for use as positive electrodes, *e.g.*, lithiated chromium oxides (the capacity of ~200 mA h g⁻¹),²¹³ $\text{LiCo}_y\text{Ni}_{1-y}\text{VO}_4$,²¹⁴ LiVOPO_4 ²¹⁵ and LiFePO_4 .^{216–219} The latter compound exhibits a theoretical specific capacity of 170 mA h g⁻¹. The prospects of using these materials are still unclear, although the use of such a cheap compound as LiFePO_4 as the active material for positive electrodes seems to be challenging.

The materials based on vanadium oxides exhibited sufficiently high specific capacities; however, their voltage changed with the discharge in a very wide range, which cannot be tolerated in chemical cells designed for power supply of electronic equipment.

3. Electrolytes for lithium and lithium-ion rechargeable batteries

In lithium-ion rechargeable batteries, liquid electrolytes, which represent solutions of lithium salts in aprotic organic solvents, were used.^{220, 221} As was mentioned above, in rechargeable batteries with metallic lithium electrodes, the use of liquid electrolytes poses certain problems; hence, the efforts of researchers were focused on the search for solid polymeric electrolytes (SPE). The processes of dendrite formation and encapsulation were assumed to be eliminated at the metal lithium/SPE interface. At the same time, the possibility of using polymeric electrolytes in lithium-ion batteries was also widely discussed.

An electrolyte for a lithium-ion rechargeable battery should exhibit high conductivity. As a rule, liquid electrolytes have a conductivity in the range from 0.001 to 0.01 S cm⁻¹. The electrolyte should be resistant toward oxidation and reduction, in other words, have a wide ‘electrochemical window’.[‡] The potential range of electrolyte stability is ~5 V. As was mentioned above, the stability of electrolytes largely depends on the formation of passive films on the electrode surface. These films are conductive with respect to lithium ions and do not prevent their intercalation and deintercalation. At the same time, the films should exhibit a minimum electronic conductivity to avoid corrosion (self-discharge) of the electrode. For this very reason, the film material should not dissolve in the electrolyte. Moreover, these films should be sufficiently elastic to avoid destruction during electrode volume changes in the discharge and charge processes.

Various combinations of solvents (both individual and mixed) and lithium salts intended for use as the electrolytes were described; however, only some of them are applied in practice.

Propylene and ethylene carbonates (PC and EC) are commonly used as the solvents. Solvents based on PC are reduced on graphite negative electrodes; hence, EC was proposed as the substitute for PC. At the same time, PC has a number of advantages over EC: the solubility of lithium salts is higher in PC, its freezing point (–54 °C) is substantially lower than the freezing point of EC (+36 °C). Moreover, in certain cases, the use of PC is preferential for improvement of positive electrode characteristics. As a rule, PC and EC are used as their mixtures

[†] If a cell is completely discharged in 1 h, this mode is designated as 1C; if a cell is discharged in 2 h, the mode is designated as 0.5C or C/2; if the total discharge takes 0.5 h, then the mode is 2C, *etc.*

[‡] The difference between the potential of the beginning of anodic oxidation and the potential of the beginning of cathodic reduction.

with less viscous, although less polar, solvents such as 1,2-dimethoxyethane, dimethyl carbonate and diethyl carbonate.

Lithium hexafluorophosphate and tetrafluoroborate are used most often as lithium salts; the possibilities of using lithium hexafluoroarsenate and perchlorate were also examined. Merck (Germany) produces ready-for-use electrolytes for lithium-ion batteries of the following types: LP20, LP30 and LP40, where electrolytes represent 1 M LiPF₆ solutions in the following solvent mixtures: PC–diethyl carbonate (1 : 4), EC–dimethyl carbonate (1 : 1) and EC–diethyl carbonate (1 : 1), respectively.

In recent years, the following lithium salts were proposed for use as lithium-ion batteries, *viz.*, lithium trifluoromethanesulfonate (triflate), bis(trifluoromethylsulfonyl)imide and tris(trifluoromethylsulfonyl)methanide and their derivatives. The derivatives involved such compounds as cyclic imides Li[N(SO₂)(CF₃)_n(SO₂)], where $1 < n < 4$,^{222, 223} an asymmetrical methanide Li[C(SO₂CF₃)₂(SO₂C₄F₉)] and bismethanide Li₂[(C₂(SO₂CF₃)₄(S₂O₄C₃F₆))₂],²²⁴ imides with long fluoroalkyl chains,²²⁵ lithium hexafluorotrimethylenebis(sulfonyl)di[bis(trifluoromethylsulfonyl)methanide],²²⁶ *etc.*

Boron-containing compounds, particularly, different borates and chelatoborates were used in lithium-ion batteries as the additives that extend the potential range of electrolyte stability, increase the solubility of salts and decrease the corrosive action of the electrolyte on the current lead material (*e.g.*, aluminium).^{227–235} Of great interest is the hexamethoxycyclotriphosphazene [NP(OCH₃)₂]₃ additive, which favours a decrease in the inflammability of lithium-ion batteries.²³⁶

VII. Polymeric electrolytes for lithium-ion batteries

Among solid ionic conductors which can be used at ambient temperature, the SPE with a relatively fast ion transfer are most promising. Thin films fabricated of these polymeric electrolytes are characterised by elasticity (mobility), adequate mechanical properties, a low electronic conductivity (10^{-14} S cm⁻¹ at room temperature), a wide electrochemical window of stability (3–4 V) and are compatible with the electrodes of alkali metals.

At the same time, the use of SPE is limited due to the following reasons: first, they have a low ionic conductivity at ordinary temperatures (from 10^{-5} to 10^{-8} S cm⁻¹); second, not only lithium ions, but also anions take part in the charge transfer, which can give rise to concentration polarisation; third, like liquid electrolytes, they can form a transition layer with a high resistance upon contact with the electrode (both positive and negative) material.

Armand *et al.*²³⁷ were the first to propose the use in lithium cells of a complex of a lithium salt with a polymer [poly(ethylene oxide), PEO]. The conductivity of such a PEO–LiSCN complex system at room temperature was 10^{-8} S cm⁻¹.^{237, 238} These rechargeable batteries could operate only at temperatures above 60 °C, because it was only under these conditions that the conductivity of the electrolyte solution had acceptable values for practice. Nonetheless, the interest in these electrodes was so high that the extensive research undertaken has soon produced polymeric electrolytes with conductivities of $\sim 10^{-3}$ S cm⁻¹ at room temperature, which is comparable with the conductivity of liquid electrolytes.

An important requirement to SPE is their mechanical strength, because, to decrease the resistance, these electrodes are mainly used as thin films with thicknesses of 0.0025–0.005 cm commensurable with the thicknesses of porous separators based on polypropylene and polyethylene, which divide the electrodes in lithium batteries with liquid electrolytes. A solid polymeric electrolyte should also withstand the pressures induced by morphological changes in the electrode material during the lithium cell cycling. Thus, SPE, on the one hand, should provide ionic conduction typical of liquid electrolytes and, on the other hand,

should be spatially stable, *i.e.*, retain their solid shapes. Modern SPE fulfil all these requirements.

We can single out two large classes of polymeric electrolytes with conductivities above 10^{-5} S cm⁻¹ at room temperature. The first class involves ‘solution-free’ SPE. In addition to polymers, these SPE contain lithium salts. The second class comprises SPE ‘with solvents’, which, in addition to polymers and lithium salts, contain liquid solvents called plasticisers. These two SPE classes may have polymeric matrices with different structures.

1. Solid electrolytes with the polymer–lithium salt composition

Solid electrolytes based on crystalline polymers have low conductivities, whereas those based on amorphous polymers exhibit higher conductivities. Thus, the SPE conductivity can be increased by decreasing the degree of crystallinity of a polymer by changing its structure. Table 1 lists the characteristics of certain polymers; Table 2 lists the SPE conductivities.

Table 1. Properties of certain polymers used as the electrolyte matrices.²³⁹

Polymer ^a	Polymer unit	<i>T</i> _g / °C	m.p. / °C
PEO	–CH ₂ CH ₂ O–	–64	65
PPO	–CH(Me)CH ₂ O–	–60	see ^b
POO	–(CH ₂ O)–(CH ₂ CH ₂ O)–	–66	13
MEEP	$\begin{array}{c} \text{OCH}_2\text{CH}_2\text{OCH}_2\text{CH}_2\text{OMe} \\ \\ \text{—P=N—} \\ \\ \text{OCH}_2\text{CH}_2\text{OCH}_2\text{CH}_2\text{OMe} \end{array}$	–83	see ^b
PDMS	–Si(CH ₃) ₂ O–	–127	–40
PAN	–CH ₂ CH(CN)–	125	317
PMMA	–CH ₂ C(Me)(CO ₂ Me)–	105	see ^b
PVC	–CH ₂ CHCl–	82	see ^b
PVDF	–CH ₂ CF ₂ –	–40	171

^a The following abbreviations were used: PEO, poly(ethylene oxide); PPO, poly(propylene oxide); POO, poly(oxyethylene oligooxyethylene); MEEP, poly{bis[2-(2-methoxyethoxy)ethoxy]phosphazene}; PDMS, poly(dimethylsiloxane); PAN, poly(acrylonitrile); PMMA, poly(methyl methacrylate); PVC, poly(vinyl chloride); PVDF, poly(vinylidene difluoride). ^b Amorphous polymer.

Table 2. Composition and bulk conductivity with respect to Li⁺ ions for solid polymeric electrolytes.^{237, 238, 240}

Electrolyte	Conductivity at 20 °C / S cm ⁻¹
(PEO) ₈ LiClO ₄	10^{-5}
(PPO) ₈ LiClO ₄	10^{-8}
(POO) ₂₅ LiCF ₃ SO ₃	3×10^{-5}
(MEEP) ₄ LiBF ₄	2×10^{-5}

Back in 1979, it was pointed out²³⁸ that PEO exhibits good solvating ability towards those Li⁺ ions and ions of other metals located in a favourable position relative to the donor oxygen atoms of the polymeric chain. By changing the oxygen atom position in the chain, the solvating ability and the temperature transitions in the polymer can be changed. For example, PEO can form polymeric electrolytes with salts of alkali and transition metals.²⁴¹ Moreover, the existence of various PEO complexes with LiBF₄, LiPF₆ and LiB₄,²⁴² LiAsF₆,²⁴³ LiSCN,²⁴⁴ LiCF₃SO₃ and LiClO₄,²⁴⁵ LiN(CF₃SO₂)₂,^{246, 247} has been reported.

The use of inorganic additives in the form of fine powders of Al₂O₃ or LiAlO₂ was proposed to enhance the mechanical strength of an electrolyte based on PEO and a lithium salt.^{248–254} Such additives, first, prevent crystallisation of the polymer and, second, can absorb water, which allows one to

reduce the lithium electrode passivation. At room temperature, the ionic conductivity of an electrolyte with the composition $(\text{PEO})_8\text{LiClO}_4$ was $10^{-5} \text{ S cm}^{-1}$, whereas the conductivity of the $(\text{PEO})_8\text{LiClO}_4 + 10 \text{ mass \% LiAlO}_2$ composition was $10^{-4} \text{ S cm}^{-1}$.

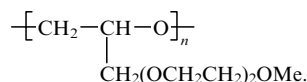
It was proposed²⁵⁵ to modify a polymeric electrolyte based on PEO and LiBF_4 using finely dispersed Al_2O_3 powders with $\sim 10 \text{ }\mu\text{m}$ particles as well as by modified particles measuring $1.3 \times 10^{-2} \text{ }\mu\text{m}$. The conductivity of the latter SPE was higher by an order of magnitude as compared with SPE modified by $10 \text{ }\mu\text{m}$ particles.

Introduction of $\gamma\text{-LiAlO}_2$ to a polymeric electrolyte based on PEO and $\text{LiN}(\text{CF}_3\text{SO}_2)_2$ resulted in a substantial decrease in the degree of crystallinity and an increase in the stability of the Li/electrolyte interface.²⁵⁶

The effect of various types of fine powders added to a polymeric electrolyte on the conductivity and mechanical strength of PEO-based SPE was also studied.^{257,258}

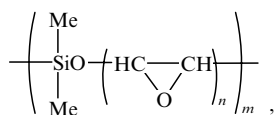
Using LiClO_4 complexes with a number of aliphatic polyesters (PEst) synthesised by a reaction of poly(ethylene glycol) (PEG) ($M_w = 300, 1000$) with diacid chlorides $(\text{ClOC}[\text{CH}_2]_n\text{COCl}$, $n = 3-8, 10$) as the examples, the effect of the polymer structure on its ionic conductivity was studied.²⁵⁹ The general composition of these complexes can be expressed by the formula $\text{PEst}(m,n)$, where m is the number of ethylene groups and n is the number of methylene groups; e.g., $\text{PEst}(6,8)$ is $[-(\text{OCH}_2\text{CH}_2)_6\text{O}-\text{CO}(\text{CH}_2)_8\text{CO}-]$. In contrast to the $\text{PEO}-\text{LiClO}_4$ system with a degree of crystallinity of 0.4, the $\text{PEst}(m,n)-\text{LiClO}_4$ systems are totally amorphous, and their ionic conductivity varies in the range from 2.5×10^{-5} to $4.1 \times 10^{-5} \text{ S cm}^{-1}$. The degree of crystallinity of PEO can be reduced by shortening its chain and decreasing its molecular mass;²⁶⁰ however, low-molecular PEO with short chains represent viscous liquids even after the formation of complexes with lithium salts and could not form SPE.

With the aim of decreasing the degree of crystallinity, comb-like polymers with short PEO side-chains attached to the main chain were synthesised, e.g., poly[2-(2-methoxy)ethoxy]ethyl glycidyl ether

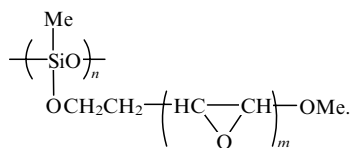


A complex of this amorphous polymer ($T_g = -57^\circ\text{C}$) with LiClO_4 had a conductivity of an order of magnitude of $10^{-5} \text{ S cm}^{-1}$ at room temperature.

A search for amorphous polymers has produced materials with highly mobile inorganic skeletons based on polysiloxanes $(-\text{SiR}_2\text{O}-)_n$ and polyphosphazenes $(\text{P}=\text{N}-)_n$. Siloxane polymers can be exemplified by poly(dimethylsiloxaneoligoethylene oxide)



and poly{[ω -methoxyoligo(ethylene oxide)ethoxy]methylsiloxane}



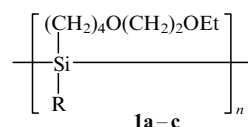
A maximum conductivity achieved using electrolytes of these types (which also represent viscous liquids) is $10^{-4} \text{ S cm}^{-1}$ (Refs 261, 262). Cross-linking of polymers decreased the conductivity to $10^{-5} \text{ S cm}^{-1}$ at room temperature. The drawback of these polymers is the sensitivity of $\text{Si}-\text{O}-\text{C}$ bonds to hydrolysis and their structural degradation with time. This problem can be

solved, e.g., by synthesising copolymers with stable $\text{Si}-\text{C}$ bonds, which has been achieved by grafting PEO to polysiloxanes.²⁶³

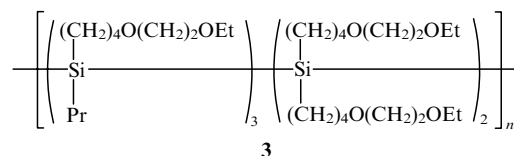
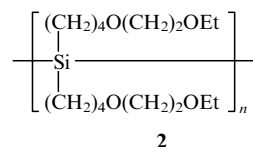
Electrolytes based on such a polymer ($-77^\circ\text{C} < T_g < -54^\circ\text{C}$) exhibited conductivities of $10^{-5} \text{ S cm}^{-1}$ at room temperature.

A modified polymeric electrolyte based on MEEP (see Table 1) was described.²⁶⁴ Complexes of MEEP with lithium salts had a low stability. The authors proposed to add LiAlCl_4 to such an electrolyte, which allowed them to fabricate MEEP- $(\text{LiAlCl}_4)_n$ films. The mechanical properties of spatially unstable MEEP-lithium salt complex systems were substantially improved as a result of formation of complexes with such polymers as PEO, PPO, poly(ethylene glycol diacrylate) and poly(vinylpyrrolidone). An electrolyte containing 55 mass % MEEP + 45 mass % PEO- $[\text{LiN}(\text{CF}_3\text{SO}_2)_2]_{0.13}$ had a conductivity of $6.7 \times 10^{-5} \text{ S cm}^{-1}$ at room temperature. Such electrolytes remained stable up to 4.5 V. A Li/TiS₂ cell with these electrolytes had a cycle life exceeding 200 charge-discharge cycles.

Results²⁶⁵ obtained in line with these studies should be considered as less successful. The authors have obtained a number of polysilane polymers: **1a-c**, **2** and **3**



R = Me (**a**), Pr (**b**), C_8H_{17} (**c**).



Polymers **1b** and **2** with 8 oxygen atoms per lithium ion exhibited a maximum ionic conductivity equal to $1.9 \times 10^{-7} \text{ S cm}^{-1}$.

The degree of crystallinity can be reduced by cross-linking the polymers. Such polymeric nets exhibited relatively high conductivities ($1.5 \times 10^{-5} \text{ S cm}^{-1}$ at 25°C for a LiClO_4 salt) and an acceptable mechanical strength. This approach was put forward in Refs 266-268 and involved cross-linking of low-molecular PEO ($M_w = 600, 1000, 2000$) and block-copolymers PEO-PPO-PEO with urethane and cyclosiloxane. Polymeric electrolytes based on PEO with $M_w = 2000$ which contained either LiCF_3SO_3 or $\text{LiN}(\text{CF}_3\text{SO}_2)_2$ and electrolytes with the composition $\text{PEG}-\text{LiCF}_3\text{SO}_3$ with an addition of poly(ethylene glycol dimethyl ether) (PEGDME) with $M_w = 500$ were studied.²⁶⁹ The following electrochemical properties of these three electrolytes were examined: ionic conductivity, electrochemical stability window, reduction and the resistance and stability of the lithium electrode/electrolyte interface. Moreover, prototypes of lithium cells with composite cathodes based on LiMn_2O_4 were tested with the aim of studying the performance of these electrolytes in solid lithium batteries. In SPE containing $\text{LiN}(\text{CF}_3\text{SO}_3)_2$, a conductivity of $10^{-4} \text{ S cm}^{-1}$ required for their practical application was achieved only at 60°C . An addition of PEGDME decreased the resistance of the lithium electrode/electrolyte interface and trebled the specific capacity (90 mA h g^{-1}).

A new method of SPE preparation by dissolving the polymers with high glass transition temperatures ($T_g > 90^\circ\text{C}$) in a LiCF_3SO_3 melt has been described.^{270,271} Such polymers as poly(*N,N*-dimethylacrylamide), poly(acrylonitrile) (PAN), poly-

(vinylpyrrolidone) and its copolymer with vinyl acetate were studied. At 45 °C, the conductivity of a PAN–LiCF₃SO₃ (75 mass %) electrolyte did not exceed 10^{−6} S cm^{−1}.

2. Plasticised polymeric electrolytes

In contrast to SPE with the polymer–salt composition, plasticised polymeric electrolytes contain organic solvents which are confined within the swollen polymeric matrix so that these electrolytes resemble rubber in their consistency. Plasticised electrolytes are also called polymeric gel-electrolytes (PGE). They can be obtained by adding plasticisers, *viz.*, polar aprotic solvents with high boiling points and high dielectric constants to SPE. Table 3 shows typical solvents-plasticisers.

Table 3. Certain organic solvents used as plasticisers.²⁷²

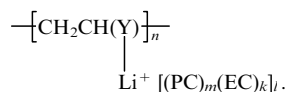
Solvent-plasticiser	m.p. /°C	b.p. /°C	Dielectric constant at 25 °C	Viscosity /10 ^{−3} Pa s
Ethylene carbonate	36	248	95.3	1.9
Propylene carbonate	−70	240	65.1	2.53
γ-Butyrolactone	−43.5	204	39	1.75
Dimethylformamide	−61	153	36.7	0.8
1,2-Dimethoxyethane ^a	−70	85	5.5	0.46

^a Used only as mixtures with high-boiling plasticisers added to decrease the viscosity.

The conductivity of PGE depends on the solvent content, its viscosity and dielectric constant. Polar solvents with low viscosities such as *N*-dimethylformamide (DMF) and γ-butyrolactone (BL) substantially increase the conductivity in lithium ions. The activation energy of conductivity decreases dramatically with an increase in the solvent-to-lithium salt molar ratio. In fact, lithium ions travel in the liquid electrolyte confined by a polymeric matrix. Hence, to obtain a PGE with an acceptable conductivity, the amount of DMF required should be only a third of that required for more viscous PC.

Solvents-plasticisers solvate Li⁺ ions facilitating their transport (this phenomenon was not observed for polyethers in which an ion travels along the polymer chain). The ‘degree of assistance’ to the ionic transport probably depends on the rate at which the ions form complexes with the polymeric chain rather than with the solvents-plasticisers.

The structures of plasticised polymeric electrolytes are still not clearly understood. The PEG structure in which Li⁺ forms a complex both with the polymeric network and the solvent has been hypothesised²⁷³ for electrolytes based on PAN (Y = CN) and PVC (Y = Cl) in a mixture of propylene carbonate–ethylene carbonate (PC/EC) solvents



To date, a large number of PGE that consist of lithium salts and plasticising organic electrolytes are known. The important advantage of PGE as compared with SPE is their high ionic conductivities at room temperature, which approaches the conductivity of liquid electrolytes. However, in practical applications of PGE, a number of other characteristics should be taken into account, *e.g.*, their ability to confine electrolyte, mechanical strength and conductivity in a wide temperature range. In particular, for multicomponent PGE, solvent losses due to leakage and vaporisation can hardly be avoided.^{274, 275} This results in a decrease in the cell resistance and impairs the electrolyte–electrode contact. The main parameter that characterises the solvent

confinement in the PGE is the affinity between the polymeric matrix and the organic solvent. This parameter also affects the mechanical strength of the PGE film and its conductivity in a wide temperature range, especially in thin-film cells which contain electrodes with high surface areas. Low degrees of affinity between a polymer and an electrolyte can result in separation of PGE into predominantly polymeric and solvent-enriched microphases. As a consequence, the mechanical strength can increase due to the formation of a polymeric network. The electrolyte electrochemical stability in lithium chemical power sources can be increased if highly polar, easily freezing solvents are used (*e.g.*, ethylene carbonate with m.p. = 36 °C). It may be assumed that an increase in the degree of solvent–polymer affinity will allow one to eliminate the problem of the increase in the PGE resistance with a decrease in the temperature, because the interaction of solvent molecules with the polymer will prevent their ordering during freezing.

Properties of PGE which contained PVDF, a copolymer of vinylidene fluoride with hexafluoropropylene (PVDF–HFP), PAN (*M_w* = 150 000) and PMMA (*M_w* = 12 000) as the polymeric components were compared,²⁷⁶ which revealed the following features. The solvent-loss rate increased in the order PMMA ≤ PAN << PVDF–HFP ≤ PVDF in accordance with the increase in the solvent affinity to the polymer and the increase in the degree of crystallinity. Polymers with low degrees of crystallinity swelled more easily and better confined the solvent, the latter being uniformly distributed throughout the polymeric matrix.

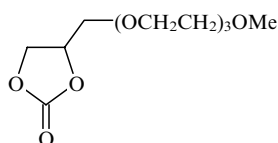
In some studies,^{277, 278} PGE based on chemically cross-linked PEO and LiBF₄ and LiN(CF₃SO₂)₂ were plasticised by PC and BL, then their ionic conductivities were compared to the conductivities of liquid electrolytes without polymers. Although the degree of dissociation of salts in PGE was higher, the conductivity appeared to be lower due to specific capture of lithium ions by the polymeric matrix.

Itoh *et al.*²⁷⁹ dissolved LiN(CF₃SO₂)₂ in PEGDME (*M_w* = 400–500) and then added γ-LiAlO₂. The solution obtained was mixed with PEO (*M_w* = 4 000 000) and a liquid electrolyte was added. The compositions thus prepared contained different amounts of the following liquid components: dimethyl carbonate (DMC), diethyl carbonate (DEC), EC and PC. These reagents were used for increasing the amorphous phase fraction in the polymeric composite membrane. Impedance measurements have shown that the maximum stability with respect to Li electrodes was observed for the following compositions (mass %): 13.6 PEO + 77.3 lithium salt solution in PEGDME + 9.1 γ-LiAlO₂ (I) and 18.2 PEO + 54.5 lithium salt solution in PEGDME + 18.2 DMC + 9.1 γ-LiAlO₂ (II). At the same time, composition (II) displayed a high ionic conductivity, *viz.*, 2 × 10^{−3} S cm^{−1} (for composition I, the ionic conductivity was 0.09 × 10^{−3} S cm^{−1}).

The main disadvantage of using PC and oligomeric ethers as the plasticisers is the low stability of the resulting films due to the solubility of the linear PEO in these solvents. To solve this problem, two approaches were suggested: (1) plasticisation of cross-linked polymeric nets which involve –CH₂CH₂O– units; (2) plasticisation of polymers which do not involve such units but are either insoluble or poorly soluble in plasticisers.

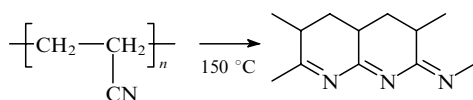
It was shown²⁷⁷ that the problem of solubility of chemically linked PEO in PC can be solved using the first approach. Although the cross-linked polymer studied was amorphous and contained the –CH₂CH₂O– unit, a non-plasticised polymeric electrolyte on its basis with addition of LiCF₃SO₃ had a conductivity of 1.4 × 10^{−6} S cm^{−1} at 25 °C. Addition of 50 mass % PC increased the conductivity of the system to 8 × 10^{−4} S cm^{−1}, while the mechanical properties allowed its application as a film.

A new plasticiser, *viz.*, a modified carbonate (MC), was synthesised,²⁸⁰ by addition of three ethylene oxide groups to propylene carbonate.



The conductivity of a PEO–LiCF₃SO₃ complex rapidly increased to 5×10^{-5} S cm⁻¹ at room temperature upon introduction of 50 mass % MC. It was assumed that this plasticiser increases the conductivity throughout the complex system bulk, in contrast to common plasticisers that provide conduction only in the liquid phase. It was assumed that MC favours a deeper dissociation of the salt as compared with PC.

A large number of studies were devoted to PAN-based PGE obtained by heating the polymer, plasticiser and lithium salt to 130–150 °C, which resulted in cross-linking along the C–N bonds



Although the amount of PAN did not exceed 20 mass %, the electrolyte obtained resembled rubber in its consistency.

Table 4 shows the conductivities of PGE based on PAN with additions of lithium salts such as LiClO₄, LiAsF₆, LiCF₃SO₃, LiN(CF₃SO₂)₂ and LiPF₆ (Refs 273, 281). PC, EC, BL, *N*-methylpyrrolidone (*N*-MP) and their mixtures were used as plasticisers.

Table 4. Conductivities of electrolytes based on PAN at 20 °C.

Electrolyte composition (mol. %)	Conductivity at 20 °C / S cm ⁻¹
21 PAN + 38 EC/33 PC + 8 LiClO ₄	1.7×10^{-3}
21 PAN + 38 EC/33 PC + 8 LiAsF ₆	2.1×10^{-3}
16 PAN + 68 PC + 16 LiClO ₄	8.6×10^{-4}
21 PAN + 18 BL/20 EC/33 PC + 8 LiClO ₄	2.3×10^{-3}
21 PAN + 40 EC/36 PC + 3 LiN(CF ₃ SO ₂) ₂	1.5×10^{-3}
21 PAN + 61 EC/13 PC + 5 LiCF ₃ SO ₃	1.1×10^{-3}
21 PAN + 61 EC/13 PC + 5 LiBF ₄	3.5×10^{-4}
21 PAN + 33 PC/30 BL/8 <i>N</i> -MP + 8 LiPF ₆	2.2×10^{-3}

Polymeric gel-electrolytes based on PAN were also modified by introducing crown ethers such as 15-crown-5 and benzo-15-crown-5.²⁸² Earlier, the effect of these crown ethers as well as 2,4-dioxo-16-crown-5 on the conductivity of PEO-based solid electrolytes was studied.²⁸³ It was found that the introduction of 15-crown-5 and 2,4-dioxo-16-crown-5 increases the ionic conductivity of a film electrolyte approximately by an order of magnitude, whereas the addition of benzo-15-crown-5 does not affect this electrolyte characteristic. A gel-electrolyte with the following composition: 8.5 mass % PAN + 81 mass % PC + 3 mass % LiClO₄ + 7.5 mass % 15-crown-5 had a conductivity of 10^{-3} S cm⁻¹ at 20 °C.²⁸²

Films prepared of a composite polymeric electrolyte involving zeolite powder dispersed in a PAN-based gel with an addition of LiAsF₆ were studied.²⁸⁴ Gel-electrolytes based on a mixture of PC/EC and PAN with addition of LiAsF₆ had ionic conductivities exceeding 10^{-3} S cm⁻¹ at room temperature. The addition of zeolite powder increased the ionic conductivity at low temperatures due to high degrees of amorphousness of the composites. The lithium electrode/electrolyte interface was studied using the impedance spectroscopy technique. The resistance of charge transfer across the Li/PGE interface was found to decrease, which indicates a decrease in the area occupied by the passive film on the surface of lithium. According to results of cyclic voltammetry, for Li/LiCoO₂ cells, an introduction of PAN and zeolite powder into a PC/EC electrolyte containing LiAsF₆ did

not change the window of electrochemical stability, and, at a current density of 0.5 mA cm⁻², the capacity loss during cycling did not exceed the corresponding values for liquid electrolytes.

A highly conducting PAN-based PGE was prepared²⁸⁵ using EC/DMC solutions of either LiPF₆ or LiC(CH₃SO₂)₃ as the plasticisers. The PGE preparation involved the following stages:

- (1) dissolution of a lithium salt in EC/DMC;
- (2) addition of PAN to the solution obtained and stirring for several hours at room temperature;
- (3) casting of the resulting liquid solution on an aluminium support preheated to 90 °C for no longer than 30 s for cross-linking of PAN;
- (4) cooling of the gel obtained to room temperature.

A LiPF₆ + EC + DMC + PAN composition with a molar ratio of 4 : 60 : 20 : 16 had a conductivity of 5.9×10^{-3} S cm⁻¹ and a break-down voltage of 4.5 V.

Ionic conductivity of a polymeric electrolyte based on PAN and lithium methacrylate (PAN–LiMA) with an addition of EC-dissolved LiClO₄ was 2.4×10^{-4} at 10 °C and 1.9×10^{-3} S cm⁻¹ at 25 °C.²⁸⁶

A copolymer of acrylonitrile with butadiene had an ultimate strength of 3.0 MPa and a conductivity of 10^{-3} S cm⁻¹.²⁸⁷

A new copolymer of PAN with bis[2-(2-methoxyethoxy)-ethyl]itaconate (PANI) was synthesised.²⁸⁸ The maximum conductivity, namely 1.9×10^{-3} S cm⁻¹, was found for a gel-electrolyte of the following composition: 25 mass % PAN + 10 mass % PANI + 50 mass % EC/BL + 15 mass % LiClO₄.

Polymeric electrolytes were also prepared based on PVC.²⁸⁹ They were obtained by dissolution of PVC in THF and subsequent addition of plasticisers with lithium salts. Then, the solution was cast on a support and dried at room temperature up to complete evaporation of THF. For an electrolyte of the following composition: 15 mass % PVC + 40 mass % PC + 40 mass % EC + 5 mass % LiClO₄, the conductivity of 1.2×10^{-3} S cm⁻¹ was reached at room temperature. Attempts to prepare an electrolyte by dissolving PVC directly in PC and EC have failed,²⁹⁰ because these polymers do not dissolve PVC even at elevated temperatures. This obstacle was bypassed using THF which dissolves all the electrolyte components.

The use of PVDF and PC-solutions of LiClO₄ as the polymeric matrix and the plasticiser, respectively, made it possible to obtain PGE with a conductivity in the range from 10^{-5} to 10^{-3} S cm⁻¹ at room temperature.²⁹¹

In recent years, the active search for polymeric composites as well as binary and ternary copolymers which can be used as polymeric matrices for electrolytes has been in progress.^{292–299}

It was shown^{282, 300, 301} that, being used as effective protective coatings for lithium electrodes, the polyacetylene (PA)/porous polyethylene (PE) and PA/polypropylene composites play the additional role of electrolyte carriers and conductors, because PA present in their compositions exhibit both ionic and electronic conductivity.

A constantly increasing number of publications devoted to synthesis of new PGE using photopolymerisation have appeared in recent years.^{302, 303} For example, this method was used for the synthesis of poly(ethylene glycol diacrylate). Synthesis of a gel-electrolyte by UV-irradiation of a mixture of oligo(urethane methacrylate) and poly(ethylene glycol monomethacrylate) has been reported;^{304, 305} the PGE conductivity was of an order of magnitude of 10^{-3} S cm⁻¹.

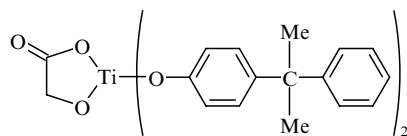
An ethylene oxide/propylene oxide (80 : 20) copolymer with acrylate groups at the macromonomer's termini that could be cross-linked under the action of UV-radiation was synthesised.³⁰⁶ EC/PC (1 : 1, by volume); EC/BL (1 : 1, by volume); PC; PC/BL (1 : 1, by volume); BL and LiBF₄ (1 M) were used as the plasticisers. The polymeric films obtained exhibited good mechanical properties in a wide range of concentrations of additives to liquid electrolytes. Their shear moduli decreased with an increase in the liquid component content, however, remaining sufficiently high, viz., 10 MPa even for a liquid content of 90 mass %. The ionic

conductivity of a composition with 1 M LiBF₄/BL decreased from 3 to 1×10^{-3} S cm⁻¹ with a decrease in the temperature from +20 to -20 °C.

Recently, it was proposed to use ternary copolymers as the polymeric gel-electrolytes.³⁰⁷ For example, ternary polymeric electrolytes were prepared by casting from a solution of a homogeneous mixture containing 18 mass % poly[(acrylonitrile)(methyl methacrylate)styrene] [poly(AMS)], 73 mass % 1 M LiClO₄ solution in EC/DMC (1:1, by volume) and 9 mass % silica. The Li/PGE/carbon cell had a reversible capacitance of 305 mA h g⁻¹ in a voltage range of 0.01–1.5 V and a cycling efficiency of 99%.

The next work by the same authors³⁰⁸ dealt with a PGE which contained 12 mass % poly(AMS), 75 mass % plasticiser and 13 mass % SiO₂. The plasticiser represented a 1 M solution of LiBF₄ in either EC/DMC (1:1, by volume) or EC/DMC/BL (5:4:1, by volume) (BL was added to increase the ionic conductivity). LiCoO₂ was used as the cathodic material. Indeed, the LiBF₄ + EC + DMC + γ -BL electrolyte added to the polymer has demonstrated a somewhat higher ionic conductivity (6.1×10^{-3} S cm⁻¹) as compared with the LiBF₄ + EC + DMC electrolyte (5.2×10^{-3} S cm⁻¹). The PGE films obtained were 60–80 μ m thick and had satisfactory mechanical properties.

Composite electrolytes based on a mixture of lithium-ion-conducting ceramics Li_{1.3}Al_{0.3}Ti_{1.7}(PO₄)₃ and a poly(ether urethane) electrolyte have been proposed.³⁰⁹ Electron microscopy studies have shown the ceramic and polymeric phases to be divided by ~ 1 μ m interlayers. The conductivity of a dry composite did not exceed that of the initial polymeric electrolyte. Under the action of solvent vapour (DMF, acetonitrile, water), the conductivity increased substantially as compared with a polymer subjected to a simpler plasticisation procedure. Treatment of the ceramics with a compatibilising agent



improved the adhesion on the polymer–ceramics interface but decreased the total conductivity of the specimen studied.

A polymeric matrix has a strong effect on the dendrite formation in PGE. Inhibition of lithium dendrite formation in a PAN-based electrolyte was studied.³¹⁰ The electrolytes used were obtained by dissolving PAN (up to 17 mass %) in a PC/EC solvent mixture (1:1, by volume) containing LiClO₄ (1 M) at 120–140 °C with subsequent cooling to -15 °C for 16 h. Upon electrodeposition of lithium for 1 h from liquid electrolytes containing up to 3 mass % PAN, dendrites were observed to be formed on the lithium/electrolyte interface, whereas in a gel-electrolyte (5 mass %–17 mass % PAN) their formation was suppressed. Taking into account the increase in the bulk resistance with an increase in the PAN content, its optimal concentration in the electrolyte was found to be 5 mass %–10 mass %.

A metallic lithium electrode in contact with a gel-like PAN-based electrolyte which contained two lithium salts (LiBF₄ and LiPF₆) was precycled to decrease the bulk resistance.³¹¹ The cycling was carried out in the range from +0.5 to -0.5 V at 20 °C immediately after the Li/PGE/Li cell was assembled. For cells with LiBF₄-containing PGE, the impedance values measured after storage for 230 days at 20 °C were below 100 Ω . Cells with LiPF₆ needed to be precycled at the potentials > 0.5 V and at 60 °C. The impedance values at 10 kHz that determine the bulk resistance of the gel-electrolyte were the same for both types of cells and remained unchanged during storage. This was also confirmed by the example of a Li/PGE/(1,3,4-thiadiazole-2,5-dithiol + polyaniline-based composite cathode) cell. According to XPS data, only a LiF–LiOH layer was retained upon cycling in a gel-electrolyte containing LiBF₄, whereas, in a gel-electrolyte containing LiPF₆, a dense and thin LiF interlayer was ‘incorporated’

into the LiF–LiOH mixed layer. It was assumed that the layer containing LiF and LiOH formed during preliminary cycling stabilises the Li/PGE interface.

Electrolyte based on the following polymers were studied:³¹² dimethyl ether of tetra(ethylene glycol) (tetraglyme), dimethyl ether of poly(ethylene glycol) ($M_w = 400$) and poly(methylene ethylene oxide). The study was aimed at elucidation of the kinetics of decomposition of liquid and solid polyether electrolytes, which contained either LiPF₆ or complexes based on this salt and exhibited high thermal stability and advanced electrochemical properties resembling those of a pure salt. Lithium bis(diglyme) hexafluorophosphate³¹³ and lithium (pentamethyldiethylenetriamine) hexafluorophosphate³¹⁴ were shown to exhibit advanced thermal stability and conductivity in nonaqueous media.³¹⁵

In recent years, attention is focused on electrolytes based on the PVDF–HFP copolymer called Kynar in the industry. Using LiClO₄, LiPF₆³¹⁶ and LiN(CF₃SO₂)₂,³¹⁷ as well as the EC/ethyl methyl carbonate plasticising mixtures, the PVDF–HFP electrolyte films with advanced mechanical and electrochemical properties were obtained. In another study,³¹⁸ PVDF–HFP membranes were first cast using such solvents as acetone, THF, ethyl methyl ketone and *N*-MP and then impregnated with a 1 M solution of LiBF₄ in PC. The polymeric electrolytes obtained had a conductivity of an order of magnitude of 10^{-3} S cm⁻¹.

Syntheses of new gel-electrolytes based on PVDF^{319–321} and PVDF–HFP^{322–327} have been reported.

The search for new polymeric electrolyte compositions for lithium-ion cells is in progress. About 100 publications on this subject appear annually. For a deeper insight into the state-of-the-art of this field, the readers are directed to the reviews^{239, 328, 329} and the book.²⁴²

VIII. Conclusion

In the past decade, lithium-ion rechargeable batteries have occupied a significant place in the power source market. They are extensively used in portable electronic devices. At present, active research on the development of large batteries, particularly, for electric vehicles is in progress. Success achieved in elaboration of lithium-ion cells is determined by the progress in the research fields of intercalation processes and development of high-performance intercalation materials. Despite the evident achievements, many problems remain to be solved.

While this review was in the stage of preparation, interesting publications devoted to lithium rechargeable batteries have appeared. For example, interesting information can be found in the Proceedings of the 10th International Meeting on Lithium Batteries which took place in Como (Italy) in 2000 (see Refs 330–353) as well as from the materials of the Joint Meeting of the International Society of Electrochemistry and the Electrochemical Society (USA) held in San-Francisco (USA) in 2001.^{354–390} The studies that deal with nanomaterials (such as fullerenes and nanotubes) used for negative electrodes in lithium-ion cells³⁸⁴ and, as a consequence, the new developments in the technology of nanosize materials^{341, 346, 354, 373, 390} deserve attention.³⁸⁴ The research aimed at the development of new materials for both negative^{347, 349, 350, 364, 382, 386, 387} and positive electrodes^{332, 360–362, 368, 370} as well as for electrolytes^{330, 345, 362, 375} is noteworthy. Finally, generalising reviews^{329, 335, 340, 376} should be mentioned.

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Structure of X-ray photoelectron spectra of lanthanide compounds†

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Abstract. The results of the X-ray photoelectron spectroscopy studies of the electronic structures of trifluorides, oxides and other compounds of Sc, Y and lanthanides (Ln) from La to Lu, except for Pm, in the binding energy range from 0 to 1350 eV are generalised. The established dependences of the Ln4f binding energies and the relative intensities of lines on the atomic number Z do not contradict the theoretical data stating that the Ln4f atomic orbitals (AO) participate markedly in the formation of molecular orbitals (MO) in the lanthanide compounds. It is established that inner valence molecular orbitals (IVMO) composed of the metal Sc3p, Y4p, Ln5p AO and the ligand L(O,F)2s AO are formed in these systems in addition to the outer valence molecular orbitals (OVMO). It is shown that the spectral fine structure caused by multiplet splitting, many-body perturbation and dynamic effects is correlated with the lanthanide oxidation state, the spin state of ions and the mechanisms of the secondary electronic processes accompanying the photoemission and can serve as a characteristic for identification of lanthanide compounds. Charge induction is discussed using titanium and niobium double oxides as examples. The bibliography includes 206 references.

I. Introduction

The lanthanide (Ln) group includes elements with atomic numbers (Z) in the $58 \leq Z \leq 71$ range. Together with scandium, yttrium, and lanthanum, they form the class of rare earth elements (REE) and can be divided into two subgroups, namely, cerium [(La), Ce, Pr, Nd, Pm, Sm, Eu] and yttrium (Gd, Tb, Dy, Ho, Er, Tm, Yb, Lu) subgroups. The electronic configurations of lanthanide atoms can be expressed by the general formula $\{Xe\}4f^n5d^m6s^2$, where $0 \leq n \leq 14$, $m = 0, 1$. In the ground state, lanthanides, except for lanthanum, gadolinium, lutetium and, possibly, terbium, contain no Ln5d electrons ($m = 0$); however, transition of one or two electrons from the Ln4f to the Ln5d shell does not require much energy. In compounds, lanthanides can

exhibit different valences, II, III and IV, the trivalent state being the most typical.^{1–4}

Metallic lanthanides, their chemical compounds and alloys are extensively used in various branches of science and engineering. Thus the rare earth element alloys of the SmCo₅ type are used to produce permanent magnets possessing tremendous energy.^{5,6} Samarium, europium and gadolinium, characterised by high absorption ratios for thermal neutrons, and their compounds are used in nuclear industry. Oxides of these lanthanides are parts of protective ceramic coatings of nuclear reactors; they are suitable for the manufacture of control rods.⁵ Lanthanide additives are used in catalysis.^{7,8} Yttrium, lanthanum and other lanthanides are employed to produce high-temperature superconductors. The development of efficient processes for the isolation of pure lanthanides and for the preparation of their compounds possessing specified physicochemical properties requires the knowledge of their electronic structures and types of chemical bonding. For this purpose, rare earth metals are actively studied by X-ray photoelectron spectroscopy (XPS).^{9–17}

Currently, XPS studies of the electronic structures of substances are performed using expensive spectrometers operating with both X-ray and synchrotron exciting radiations. However, the use of these spectrometers for the investigation of lanthanide compounds is associated with a number of problems because, due to the presence of unpaired Ln4f electrons and specific features of chemical bonding in these compounds and to secondary electronic processes which accompany electron photoemission, the X-ray photoelectron (XPS) spectra of these compounds in the binding energy (E_b) range from 0 to 1350 eV (in which the XPS spectra are normally recorded) contain complex fine structures. This hampers the quantitative elemental analysis of lanthanide compounds and makes difficult the determination of their oxidation states on the basis of the traditional characteristics of the XPS spectra (line intensities and chemical shifts). Therefore, the efforts of researchers are concentrated on the interpretation of the fine structure of the spectra of lanthanide compounds, elucidation of the reasons for its appearance and identification of the relationship between the spectral structure characteristics and the physicochemical properties of compounds.^{5,18}

Thus the effect of the degree of occupancy of the Ln4f shell of lanthanide compounds on the structure of their spectra and the giant Coster-Kronig electron transition phenomenon (dynamic effect) within the core and valence electron shells have been studied by XPS.^{19,20} In addition, the degree of participation of relatively low-lying occupied orbitals of neighbouring atoms in

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the formation of inner valence molecular orbitals (IVMO) has been determined.¹⁸ Since an increase in the atomic number (Z) of lanthanides in the range of $57 \leq Z \leq 71$ entails an increase in the $\text{Ln}5p_{3/2}$ electron binding energy [$E_b(\text{Ln}5p_{3/2})$] in their oxides from 17.7 to 27.5 eV, while the oxygen $\text{O}2s$ electron binding energy [$E_b(\text{O}2s)$] is an intermediate value, these compounds are convenient objects for investigating the influence of the difference between the energies of the $\text{Ln}5p$ and $\text{O}2s$ atomic orbitals (AO) on the efficiency of their participation in the IVMO.¹⁸ For example, the $\text{Ln}-\text{O}$ bond lengths (R) in the lanthanide oxides Ln_2O_3 are rather great (~ 0.240 nm); therefore, the formation of IVMO for lanthanide oxides of the beginning of the row is not very efficient. However, in the case of LnO oxides in the gas phase, the $\text{Ln}-\text{O}$ distance is rather short (~ 0.180 nm);²¹ therefore, participation of the $\text{Ln}5p$ and $\text{O}2s$ AO in the formation of IVMO can be substantial; this should be taken into account when investigating the interaction between the atoms contained in the monoxides.

Analysis of the fine spectral structure (besides line intensities and chemical shifts) extends substantially the scope of XPS in the study of lanthanides and their compounds. This is the most adequate technique for determination of the lanthanide oxidation states in compounds, which is widely used in practice.^{6, 7, 12–17, 22–33} Considerable attention is also devoted to the theoretical examination of the multielectron processes which accompany the photoemission of electrons and account for the fine structure observed in the XPS spectra.^{34–41}

In this review, we present the results of XPS investigations of the electronic structures of several series of stable compounds of lanthanides (except for Pm, which is difficult to obtain), Sc, Y and La. The correlations between characteristics of the XPS spectra, physicochemical properties of these compounds and the nature of chemical bonding in them are discussed. Attention is focused on lanthanide trifluorides and oxides. The lanthanide compounds under consideration are rather stable against oxidation in air, high vacuum and X-radiation. Since some of lanthanide oxides have a variable stoichiometric composition inconsistent with the general formula Ln_2O_3 , analysis of the structures of the XPS spectra of these compounds is accompanied by comparison with analogous spectra of some LnL_3 complexes containing Ln^{3+} ions and organic ligands (L). These compounds can be regarded as clusters consisting of condensed molecules rather than as solids with a band electronic structure. Conversely, lanthanide oxides and niobates are solids in which the lanthanide ions occupy the crystal lattice points and are surrounded by oxygen atoms.

II. Lanthanide trifluorides

The lanthanide trifluorides LnF_3 ($\text{Ln} = \text{La}-\text{Lu}$, except for Pm) are relatively stable compounds; the metal ions Ln^{3+} in them are formally trivalent.^{1–4} No noticeable changes were detected in the XPS spectra of these compounds during recording of the spectra using the sample preparation procedure proposed by Teterin *et al.*⁴² In addition to this study,⁴² data on the XPS spectra of some lanthanide fluorides can be found in other publications.^{43–54}

The X-ray photoelectron spectra of lanthanide trifluorides in the binding energy range from 0 to 1350 eV exhibit fine structure for virtually all electron levels.^{42, 52, 55} To analyse XPS spectra and elucidate the relationship between the structural characteristics and the properties of substances, it is convenient to distinguish three conventional spectral ranges.

1. Electron binding energy in the range from 0 to ~ 15 eV. For lanthanide trifluorides, this range of XPS spectra exhibits a poorly resolved structure related to the electrons of outer valence molecule orbitals (OVMO), which are largely formed from the partially filled $\text{Ln}5d$, $\text{Ln}6s$ and $\text{F}2p$ AO. A structure caused by $\text{Ln}4f$ electrons also arises in this region. Theoretical calculations suggest^{54–59} significant participation of the $\text{Ln}4f$ AO in the formation of the OVMO in lanthanide compounds. In this case, in analysis of the chemical bond, the $\text{Ln}4f$ electrons cannot,

generally speaking, be classified as core electrons (as was traditionally considered before).

2. Electron binding energy in the range from ~ 15 to 50 eV. In this region, XPS spectra show relatively well resolved structure due to the electrons of the inner valence MO (IVMO),^{18, 42, 52, 55, 60–63} which are mainly composed of low-energy occupied $\text{Ln}5p$, $\text{Ln}5s$ and $\text{F}2s$ AO of neighbouring atoms. The structure of the IVMO spectra can be used to characterise the structures of the compounds under study and even to estimate the bond lengths in them.

3. Electron binding energy of > 50 eV. This XPS range is typical of electrons of inner (core) MO; specifically, for lanthanide trifluorides, the spectra of the core AO are mainly recorded. These include the $\text{Ln}3p_{3/2}$, $\text{Ln}3d$, $\text{Ln}4s$, $\text{Ln}4p$, $\text{Ln}4d$ and $\text{F}1s$ AO. Both the energy region of the binding energies of these electrons and the low-energy part of the XPS spectra of the compounds in question can be subject to various effects resulting in a more complex spectral structure.^{18, 38–40} Since these effects can arise simultaneously in any binding energy region, when interpreting spectral structure corresponding to individual shells, one should also take into account the structure displayed in other spectral regions. Therefore, when investigating lanthanide compounds by the XPS method, it is expedient to measure the spectrum over the whole experimentally accessible range (Table 1). It should be noted that one or another mechanism giving rise to the fine structure shows itself with variable probability in the spectra of electrons of different shells; this markedly facilitates interpretation of the spectra.

To identify the structural features of the low-energy XPS spectra of lanthanide fluorides, the spectra of scandium and yttrium fluorides have also been studied.^{52, 55}

1. The spectral region of electrons of the outer valence molecular orbitals

The spectra of the outer valence MO of scandium, yttrium and lanthanum trifluorides,^{52, 55} which contain no $4f$ electrons, are largely due to the $\text{M}nd$, $\text{M}(n+1)s^2$ and $\text{F}2p$ electrons of the neighbouring metal (M) and fluorine atoms, respectively (Fig. 1). They are displayed as 3.7-, 3.3- and 2.9-eV wide bell-shaped lines with smeared structures characterised by weighted-mean electron binding energies of 8.9, 8.9 and 8.4 eV, respectively. Comparison of these values with the positions of the maxima of these broadened lines (see Table 1) shows that the line in the spectrum of YF_3 is the most symmetrical. The lines related to the $\text{F}2p$ and $\text{F}2s$ electrons are approximately 21 eV apart (see Table 1). In the spectra of lanthanide trifluorides containing $\text{Ln}4f$ electrons, the line intensity markedly increases with an increase in the metal nuclear charge (Z) due to the increase in the number of these electrons (n_{4f}) (Fig. 2). With the assumption that the $\text{Ln}4f$ electrons do not participate in the formation of chemical bonds in the trifluorides, the spectral structure should be mainly governed by the final state of the ion which arises after photoemission of an $\text{Ln}4f$ electron.^{43, 51, 53, 54, 64–67}

In the XPS spectra of LnF_3 for lanthanides at the beginning of the row, the $\text{Ln}4f$ lines are located at lower binding energies than the OVMO lines (Fig. 3, see also Fig. 2). As the atomic number (Z) of lanthanides and, correspondingly, the n_{4f} number increase (the relationship between these values is considered below), the binding energy of the $\text{Ln}4f$ electrons noticeably increases, and their spectrum overlaps with the line of the OVMO electrons.^{37, 67, 68}

Ln^{3+}	n_{4f}	Z	Ln^{3+}	n_{4f}	Z	Ln^{3+}	n_{4f}	Z
La^{3+}	0	57	Sm^{3+}	5	62	Ho^{3+}	10	67
Ce^{3+}	1	58	Eu^{3+}	6	63	Er^{3+}	11	68
Pr^{3+}	2	59	Gd^{3+}	7	64	Tm^{3+}	12	69
Nd^{3+}	3	60	Tb^{3+}	8	65	Yb^{3+}	13	70
Pm^{3+}	4	61	Dy^{3+}	9	66	Lu^{3+}	14	71

Table 1. Electron binding energies (E_b , eV) for the basic lines and satellites in the XPS spectra of lanthanide trifluorides.⁴²

Compound	OVMO	Ln5 $p_{3/2}$	Ln5 $p_{1/2}$	F2s	Ln5s	Ln4 $d_{5/2, 3/2}$	Ln4 $p_{3/2, 1/2}$ (see ^{a, b})	Ln4s	Ln3 $d_{5/2}$ (see ^b)	Ln3 $d_{3/2}$	F1s
LaF ₃	—; 8.1	18.6	20.8	29.3	36.4	104.4; 107.5; 120.3; 134.6; 137.7	198.1; 203.4; 213.1; (231.5)	276.9	837.3; (841.6)	854.1; (858.3)	685.1
CeF ₃	3.4; 8.4	19.4	22.4	29.5	38.0	110.7; 112.8; 125.7; 135.7; 143.2	208.2; 223.9; 243.5; 250.1	289.4; 291.0	884.7; (888.2)	903.3; (906.3)	685.4
PrF ₃	5.2; 8.3	20.1	23.8	29.6	39.4; 40.5	118.4; 137.2; 147.6; 151.8; 169.6	219.1; 233.4; —; (251.4)	306.5; 309.5	934.4	955.2	685.3
NdF ₃	6.5; 8.0	20.7	24.4	29.4	40.4; 41.7	122.8; 139.4; 136.3; 154.0; 160.0	229.6; 246.4; 259.9; (266.0)	319.0; 321.8	982.6	1005.6	685.1
SmF ₃	7.5; 9.2	22.1	26.4	29.7	43.1; 45.5	132.3; 134.5; 137.3; 154.1; 164.0	251.8; 269.0	348.2; 352.1	1084.4; (1099.4)	1111.4	685.2
EuF ₃	8.3; 11.8	22.4	unknown	29.2	43.8; 46.4	137.1; 142.6; 152.0 158.7; 168.2	261.9	365.5; 370.2	1135.3	1164.8; (1167.5)	685.0
CdF ₃	—; 9.8	22.9	the same	29.2	45.4; 48.5	143.4; 148.6; 159.3 172.0; 183.0	272.7; 278.7; 289.4	379.8; 388.1	1187; (1200.2)	1219.8	684.8
TbF ₃	4.2; 9.4	23.9	"	29.1	46.8; 49.5	147.5; 151.2; 155.0; 167.0; 178.8	288.5; 306.6; —; (322.6)		1242.6	1277.3	685.1
DyF ₃	5.9; 9.7	24.5	"	29.4	49.2; 51.5	155.1; 157.3; 162.1; 173.6; 183.9	297.3; 301.3; —; (336.9)	415.4; 421.1	1297.6	1335.6; (1351.0)	685.2
HoF ₃	8.0; 11.1	26.2	33.0	30.4	50.3; 52.3	163.1; 168.1; 177.2; 187.0; 191.4	309.9; 315.0; 322.6; (347.0)	433.7; 438.2	1356.5; (1346.1)	unknown	685.2
ErF ₃	7.7; 10.8	26.1	32.9	29.7	53.8; 55.1	170.2; 173.6; 185.1; 194.1; 197.7	321.3; 327.3; —; (366.7)	452.1; 455.6	unknown	the same	685.4
TmF ₃	7.5; 10.8	26.8	34.0	29.8	55.0; 56.0	177.9; 201.0; 185.8; 192.4; 204.1	334.4; 339.6; —; (392.4)	470.9; 472.4	the same	"	685.4
YbF ₃	8.8; 12.6	27.2	34.7	29.6	57.0; 57.7	186.3; 189.3; 194.1 200.7; 206.2	347.2; 351.2; —; (399.0)	489.3; 491.3	"	"	685.2
LuF ₃	—; 10.2	28.4	35.7	unknown	59.0	197.3; 207.3	361.1; 414.3	508.9	"	"	685.5
YF ₃	—; 8.9	26.1 ^c	unknown	29.9	47.1 ^d	159.4; 161.3 ^e	302.5; 314.5 ^f	397.0 ^g	—	—	685.2
ScF ₃	—; 8.7	33.9 ^h	the same	29.4	55.3 ⁱ	unknown	405.0; 409.3 ^j	503.9 ^k	—	—	685.6

Note. The binding energies are presented for the peaks with respect to the C1s binding energy for hydrocarbons on the sample surface [$E_b(\text{C1s}) = 285.0$ eV]. ^a Weighted-mean energies for electrons in a complex structure. ^b The values in parentheses are satellite or shoulder energies. ^c The Y4 $p_{3/2, 1/2}$ line. ^d The Y4s line. ^e The Y3 $d_{5/2, 3/2}$ lines. ^f The Y3 $p_{3/2, 1/2}$ lines. ^g The Y3s line. ^h The Sc3 $p_{3/2, 1/2}$ line. ⁱ The Sc3s line. ^j The Sc2 $p_{3/2, 1/2}$ lines. ^k The Sc2s line.

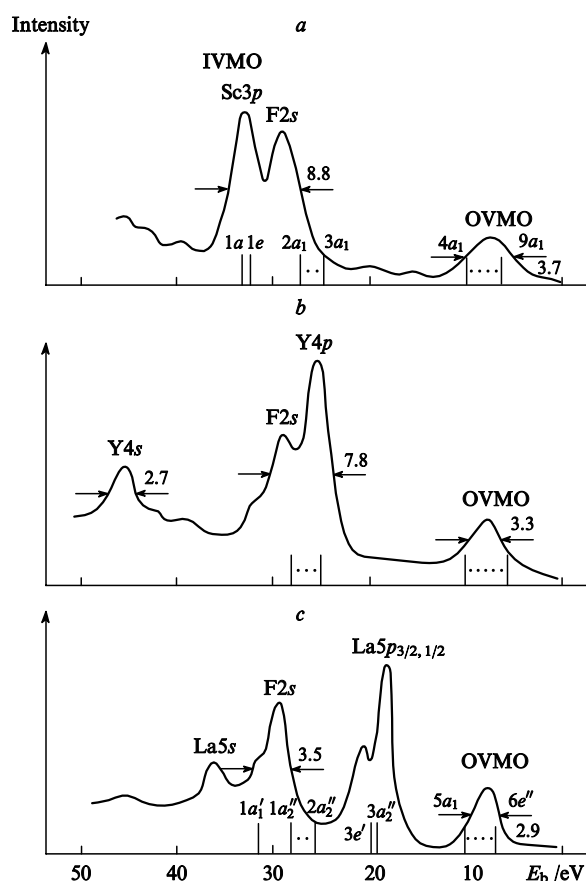


Figure 1. XPS spectra of scandium (a), yttrium (b) and lanthanum (c) trifluorides.⁵ The vertical segments show the MO energies for the ScF_6^{3-} (C_3 symmetry), YF_9^{6-} (asymmetrical) and LaF_{11}^{8-} (D_{3h} symmetry) clusters calculated in the self-consistent field (SCF) X_α -DV (discrete variation) approximation.⁶³

Starting from terbium, the spectrum of $\text{Ln}4f$ electrons starts exhibiting an extra line located at a lower binding energy than the most intense component. As the $\text{Ln}4f$ shell is being filled, this line grows approaching in intensity the high-energy component (see Fig. 2). In the $\text{Tb}4f$ spectrum of TbF_3 , this line is located at a distance of 5.2 eV from the second component. The observed splitting can be qualitatively considered using Tb^{3+} as an example.⁴³ The Tb^{3+} ion occurs in the $(4f^7)(4f^1)^1$ state, which implies the $^7F_6$ term, i.e., the $\text{Tb}4f$ shell is occupied by more than half. Photoemission of one $\text{Tb}4f$ electron gives rise to two final states: $(4f^7) - ^8S$ term and $(4f^7)(4f^1)^1 - ^{2s+1}L_J$ term. Since the former can be attained in only one way and the latter, in seven ways, the intensity ratio of the two components arising in the $\text{Tb}4f$ spectrum is expected to be 1 : 7; this is close to the experimental value (see Fig. 2).

The photoemission of an electron with the $\beta(\downarrow)$ spin is known^{43,69} to require less energy than the removal of an electron with the $\alpha(\uparrow)$ spin. The results of SCF X_α -DV (discrete variation) calculations (with allowance for spin polarisation)⁶⁹ for exchange splitting in the $\text{Ln}4f$ spectra of REE compounds for the second half of the lanthanide row are in qualitative agreement with the corresponding experimental values (Fig. 4); for LnF_3 , they are in accord with published data.⁴³

Indeed, photoemission of an $\text{Ln}4f$ electron gives rise to a more complex final state, resulting in a further complication of the spectra of the $\text{Ln}4f$ electrons. The structure of these spectra is in satisfactory agreement with the set of levels derived from theoretical considerations of the multiplet splitting of the $\text{Ln}4f$ line for the Ln^{3+} cations.^{66,70} The results of these calculations are reflected in Fig. 2 as vertical segments below the $\text{Ln}4f$ spectra. The structure

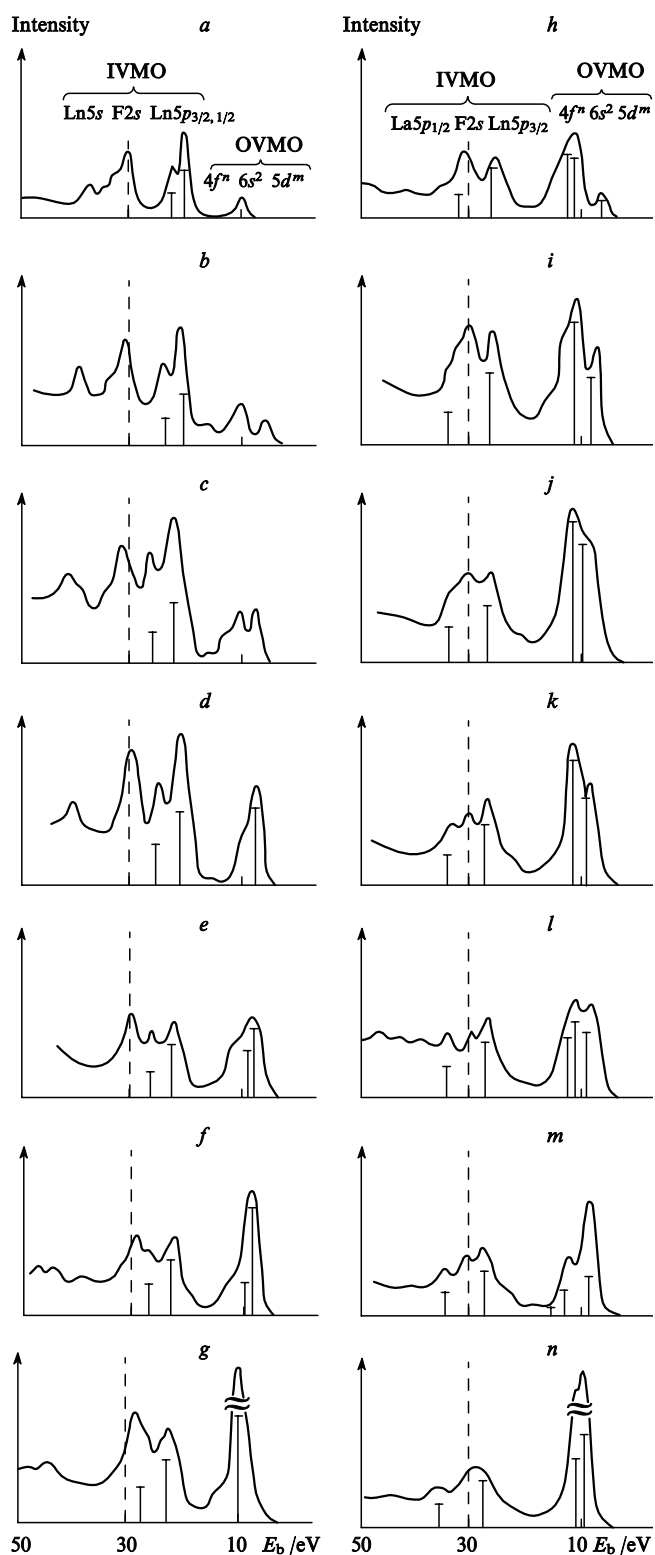


Figure 2. XPS spectra of low binding-energy electrons of lanthanide trifluorides.⁴² (a) LaF_3 , (b) CeF_3 , (c) PrF_3 , (d) NdF_3 , (e) SmF_3 , (f) EuF_3 , (g) GdF_3 , (h) TbF_3 , (i) DyF_3 , (j) HoF_3 , (k) ErF_3 , (l) TmF_3 , (m) YbF_3 , (n) LuF_3 . The vertical segments in the OVMO energy range show the $\text{Ln}4f$ lines found in the ionic approximation,⁶⁶ and those in the IVMO energy range are the lines of the $\text{Ln}5p$ and $\text{F}2s$ atomic spectra.²² The dashed lines show the positions of the $\text{F}2s$ lines of fluorine.

of the spectra of these electrons can characterise the lanthanide oxidation state in the compounds. As was to be expected, in the case of Lu^{3+} in LuF_3 , the line of $\text{Lu}4f$ electrons is split due to the

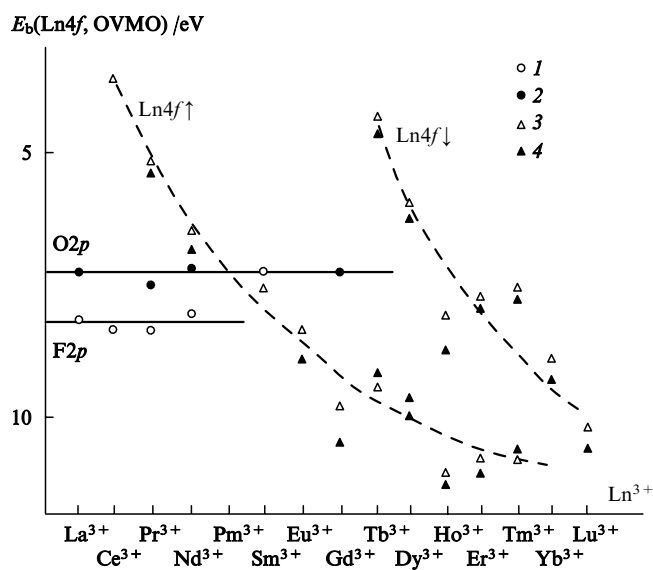


Figure 3. Binding energy (E_b) of the OVMO (1, 2) and Ln4f (3, 4) electrons vs. the number of electrons in the $\text{La}^{3+} - \text{Lu}^{3+}$ series. (1, 3) LnF_3 (see Table 1); (2, 4) Ln_2O_3 .³⁷

spin-orbit coupling into only two components, the difference between their binding energies (ΔE_{so}) being 1.2 eV in magnitude. A similar effect could be expected for the $\text{Yb}4f$ spectrum of Yb^{2+} in YbX_2 (the electronic configuration of Yb^{2+} , like that of lutetium, is $4f^{14}$); this is the case for the Yb atom⁷¹ and for the Yb metal.^{72,73} However, the structure of the spectrum of these electrons in the ytterbium fluoride (see Fig. 2) corresponds to the Yb^{3+} electronic configuration ($4f^{13}$). The structures of the spectra of the Ln4f electrons of other lanthanide ions are also unique and characterise the particular metal ion. When the energy of the exciting X-radiation increases, the intensities of the lines for the metal Ln4f electrons grow.^{74,75} Figure 5 shows the experimental values for the total relative intensity (I_{exp}) of the OVMO and the Ln4f line, found as the ratio of the total area of these spectral lines to the total area of the Ln5p and F2s lines, depending on the

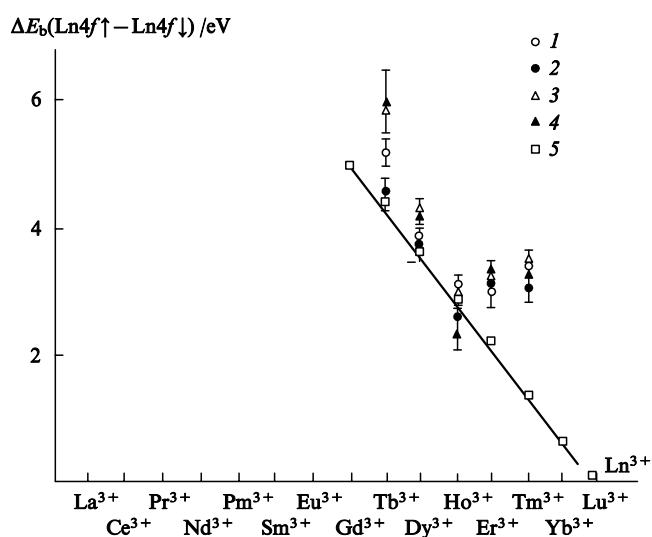


Figure 4. Splitting [$\Delta E_b(\text{Ln}4f\uparrow - \text{Ln}4f\downarrow)$] of the spectral line for the Ln4f electrons vs. the number of electrons in the $\text{La}^{3+} - \text{Lu}^{3+}$ series. (1) LnF_3 (see Table 1); (2) Ln_2O_3 ; (3) LnL_3 (L¹ is the *o*-methoxybenzoic acid residue);⁶⁷ (4) LnL_3^2 (L² is the diphenylacetic acid residue); (5) SCF X_α -DV calculations for LnVO_4 .⁶⁹

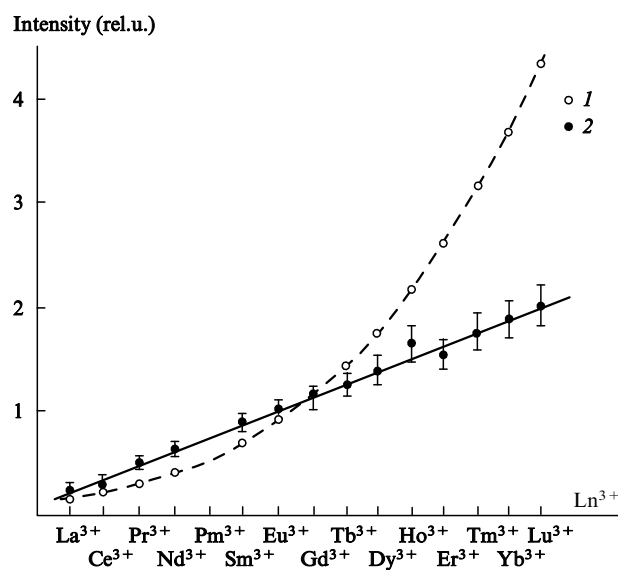


Figure 5. Relative intensity of the Ln4f line vs. the number of 4f electrons in the $\text{La}^{3+} - \text{Lu}^{3+}$ series; (1) theoretical dependence [Eqn (5)]; (2) experimental data for LnF_3 [Eqn (1)].⁶⁸

number of Ln4f electrons (n_{4f}) in lanthanide fluorides. The I_{exp} values are described approximately by the linear relation

$$I_{\text{exp}} = 0.128n_{4f} + 0.20, \quad (1)$$

derived using the least-squares method. Equation (1) reflects the experimental dependence of the relative intensity of the Ln4f spectral line on the number of these electrons in the LnF_3 molecules. The absolute term in Eqn (1), equal to 0.20, characterises the relative intensity of lines for the OVMO electrons, which are partially due to Ln5d and F2p AO. It is noteworthy that this value is somewhat greater than the corresponding theoretical value calculated without allowance for the contribution of occupied Ln4f states. This suggests that an Ln4f electron involved in the chemical bond does not lose the *f* nature (traditionally, it has been considered that the Ln4f electron passes preliminarily to the Ln5d orbital), and in the case of LaF_3 , La4f states are formed in its outer valence shell. However, verification of this hypothesis requires a more accurate experimental determination of the relative line intensities than that performed by Teterin *et al.*^{37,67,68} It is significant that such data can, in principle, provide an answer to the question discussed. The difference between the relative intensities for LnF_3 containing Ln4f electrons and the absolute term in Eqn (1) (0.20) is proportional to the number of Ln4f electrons, which slightly participate in the chemical bond, and can be used to estimate the oxidation state of lanthanides in fluorides.

The theoretical dependence of the relative intensity (I_{theor}) of the Ln4f line in the spectra of LnF_3 on the number of electrons (n_{4f}) can be derived using the data on photoionisation cross-sections for low-energy subshells.^{76,77} In this case, the expression for I_{theor} can be written in the form

$$I_{\text{theor}} = \frac{\sigma(4f)n_{4f} + \sum_i \sigma_i(\text{OVMO})n_i}{\sigma(5p)n_{5p} + 3\sigma(\text{F}2s)n_{\text{F}2s}} = \frac{\sigma(4f)n_{4f}}{\sigma(5p)n_{5p} + 3\sigma(\text{F}2s)n_{\text{F}2s}} + \frac{\sum_i \sigma_i(\text{OVMO})n_i}{\sigma(5p)n_{5p} + 3\sigma(\text{F}2s)n_{\text{F}2s}}, \quad (2)$$

where $\sigma(nl)$ is the photoionisation cross-section of the *nl* shell (*n* and *l* are the principal and orbital quantum numbers, respectively); n_{nl} is the number of electrons; the summation involves

occupied OVMO.^{37, 67, 68} The first term in this expression was found under the assumption that the Ln4*f* electrons do not participate directly in the chemical bond. To estimate the second term, the expression in the numerator was replaced by the sum of terms characterising valence AO,

$$\sum_i \sigma_i(\text{OVMO})n_i \approx \sigma(5d)n_{5d} + \sigma(6s)n_{6s} + 3\sigma(\text{F}2p)n_{\text{F}2p}. \quad (3)$$

In this rather rough approximation, the second term of Eqn (2) for LaF₃ was found to be 0.17, which is smaller than the absolute term (0.20) in Eqn (1). The corresponding values for GdF₃ and LuF₃ are 0.16 and 0.15, respectively. In particular, relation (2) can be written in the form

$$I_{\text{theor}} = \frac{\sigma(4f)n_{4f}}{\sigma(5p)n_{5p} + 3\sigma(\text{F}2s)n_{\text{F}2s}} + 0.17. \quad (4)$$

Assuming that the Ln atoms involved in the chemical bonds in LnF₃ have the configuration 4*fⁿ*5*d*¹6*s*², using the atomic photoionisation cross-sections of the Ln4*f* shell⁵² and taking into account Eqn (4), one can obtain the following expression for I_{theor} :

$$I_{\text{theor}} = 0.01 n_{4f}^{2.24} + 0.17. \quad (5)$$

The plotted function I_{theor} and the corresponding experimental data are presented in Fig. 5.

The substantial difference between the theoretical and experimental values considered can hardly be explained by errors brought about by rough calculations of some terms of Eqn (5) or by the change in the Ln4*f* line intensity caused by different scattering of low-energy electrons upon photoemission. Note that the use of the photoionisation cross-sections of the outer 3*d* electrons for Period 4 elements and various low-lying inner electron levels for any other elements reported in Refs 76 and 77 to determine the relative intensities of their lines provides, as a rule, satisfactory agreement between theoretical and experimental data within the experimental error. Among other reasons, the

observed discrepancy may be due to participation of the Ln4*f* electrons in the chemical bonds.

2. The energy region of Ln5*p* and F2*s* electrons

When investigating the structures of XPS spectra of low-energy electrons in the binding energy range from 0 to 50 eV, in particular, in the spectra of lanthanide compounds, researchers noted that some lines in this range are often substantially broader than the corresponding lines for the core electrons.^{78, 79} Indeed, it follows from the uncertainty relation $\Delta E \Delta \tau \approx h/2\pi$ (ΔE is the atomic level width, $\Delta \tau$ is the lifetime of the 'hole' formed upon photoemission of an electron, and h is Planck's constant) that the lines for the low-lying electrons should be the broadest because the parameter $\Delta \tau$ decreases with an increase in the magnitude of the atomic level energy. However, for example, in LaF₃, the width (Γ) of the F2*s* line is 3.5 eV (see Fig. 1), whereas the low-lying F1*s* electrons account for $\Gamma(\text{F}1s) = 1.6 \text{ eV}$ ⁵ (Table 2).

Whereas line broadening in the binding energy range from 0 to ~15 eV can be due to the MO formation and solid-state effects, the broadening of lines in the energy range from ~15 to 50 eV cannot be interpreted in terms of the well-known classical mechanisms of fine structure origination alone. Moreover, the XPS spectra in the Ln5*p* and F2*s* binding energy range have a more complex structure than that expected upon simple superposition of the lines due to the corresponding lanthanide and fluorine atomic shells (see Fig. 2).⁵² Therefore, it has been suggested that this structure could arise due to the formation of the inner valence molecular orbitals largely composed of the Ln5*p* and F2*s* AO of neighbouring atoms.^{18, 42} In addition, it was found that separate maxima can be distinguished in the spectra and attributed, in a certain approximation, to the Ln5*p*_{3/2} and Ln5*p*_{1/2} components of the doublet (see Fig. 2).

The overall atomic spectra of this region obtained by summation of the Sc3*p*, Y4*p*, Ln5*p*_{3/2, 1/2} and F2*s* lines for scandium, yttrium, and some lanthanide trifluorides are presented in Fig. 6. In the simulation of these spectra, the spin-orbit splitting $\Delta E_{\text{so}}(\text{Mnp})$ was varied around the corresponding value for the metal,⁸⁰ and the FWHM (full line width at half maximum) Γ and

Table 2. Spectral parameters found by comparison of the approximate atomic (calculation) and experimental XPS spectra of metal fluorides: electron binding energies (E_b , eV), spin-orbit splitting [$\Delta E_{\text{so}}(\text{M}5p)$, eV], binding energy difference between the F2*s* and F1*s* electrons [$\Delta E_b(\text{F}2s - \text{F}1s)$, eV], line widths (Γ , eV)⁵⁵ and photoionisation cross-sections (σ) at 1487 eV.⁷⁶

Compound	Ln5 <i>p</i> _{3/2}			Ln5 <i>p</i> _{1/2}		$\Delta E_{\text{so}}(\text{M}5p)$		F2 <i>s</i> (see ^a)		$\Gamma(\text{F}1s)$, experiment	$\Delta E_b(\text{F}2s - \text{F}1s)^b$	
	E_b (see ^c)	Γ	σ (see ^d)	E_b	σ	calculation	experiment ^e	E_b	Γ		calculation	experiment ^e
LaF ₃	18.6	0.9	0.458	21.1	0.230	2.4	2.3	29.5	1.6	1.6	656.6	655.8
CeF ₃	19.4	1.0	0.439	22.5	0.221	3.1	2.9	29.7	1.3	1.7	655.7	655.9
PrF ₃	21.7	1.5	0.456	25.6	0.229	3.9	unknown	31.2	2.0	2.1	654.1	655.7
NdF ₃	20.7	1.1	0.472	24.0	0.236	3.7	the same	29.6	1.4	1.5	655.5	655.7
SmF ₃	22.1	1.4	0.501	26.2	0.249	4.1	"	30.0	1.5	1.5	655.2	655.5
EuF ₃	22.4	1.7	0.515	27.0	0.255	4.6	"	29.7	2.0	1.7	655.3	655.8
GdF ₃	22.9	1.8	0.568	29.3	0.279	6.4	"	28.6	2.2	1.6	656.2	655.6
TbF ₃	23.9	1.6	0.539	30.1	0.265	6.2	6.2	29.0	1.9	1.8	656.1	656.0
DyF ₃	24.5	1.7	0.551	32.0	0.270	7.5	6.4	29.4	1.7	1.8	655.8	655.8
HoF ₃	26.2	1.9	0.562	33.5	0.274	7.3	6.7	30.6	2.1	2.5	654.6	654.8
ErF ₃	26.1	1.1	0.572	33.2	0.277	7.1	6.7	29.9	1.9	2.1	655.5	655.7
TmF ₃	26.6	1.1	0.583	34.0	0.281	7.4	6.8	29.7	1.3	1.7	655.7	655.6
YbF ₃	27.1	1.4	0.592	34.7	0.284	7.6	6.9	29.9	1.6	1.6	655.3	655.6
LuF ₃	28.4	2.5	0.645	35.7	0.304	7.3	7.0	28.7	3.2	2.1	656.8	unknown
YF ₃ (see ^f)	26.1	1.2	0.599	27.4	0.311	1.3	—	30.2	1.6	1.7	655.0	655.3
ScF ₃ (see ^g)	33.9	1.4	0.429	34.6	0.221	0.7	—	29.8	1.8	2.3	655.8	656.2

^a For the F2*s* electrons, $\sigma = 0.210$. ^b The $\Delta E(\text{F}2s - \text{F}1s)$ values for MnF₂ and MnF₃ are 655.4 and 655.2 eV, respectively. ^c Comparison of the approximate atomic spectra of Ln, Y, Sc and F with experimental spectra of the fluorides was carried out for La–Er, Y and Sc relative to the Ln5*p*_{3/2}, Y3*p*_{3/2} and Sc3*p*_{3/2} energies, and for Tm–Lu, relative to the Ln5*p*_{1/2} energies. ^d In relative units, 1 rel.u. = 13.600 barn. ^e The values for individual metals are given.⁸⁰ ^f The Y4*p*_{3/2, 1/2} energies are presented. ^g The Sc3*p*_{3/2, 1/2} energies are presented.

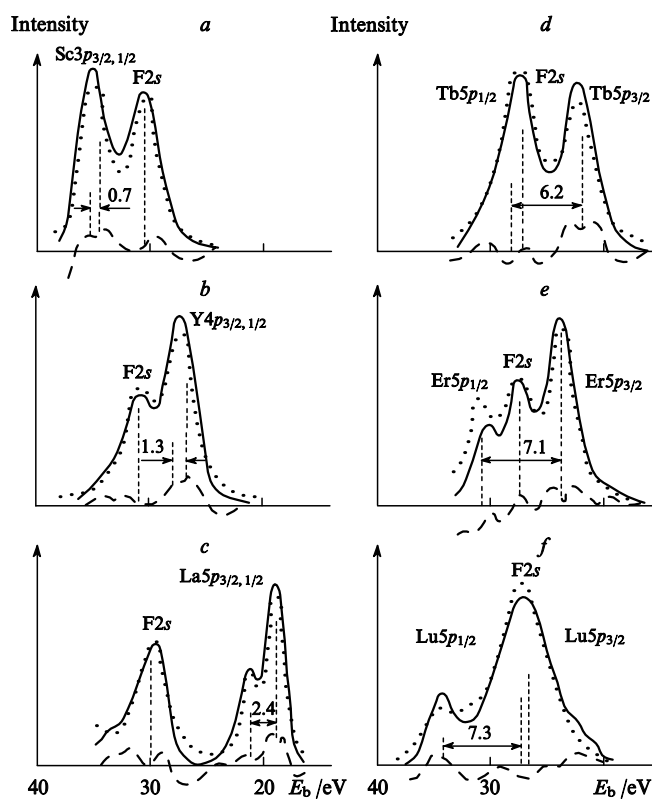


Figure 6. XPS spectra of the MF_3 fluorides in the $\text{Sc}3p$ (a), $\text{Y}4p$ (b), $\text{La}5p$ (c), $\text{Tb}5p$ (d), $\text{Er}5p$ (e), $\text{Lu}5p$ (f) and $\text{F}2s$ binding energy ranges.⁴² The continuous lines show the experimental spectra, the vertical dashed segments correspond to atomic spectra; the dots show the summarised spectra; and the dashed lines are the differences between the experimental and simulated spectra.

the $\text{F}2s$ binding energies with allowance for photoionisation cross-sections^{76,77} were varied until the best agreement with the experimental spectra was attained. It was assumed that the composition of the compounds considered corresponds to the stoichiometric formula MF_3 , and the spectral lines for their electrons have a Lorentzian form. The spectral parameters found in this way and the corresponding experimental values are presented in Table 2 and in Fig. 7. These values characterise the main features of the considered spectra and barely reflect the complex structure of the spectra. Therefore, one should not expect too large a difference between the theoretical and experimental values (see Fig. 6, Table 2). Thus the general trend for the increase in the spin-orbit splitting [$\Delta E_{\text{so}}(\text{M}5p)$] and FWHM (Γ) for $\text{Ln}5p$ electrons can be followed, but the FWHM values for the $\text{F}2s$ lines are markedly different (see Table 2).

The binding energy differences between the $\text{F}2s$ and $\text{F}1s$ electrons [$\Delta E_b(\text{F}2s - \text{F}1s)$] for the metal fluorides studied differ somewhat from the corresponding values for $3d$ -metal compounds, in particular MnF_2 and MnF_3 , in which the conditions for IVMO formation from the $\text{F}2s$ and $\text{Mn}3p$ AO are much less advantageous than those in LnF_3 . It really follows from this comparison (see Table 2, Fig. 2) that the experimental spectra in the considered energy range do not consist of separate lines but have a more complex structure. The dependence of the $\text{Ln}5p$ binding energy on the atomic number (Z) is relatively weak and is nearly linear for the whole lanthanide series (see Fig. 7). This pattern of the $E_b - Z$ curve is not typical of the core shells the energy of which follows a quadratic dependence on Z .

The $\text{F}2s$ XPS spectra for LaF_3 , CeF_3 , PrF_3 , NdF_3 and SmF_3 exhibit a clear-cut shoulder removed from the basic line by ~ 2.2 eV towards higher electron binding energies. In the spectra of other lanthanide trifluorides, this region is superimposed by the

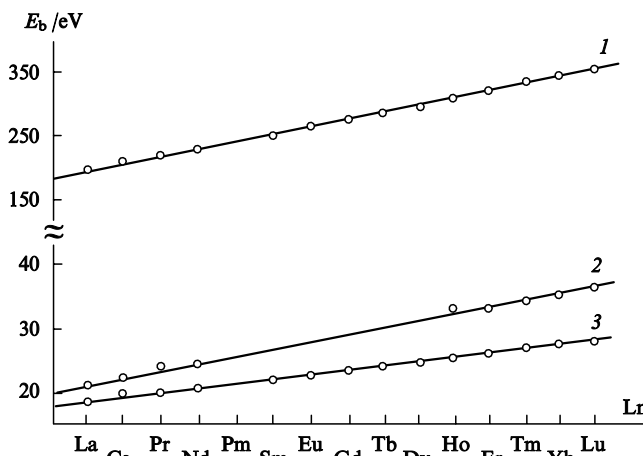


Figure 7. Binding energies (E_b) of the $\text{Ln}4p_{3/2}$ (1), $\text{Ln}5p_{1/2}$ (2) and $\text{Ln}5p_{3/2}$ electrons (3) of lanthanide trifluorides vs. the metal atomic number in the La–Lu series. The error in determination of the electron binding energies from the maxima of the corresponding lines is ± 0.2 eV.⁵

$\text{Ln}5p_{1/2}$ line, which complicates the observation of this shoulder. This extra structure cannot be due to fluorine atoms having different oxidation states because the $\text{F}1s$ line in the spectra of these compounds is rather narrow and symmetric. On passing from La to Sm, the $\text{Ln}5p_{3/2}$ and $\text{Ln}5p_{1/2}$ binding energies increase by 3.5 and 5.1 eV, respectively. Simultaneously, the shoulder at the basic $\text{F}2s$ line shifts to a much lesser extent. The absence of the corresponding shoulder at the $\text{F}1s$ line suggests that this shoulder is not due to many-body perturbation, i.e., to the so-called shake-up (or shake-down) process, which implies transition of a valence electron to a higher (or lower) excited state simultaneously with photoemission of a core electron and gives rise to shake-up (or shake-down) satellites on the side of higher (or lower) electron binding energies of the basic spectral line. In other words, the observed shoulder is not a shake-up (shake-down) satellite.^{5,42}

The same conclusion can be drawn by analysing and comparing the relative electron binding energies of satellites in the spectra of various core electrons of the fluorides studied. Complication of the structure of LnF_3 spectra in the $\text{Ln}5p$ and $\text{F}2s$ electron binding energy ranges in, for example, the spectra of LaF_3 and LuF_3 cannot be due to the multiplet splitting either, as these fluorides contain no unpaired $\text{Ln}4f$ electrons and they are diamagnetic. This splitting should result, apparently, in some broadening of the $\text{Ln}5p$ doublet lines for lanthanide trifluorides that contain unpaired $\text{Ln}4f$ electrons, which is actually observed in the spectra of fluorides of light lanthanides (see Fig. 2). This is not at variance with the results of the estimation of the influence of this factor on the $\text{Ln}5p$ spectra performed in the approximations of isolated Ln^{3+} ions⁸¹ and atoms in the metals.⁸²

On the basis of the foregoing data and with allowance for similar results for oxygen-containing lanthanide compounds,^{57–59, 78, 79, 83, 84} it was suggested that one reason for structure complication in the $\text{Ln}5p$ and $\text{F}2s$ spectral range is the formation of IVMO, mainly from the $\text{Ln}5p$ and $\text{F}2s$ AO.^{5, 18, 42, 52} The spectral structure in this energy range can be qualitatively described by considering the diagram of the IVMO levels for the clusters that reflect the surrounding of the metal atoms by the ligands in the MF_3 trifluorides (Fig. 8).

Lanthanide (La to Sm) trifluorides form a tysonite hexagonal layered lattice characterised by the D_{6h}^3 ($C6/mcm$) point group of symmetry.^{2, 85} The wavy layers of F atoms alternate in the lattice with the flat layers composed of Ln and F atoms, which form six-membered rings. The lanthanide atoms are surrounded by three fluorines. Therefore, a calculation of the electronic structure of the lanthanide trifluorides has been carried out for LnF_3 clusters with D_{3h} symmetry.⁴⁷ It has been noted² that the structures of

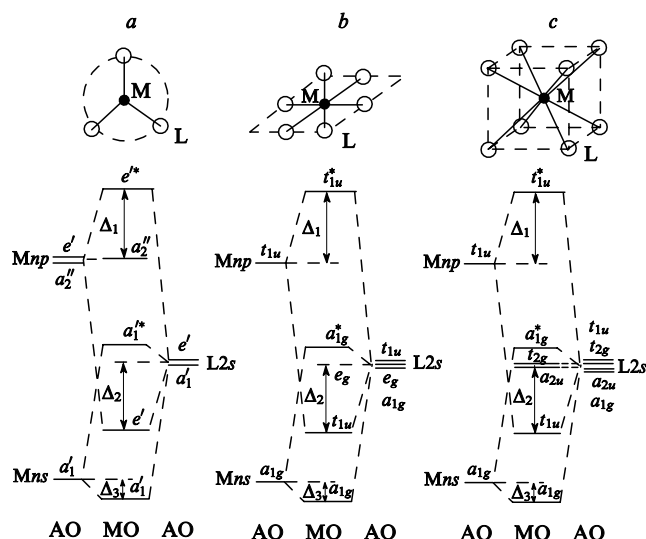


Figure 8. Diagram of IVMO formed by the metal Mnp and Mns AO and the ligand $L2s$ AO of model clusters. (a) ML_3^{n1-} (D_{3h} symmetry); (b) ML_6^{n2-} ; (c) ML_8^{n3-} (O_h symmetry).⁴²

lanthanide trifluorides from La to Ho can be regarded as a hexagonal LaF_3 (tysonite) structure, space group D_{3d}^4 ($P\bar{3}c1$). In this structure, each lanthanum atom is surrounded by nine fluorine atoms located at distances of 0.2416 to 0.2640 nm. At room temperature, lanthanide (Sm to Lu) trifluorides can also have the YF_3 structure² with an orthorhombic lattice, space group D_{2h}^{16} ($Pnma$). Each yttrium atom in the structure is surrounded by eight fluorine atoms located at distances of 0.225 to 0.232 nm. One more (ninth) fluorine is located at a distance of 0.260 nm.

To discuss qualitatively the spectral patterns in the $Ln5p$, $Y4p$, $Sc3p$ and $F2s$ energy ranges in terms of the IVMO concept, Teterin *et al.*⁴² used, instead of the real structures, structural models of the local environment of the metal atoms in fluorides resembling most closely the real structures but which are more symmetrical.⁴² Using group theory in a non-relativistic (NR) approximation for the chosen model clusters, one can describe schematically the structure and energy of the IVMO consisting of the Mns , Mnp and $L2s$ AO of the neighbouring metal and ligand atoms (see Fig. 8). The IVMO structures corresponding to different local environments of the metal are significantly different. Thus, for the ML_3^{n1-} cluster (D_{3h} symmetry), two energy levels representing the a_2' and e'^* IVMO are observed instead of one level representing the Mnp AO. In the case of ML_6^{n2-} and ML_8^{n3-} clusters (O_h symmetry), as for the metal atom, this energy range contains one level whose position can vary (see Fig. 8). The relative intensities of lines of the theoretical IVMO spectra for clusters of different symmetries are proportional to the electron photoemission cross-sections and degeneration factors for different levels (a_1' , a_{1g} , a_{2u} are non-degenerate, e' are doubly degenerate, and t_{2g} and t_{1u} are triply degenerate IVMO); thus, they should be typical and substantially different.

In the clusters in question, the interaction of the filled Mnp and $L2s$ AO gives rise to bonding (e' , t_{1u}) and antibonding (e'^* , t_{1u}^*) IVMO. If the admixtures of the vacant valence $Ln4f$, $Ln5d$ and $Ln6s$ AO in these IVMO are small, the electrons of these MO should influence only slightly the energy of the chemical bond in the cluster. A significant admixture of these AO in IVMO would weaken the antibonding nature of the e'^* (t_{1u}^*) MO and enhance the bonding nature of the e' (t_{1u}) MO. Thus, the formation of these IVMO would result in stronger binding between the neighbouring atoms.^{18, 55, 60, 86, 87} The interaction of the Mns AO with the $L2s$ AO can also give rise to couples of bonding a_1' and a_{1g} and the corresponding antibonding $a_1'^*$ and a_{1g}^* IVMO. Analogous con-

siderations concerning the influence of IVMO electrons on the chemical bonding in clusters are also applicable to these IVMO. Some IVMO such as a_2' , e_g , a_{2u} and t_{2g} are mainly formed by the Mnp and $L2s$ AO. However, vacant valence AO can also be admixed to them. If these admixtures are small, the IVMO would be of the quasi-atomic nature.

The limited resolving power of X-ray photoelectron spectrometers and line broadening caused by solid-state effects in the spectral range considered preclude elucidation of all structural details of the IVMO in lanthanide trifluorides. Nevertheless, the most clear-cut changes in the structure of the IVMO spectra compared to the structure of the spectra of the AO of neighbouring atoms are experimentally measurable. It is noteworthy that in a more rigorous approach, the real experimental spectra of lanthanide compounds should be compared with the theoretical spectra calculated using the relativistic approximations taking into account many-body processes that take place during the electron photoemission. However, no calculations of this type are available to date.

When discussing the low-binding energy spectral structure in MF_3 which are characterised by relatively low spin-orbit coupling between the low-energy filled Mnp shells, one can use the data of non-relativistic calculations. This is true for compounds such as, for example, ScF_3 , YF_3 and LaF_3 ; the spin-orbit splittings (ΔE_{so}) for the $Sc3p$, $Y4p$ and $La5p$ levels are equal to 0.7, 1.3 and 2.3 eV, respectively (see Table 2). The results of non-relativistic SCF X_α DVM calculations of the electronic structures of the ScF_6^{3-} (C_3 symmetry), non-symmetrical YF_9^{6-} and LaF_{11}^{8-} (D_{3h} symmetry) clusters (Fig. 9)⁶³ are given schematically in Figs 10, 11, 12. The structures of these clusters simulate most closely the environment of scandium, yttrium and lanthanum in ScF_3 , YF_3 and LaF_3 , respectively.

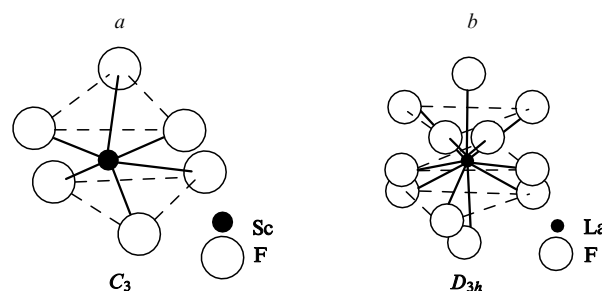


Figure 9. Structure of the ScF_6^{3-} (C_3 symmetry) (a) and LaF_{11}^{8-} (D_{3h} symmetry) clusters (b). The $Sc-F$ bond length in ScF_6^{3-} is 0.202 nm; in the LaF_{11}^{8-} cluster, the average value over five distances $\bar{R}(La-F) = 0.239$ nm, and that for the other six distances, $\bar{R}(La-F) = 0.272$ nm.⁶³

The calculations for the electronic structure of the ScF_6^{3-} cluster (C_3 symmetry) were performed using structural data² of ScF_3 , which indicate that the fluorine atoms are located at approximately equal distances from scandium; the average $\bar{R}(Sc-F)$ value is 0.202 nm, and no inversion centre is present (see Fig. 9).

According to these calculations, the broadened line near the Fermi level in the spectrum of ScF_3 is attributed to OVMO electrons (see Figs 1, 10). The spectral structure in the $Sc3p$ and $F2s$ binding energy range is due to the IVMO electrons. For the considered $Sc-F$ bond lengths in the ScF_6^{3-} cluster, noticeable mixing of the $Sc3p$ and $F2s$ AO takes place, resulting in the formation of the $1a_1$ and $3a_1$ IVMO. Therefore, the fine structure in the spectrum of the $Sc3p$ and $F2s$ electrons is attributable to the formation of these IVMO (see Figs 1, 6).

The resonance energy values $E_x^R(Sc-F)$,¹⁸ which characterise the covalent bonding between scandium and fluorine in ScF_3 imply that the greatest contribution to the stability of ScF_3 is made by the $5a_1$ OVMO and $2a_1$ and $1a_1$ IVMO electrons. Due to mixing

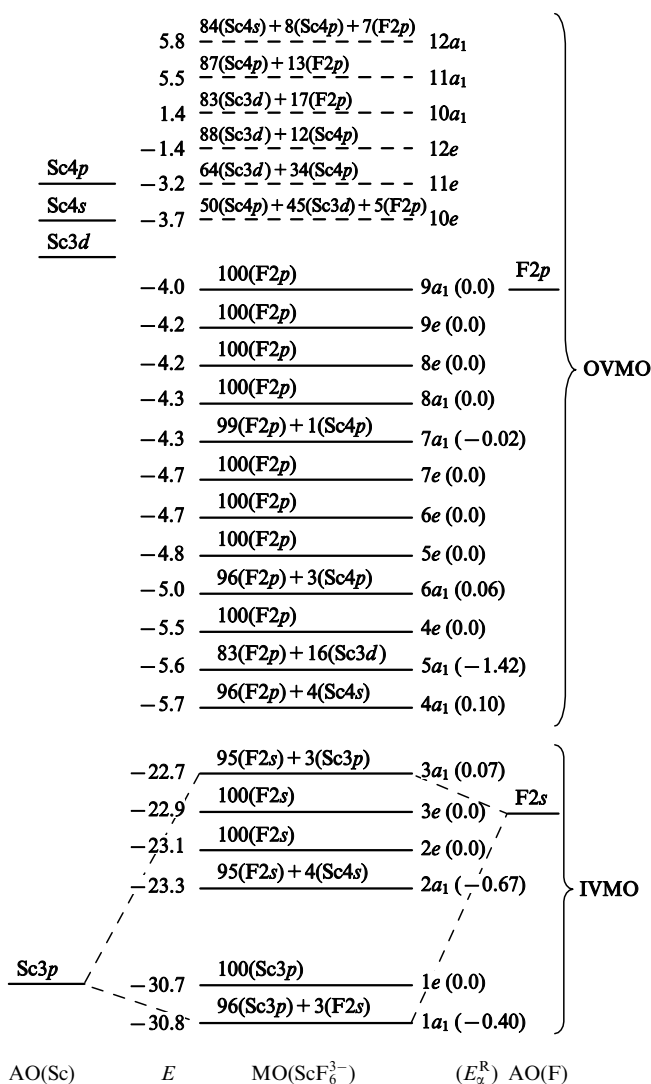


Figure 10. Diagram of the MO in the ScF_6^{3-} cluster [C_3 symmetry, $\bar{R}(\text{Sc}-\text{F}) = 0.202$ nm] calculated in the SCF X_α -DVM approximation.⁶³ The MO energies are expressed in eV (the diagram is not scaled). The values in parentheses are the resonance energies $E_\alpha^R(\text{Sc}-\text{F})$ in a.u.

of the outer and inner valence AO, as noted in a number of publications,^{18, 52, 55, 85, 86} the contribution of the bonding $1a_1$ IVMO prevails over the contribution of the antibonding $3a_1$ IVMO, and, in total, the electrons of these MO strengthen the bond. If the contribution of the $2a_1$ IVMO is taken into account, the total covalent contribution of the IVMO electrons to the chemical bond energy in the ScF_6^{3-} cluster (C_3 symmetry) would be $\sim 43\%$. Comparison of the calculated energy levels with the experimental spectra should be done using the data for the so-called transition state rather than for the ground state.⁸⁸ However, the energy levels calculated for the transition state in a narrow range of MO energies are known to be shifted relative to those found for the cluster ground state towards greater (in magnitude) E_b by a virtually constant value equal to several electron-volts (see, for example, Ref. 89). For comparison, MO energies for the ScF_6^{3-} cluster (C_3 symmetry) increased (in magnitude) by 2 eV are shown in Fig. 1 as vertical segments below the experimental XPS spectrum of scandium trifluoride. A satisfactory qualitative agreement between the experimental and theoretical results can be noted.

The structure of the yttrium local environment in YF_3 is rather complicated. Therefore, the YF_9^{6-} cluster, which has no symmetry elements and in which the metal environment resembles most

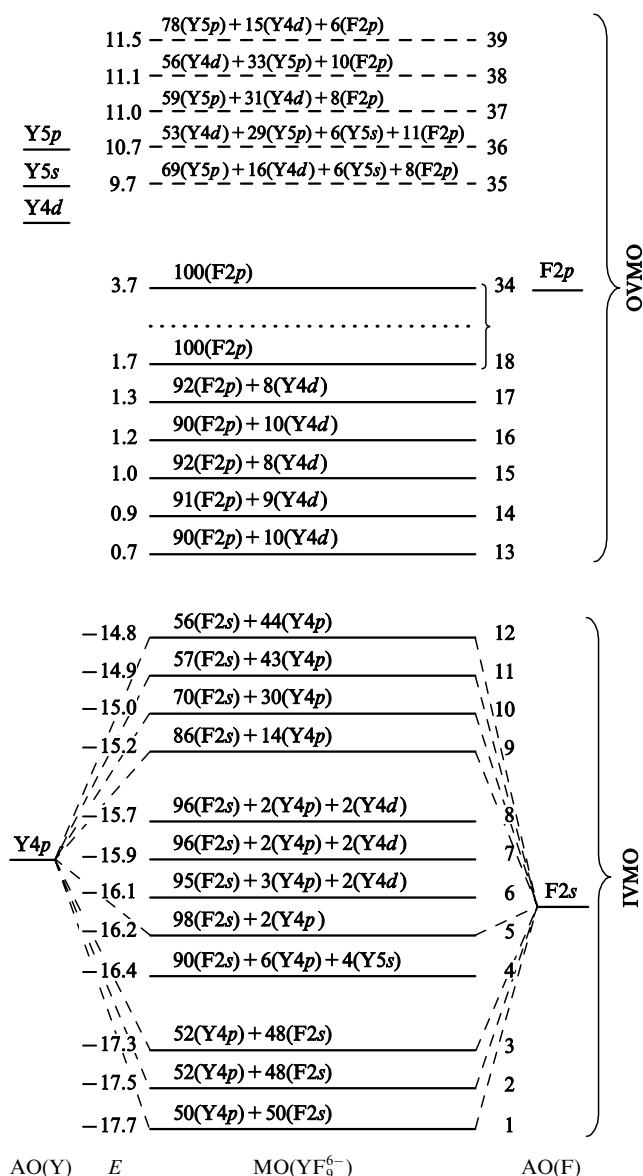


Figure 11. Diagram of MO of the asymmetrical YF_9^{6-} cluster (SCF X_α -DVM) in which the average value over eight bond lengths, $\bar{R}(\text{Y}-\text{F}) = 0.229$ nm, and for the ninth bond length, $R(\text{Y}-\text{F}) = 0.260$ nm.⁶³ The MO energies are expressed in eV (the diagram is not scaled).

closely the yttrium environment in the trifluoride, can be chosen for the electronic structure calculations. In this case, the yttrium atom is surrounded by eight fluorine atoms located at distances $\bar{R}(\text{Y}-\text{F}) = 0.229$ nm and one fluorine atom located at the distance $R(\text{Y}-\text{F}) = 0.260$ nm.^{2, 63, 90} The calculation results indicate that the higher occupied OVMO are mainly formed by the $\text{F}2p$ AO, while the lower OVMO involve the $\text{F}2p$ and $\text{Y}4d$ AO (see Fig. 11). The IVMO formation is associated with substantial mixing of the $\text{Y}4p$ and $\text{F}2s$ AO, which may be as great as 50%.

For comparison of the theoretical results of the electronic structure of the YF_9^{6-} cluster with the structure of the XPS spectrum of YF_3 , the magnitudes of the MO energy were increased by 10 eV. These results are given under the XPS spectra of yttrium trifluoride in Fig. 1 as vertical segments. The considered calculation results suggest that the spectrum in the $\text{Y}4p$ and $\text{F}2s$ binding energy range reflects the IVMO system in YF_3 . The appearance of these MO can also account for the additional structure observed in this range of the spectrum of YF_3 as shoulders next to the expected atomic lines.

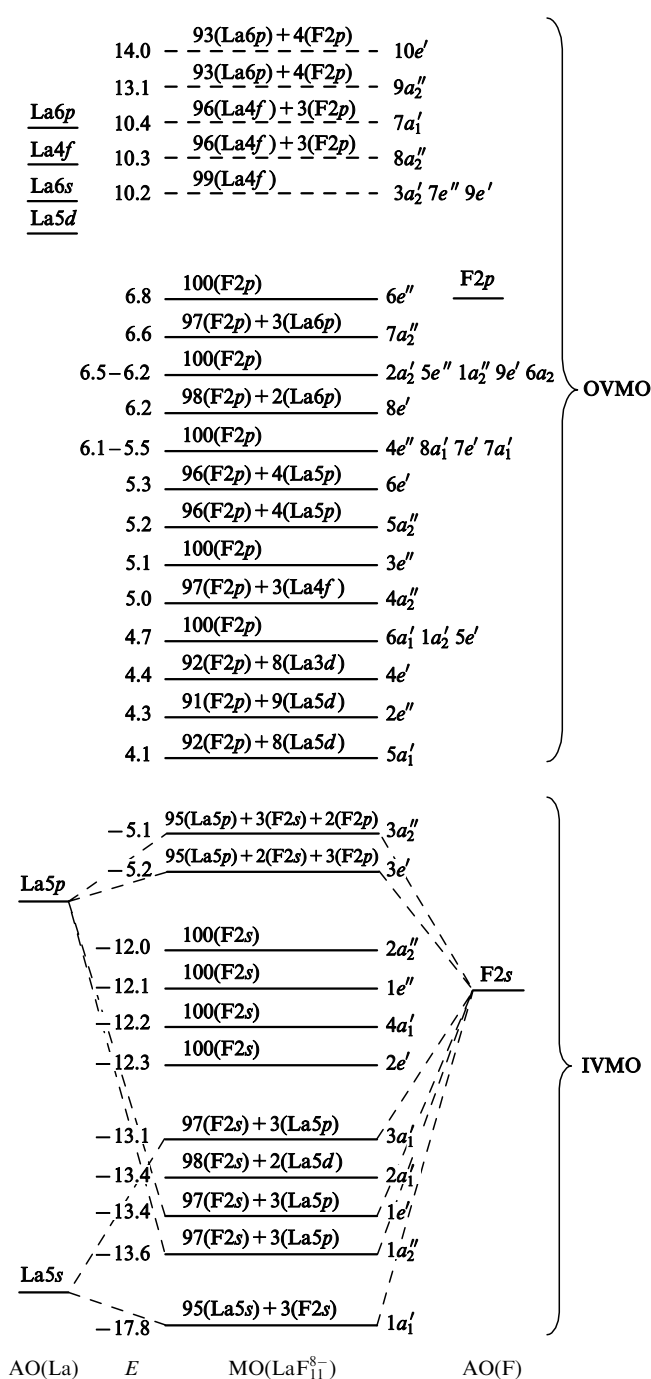


Figure 12. Diagram of MO of the LaF_{11}^{8-} cluster (D_{3h} symmetry) (SCF X_α -DVM) in which the average value over five bond lengths, $\bar{R}(\text{La}-\text{F}) = 0.239$ nm, and for the other six lengths, $\bar{R}(\text{La}-\text{F}) = 0.272$ nm.⁶³ The MO energies are expressed in eV (the diagram is not scaled).

The structure of the low binding energy XPS spectra of lanthanum trifluoride was interpreted using theoretical data for the electronic structures of the LaF_{11}^{8-} cluster (D_{3h} symmetry) obtained by non-relativistic SCF X_α -DV calculations.^{5,63} The calculations were based on the crystallographic data for LaF_3 ,^{2,63} which imply that five fluorine atoms in the LaF_{11}^{8-} cluster are located at an average distance $\bar{R}(\text{La}-\text{F}) = 0.239$ nm away from the lanthanum atom, while the other six fluorines are located at a distance $\bar{R}(\text{La}-\text{F}) = 0.272$ nm (see Fig. 9). The results of calculations are presented in Fig. 12, which shows that the overlap of the $\text{La}5s$, $\text{La}5p$ and $\text{F}2s$ AO results in the formation

of the $1a_1' - 3a_2''$ IVMO system. Due to the substantial difference between the $\text{La}5p$ and $\text{F}2s$ binding energies [the experimental $\Delta E_b(\text{La}5p_{3/2} - \text{F}2s)$ value is 10.7 eV] and long $\text{La}-\text{F}$ bonds, the degree of mixing of the $\text{La}5p$ and $\text{F}2s$ AO is not large.

To compare the results of calculations for the electronic structure of the LaF_{11}^{8-} cluster (D_{3h} symmetry) with the structure of the experimental X-ray photoelectron spectrum of LaF_3 , the absolute MO energies were increased by 14 eV (see Fig. 1).

As the chemical bond in LaF_3 is formed, the difference between the $\text{La}5p_{3/2}$ and $\text{La}3d_{5/2}$ binding energies does not change within the error of measurements. For instance, for metallic lanthanum, $\Delta E_b(\text{La}5p_{3/2} - \text{La}3d_{5/2}) = 818.6$ eV⁹¹ or 818.2 eV,⁵ and for LaF_3 , this value is 818.7 eV⁴² (see Table 1). However, the formation of IVMO of the $3e'$ and $3a_2''$ type is not expected to cause necessarily a significant increase in this energy difference (see Fig. 12) because the mixing of outer and inner valence AO during the IVMO formation may be accompanied by a substantial decrease in the antibonding type of these orbitals.¹⁸ Unfortunately, no theoretical results for the trifluorides of heavier lanthanides using either the non-relativistic or relativistic approximation are currently available. Nevertheless, it follows from the given examples that the results of theoretical calculations agree qualitatively with experimental data. This suggests that the complication of the XPS spectral structure for REE trifluorides in the region of the Mnp and $\text{F}2s$ binding energies is due to the formation of IVMO.

3. The spectra of core electrons

a. The structures of the spectra of the $\text{Ln}5s$ and $\text{Ln}4s$ electrons

It follows from theoretical calculations⁵⁶⁻⁵⁹ that the $\text{Ln}5s$ AO in lanthanide compounds can be involved in the IVMO formation. However, the concomitant changes in the $\text{Ln}5s$ spectra observed on passing from metals to compounds are difficult to detect because various effects determining the structure of the XPS spectra can show themselves in this spectral range (Fig. 13). Complication of the spectral structure in the $\text{Ln}5s$ binding energy range for the compounds considered can be related to the appearance of additional broadened lines caused by electronic Auger transitions. Thus the lines at 63 and 46 eV in the spectra of ErF_3 and TmF_3 , respectively, have been attributed⁵ to the electronic Auger transitions of the M_5NN type.⁹² Nevertheless, in many cases, the basic line for the $\text{Ln}5s$ electrons, which also has a complex structure, can be distinguished in these spectra. On the side of higher (by 14–16 eV) binding energies, a relatively intense additional structure is observed. A similar, though less intense structure is found in the spectra of electrons of other deep core shells. Therefore, many-body perturbation giving rise to shake-up satellites in the spectra might be a reason for this additional structure (see Fig. 13).

Comparison of the $\text{Ln}5p$ and $\text{Ln}5s$ binding energies (see Table 1) shows that the approximate equality $E_b(\text{Ln}5s) \approx 2E_b(\text{Ln}5p)$ holds for the lanthanide trifluorides considered. It allows the suggestion that a significant complication of the $\text{Ln}5s$ spectral structure may be caused by the dynamic effect related to the giant Coster-Kronig transitions within the $\text{Ln}5s$, $\text{Ln}5p$ and $\text{Ln}4f$ shells. As a consequence, photoemission of an $\text{Ln}5s$ electron gives rise to not only the ground final state ($\text{Ln}5s^1 5p^6 4f^n$) but also an excited final state ($\text{Ln}5s^2 5p^4 4f^{n+1}$) with an energy close to that of the ground state. This situation is sometimes considered as the interaction of the configurations of the final states, $\text{Ln}5s^1 5p^6 4f^n \leftrightarrow \text{Ln}5s^2 5p^4 4f^{n+1}$. In particular, this might be the reason for some extra peaks in the $\text{Ln}5s$ spectra (see Fig. 13).

The $\text{Ln}5s$ spectra of lanthanide compounds exhibit, in the simplest case, a structure related to multiplet splitting (ΔE_{ms}).^{44,93,94} In this case, two components arise instead of the expected single line; the splitting is proportional to the number of unpaired $\text{Ln}4f$ electrons. The greatest multiplet splitting was observed for the lanthanide trifluorides of the middle of the lanthanide row, the maximum value being found for GdF_3 : $\Delta E_{\text{ms}}(\text{Gd}^{3+}) = 3.2$ eV (see Fig. 13). The dependence of the elec-

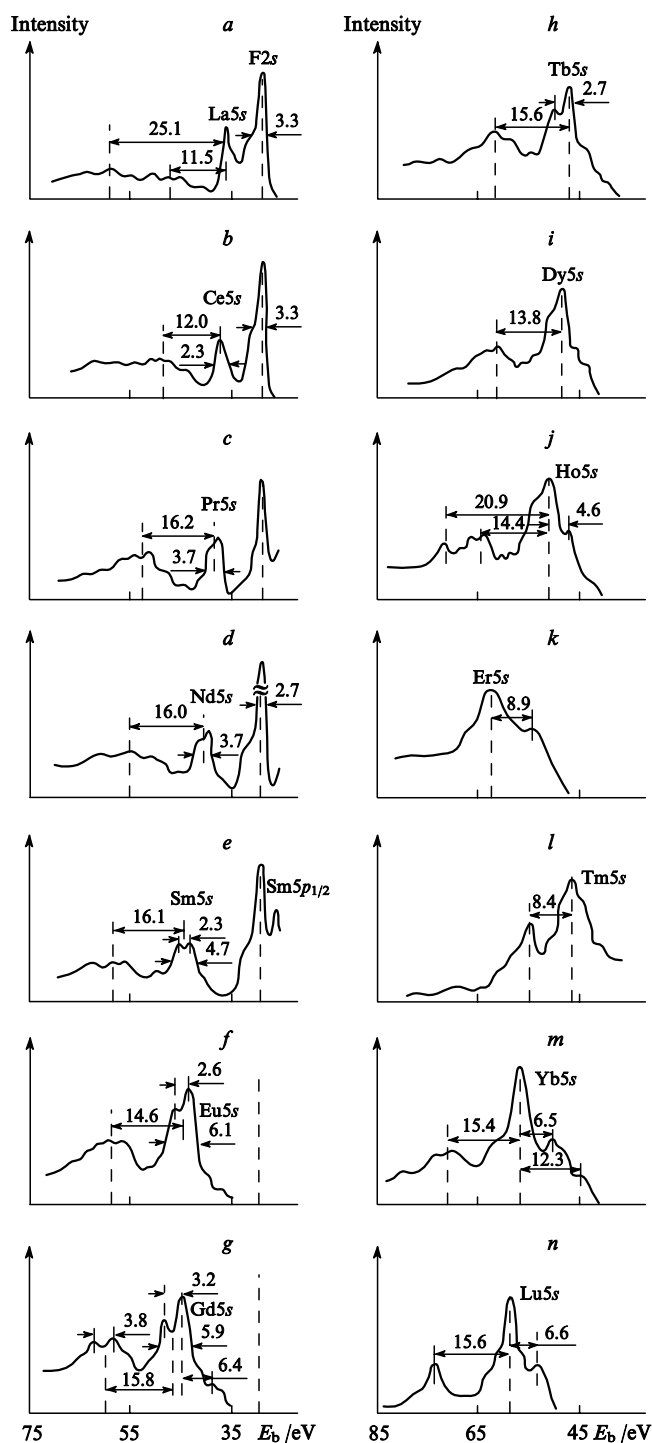


Figure 13. XPS spectra of lanthanide trifluorides in the Ln5s binding energy range.⁴² (a) LaF₃, (b) CeF₃, (c) PrF₃, (d) NdF₃, (e) SmF₃, (f) EuF₃, (g) GdF₃, (h) TbF₃, (i) DyF₃, (j) HoF₃, (k) ErF₃, (l) TmF₃, (m) YbF₃, (n) LuF₃.

tron binding energies corresponding to these two components on the lanthanide atomic number is presented in Fig. 14.

A similar structure was observed in the Ln4s spectra of lanthanide trifluorides (Fig. 15). In the case of TbF₃, DyF₃, HoF₃ and ErF₃, intense lines caused by the electronic Auger transitions of the $M_5N_{45}O_3$, $M_5N_{45}O_1$, $M_5N_4N_{45}$ and $M_4N_4N_{45}$ types, respectively, appear in the Ln4s binding energy range.⁹² In the Ln4s spectra of these compounds recorded on a spectrometer

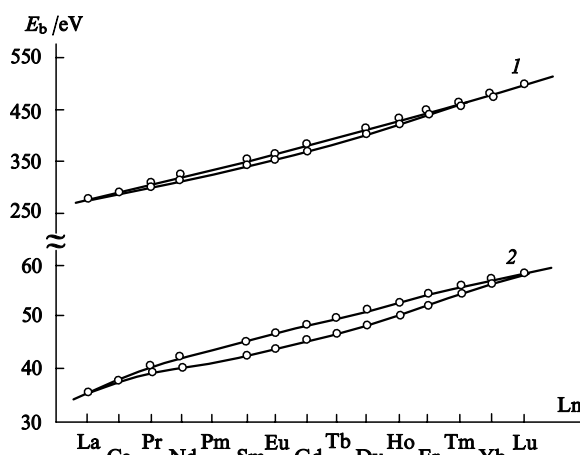


Figure 14. Binding energies (E_b) of the Ln4s (1) and Ln5s electrons (2) of lanthanide trifluorides vs. the metal atomic number in the La–Lu series.⁵ The error of determination of the electron binding energy is ± 0.2 eV.

with X-ray $MgK_{\alpha 1.2}$ excitation (1253.6 eV) instead of $AlK_{\alpha 1.2}$ excitation (1486.6 eV), as was to be expected, no Auger lines are observed around the Ln4s XPS lines.⁴⁴ In this case, the Auger lines are shifted towards the lower binding energy range by the value

$$\Delta E = E(AlK_{\alpha 1.2}) - E(MgK_{\alpha 1.2}) = 233 \text{ eV}.$$

The parameters of the Ln4s spectra of TbF₃, DyF₃, HoF₃ and ErF₃ found by Cohen *et al.*⁴⁴ allowed interpretation of some of the lines in the previously recorded spectra of these electrons⁵ (see Table 1, Fig. 13). The use of $AlK_{\alpha 1.2}$ X-ray excitation provided the possibility of recording the Ln4s spectra for the trifluorides of light lanthanides.^{42, 52}

Like the spectra of the Ln5s electrons, the spectra of the Ln4s electrons contain a structure attributable to many-body perturbation on the higher (by ~ 14 – 16 eV) binding energy side of the basic lines (see Fig. 15). Since the approximate equality

$$E_b(Ln4s) \approx E_b(Ln4p) + 2 E_b(Ln5p),$$

holds for the whole lanthanide row, the Ln4s spectra are expected to exhibit a structure caused by the dynamic effect, which results in the formation of two final states, $Ln4s^1 4p^6 5p^6 4f^n \leftrightarrow Ln4s^2 4p^5 5p^4 4f^{n+2}$.

The above rule holds worst for heavy lanthanides; therefore, the configuration interaction should be manifested in the Ln4s spectra of these metals to a lesser extent than in the case of light lanthanides (see Table 1, Fig. 15). This interaction can lead to broadening of the Ln4s lines in the spectra of lanthanide trifluorides. For Gd³⁺, this agrees with the results of theoretical calculations.⁹⁵

In the Ln4s spectra of LnF₃, as in the spectra of lanthanide metals,⁹³ multiplet splitting is about twice as effective as in the Ln5s spectra (Fig. 16, see also Fig. 15). The maximum value is reached for GdF₃, in which the Gd³⁺ ion contains the greatest number of unpaired Gd4f electrons and occurs in an energy state with the multiplicity $2S + 1 = 8$. The dependence of the multiplet splitting for the Ln4s and Ln5s lines on the multiplicity ($2S + 1$) of the state of the lanthanide ion in the trifluorides is reflected in Fig. 16, which shows the data of different researchers obtained using both $AlK_{\alpha 1.2}$ and $MgK_{\alpha 1.2}$ excitation types (The data gained with different types of excitation supplement each other.)

The multiplet splitting values (ΔE_{ms}) found by Teterin *et al.*^{5, 42} are somewhat lower than the corresponding values determined by Cohen *et al.*⁴⁴ Apparently, this is due to the fact that in determining the ΔE_{ms} values, Teterin *et al.*^{5, 42} used, whenever possible, the binding energies for the 4s and 5s electrons found

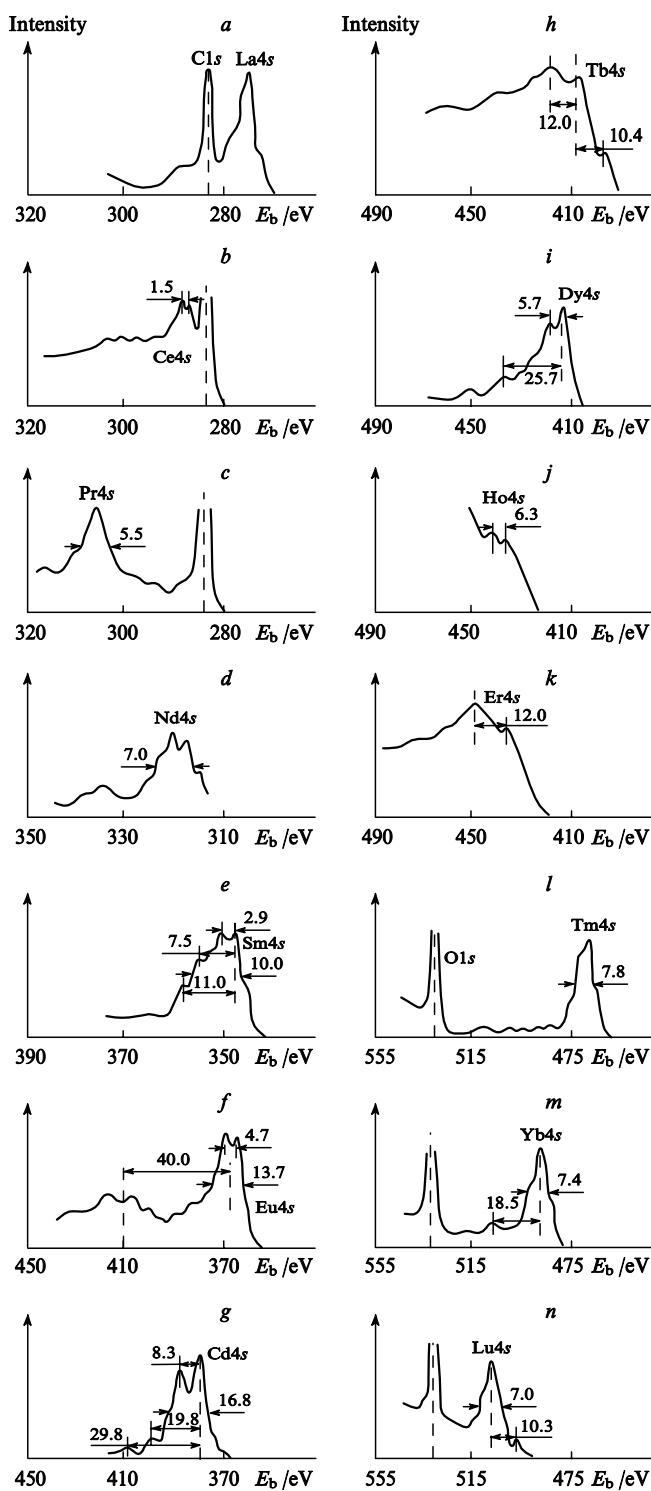


Figure 15. XPS spectra of lanthanide trifluorides in the Ln4s binding energy range.⁴² (a) LaF₃, (b) CeF₃, (c) PrF₃, (d) NdF₃, (e) SmF₃, (f) EuF₃, (g) GdF₃, (h) TbF₃, (i) DyF₃, (j) HoF₃, (k) ErF₃, (l) TmF₃, (m) YbF₃, (n) LuF₃.

from experimental positions of the peaks rather than from the resolution of lines into two components, as was done in the other publication.⁴⁴

The experimental estimates of the ΔE_{ms} values for the Ln5s electrons are consistent with the results of calculations carried out in various approximations.^{44, 69, 87, 93} In the case of Ln4s electrons, to attain agreement with the experimental data, the researchers⁹³ multiplied the determined ΔE_{ms} values by 0.55 (see Fig. 16). The

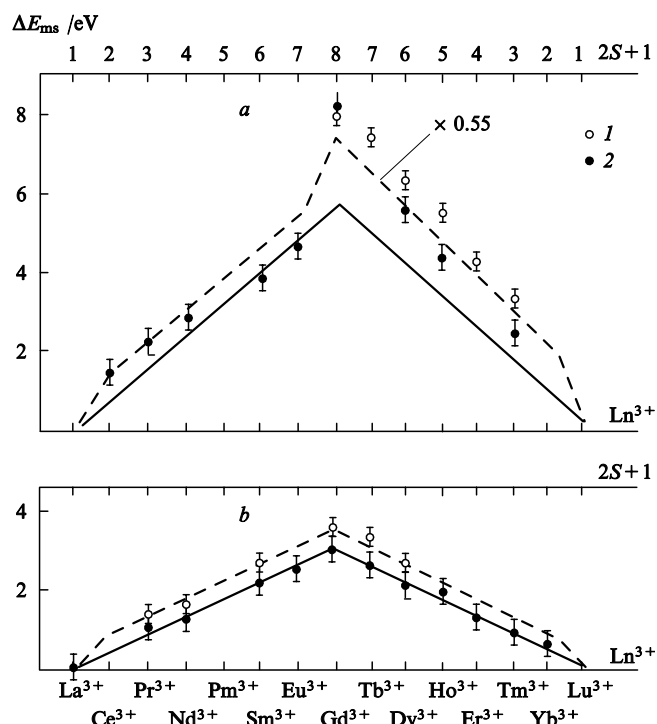


Figure 16. Multiplet splitting (ΔE_{ms}) of the Ln4s (a) and Ln5s (b) lines in the XPS spectra of lanthanide trifluorides. (1) Data of Ref. 44 (MgK_{α1,2} excitation); (2) data of Ref. 52 (AlK_{α1,2} excitation); the continuous line shows the results of the SCF X_α-DVM calculations;⁶⁹ the dashed line shows the results of *ab initio* calculations;^{44, 93} the dependence of $\Delta E_{ms}(\text{Ln}4s)$ on the multiplicity ($2S+1$) has been multiplied by 0.55.⁹³

symmetrical pattern of the calculated E_{ms} – multiplicity plots can be explained by the fact that, as the Ln4f shell of the Ln³⁺ ions is being occupied by electrons, the total spin (S) initially increases (from La³⁺ to Gd³⁺) and then gradually decreases to zero. Thus, it can be seen from Fig. 16 that the magnitude of splitting of the Ln4s and Ln5s lines characterises the number of unpaired electrons in the lanthanide ions and, as a consequence, the lanthanide oxidation state in the compound. For example, splitting of the Ce4s line, $\Delta E_{ms}(\text{Ce}4s) = 1.5$ eV, in the XPS spectrum points unambiguously to the trivalent state of the cerium ion in the fluoride. The maximum splitting of the Gd5s and Gd4s lines is also consistent with the fact that gadolinium is trivalent in the fluoride considered (see Fig. 16). In this connection, it should be noted that the structure of the Ln4s and Ln5s spectra can be useful in the determination of the oxidation and spin states of lanthanides in compounds.

b. The structures of the spectra of the Ln4d electrons

The spectra of Ln4d electrons in lanthanide fluorides exhibit a complex fine structure in an energy range of ~40 eV (Fig. 17, see also Table 1). It is noteworthy that the greatest spin–orbit splitting $\Delta E_{so}(\text{Ln}4d)$ over the lanthanide row was found for Lu and was as low as 10 eV. For other lanthanides, the corresponding $\Delta E_{so}(\text{Ln}4d)$ values cannot be determined experimentally due to the complicated structure of the Ln4d XPS spectra. In the region of the Dy4d, Ho4d, and Tm4d spectra at 231, 163 and 235 eV, the lines for Auger electrons can arise, caused by L_1MN , L_1MN and $M_5N_5O_3$ type transitions, respectively.⁹² The lines observed at 187 and 207 eV in the Yb4d spectrum might also be Auger lines caused by the $M_5N_5O_1$ and $M_5N_4O_2$ electronic transitions (see Fig. 17). The spectra can also become complicated due to many-body perturbation accompanied by the formation of shake-up satellites on the higher binding energy side of the basic lines, for example, at $\Delta E_b = 14–16$ eV. As has already been noted with regard to the Ln4s and Ln5s spectra (see Fig. 13, 15), the

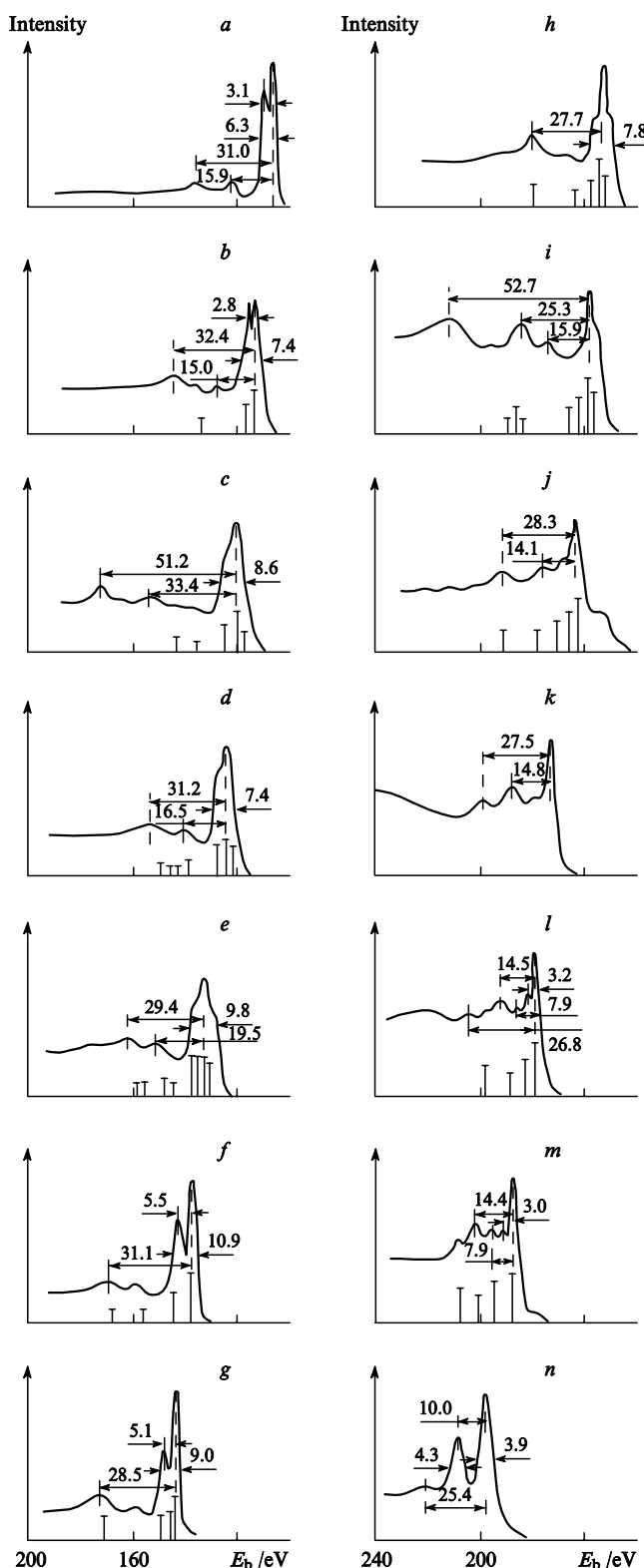


Figure 17. XPS spectra of lanthanide trifluorides in the Ln4d binding energy range.⁵² (a) LaF₃, (b) CeF₃, (c) PrF₃, (d) NdF₃, (e) SmF₃, (f) EuF₃, (g) GdF₃, (h) TbF₃, (i) DyF₃, (j) HoF₃, (k) ErF₃, (l) TmF₃, (m) YbF₃, (n) LuF₃. Vertical segments show the calculation results for the spectra of these electrons in the Ln³⁺ ions with allowance for the multiplet splitting.⁶⁶

intensity of these satellites should not be high. Among the lanthanide electronic configurations that can arise after photoemission of the Ln4d electrons upon the giant Coster-Kronig transitions between the core and valence shells, the

$\text{Ln}4d^9 5s^2 5p^6 4f^n \leftrightarrow \text{Ln}4d^{10} 5s^0 5p^5 4f^{n+2}$ configurations are the most probable. However, since the approximate equality

$$E_b(\text{Ln}4d) \approx 2 E_b(\text{Ln}5s) + E_b(\text{Ln}5p)$$

scarcely holds for lanthanides (see Table 1), it has been suggested⁴² that the structure related to the dynamic effect would not be pronounced in the Ln4d spectra.

The structure of the Ln4d spectra depends on the atomic number of the lanthanide (Z), the simplest structures being observed for LaF₃^{50, 52} and LuF₃. These fluorides contain no unpaired Ln4f electrons, and their Ln4d spectra exhibit sharp doublets related to the spin-orbit coupling. The spin-orbit splitting markedly increases by the end of the lanthanide row; indeed, it amounts to 3.1 and 10.0 eV for LaF₃ and LuF₃, respectively (see Fig. 17). The extra structure detected in the Ln4d spectra of these compounds may also be due to both the many-body perturbation and (to a lesser degree) the dynamic effect.

The Ln4d spectra of lanthanides containing the unpaired Ln4f electrons are expected to manifest multiplet splitting.^{38, 45, 96} The multiplet splitting was first observed in the spectra of 3d elements and europium.^{97, 98} Unlike the Ln5s spectra in which the line is split into two components, in the case of Ln4d spectra, the final state of the ion after photoemission of these electrons can be rather complicated. In particular, in the Ln4d spectra of most lanthanide trifluorides, the multiplet splitting gives rise to a more complicated structure in a binding energy range of ~40 eV (see Fig. 17). The results of calculations^{45, 66} of the multiplet structure of the Ln4d spectra of Ln³⁺ ions are presented in Fig. 17 as vertical segments under the experimental spectra. Qualitative agreement between the theoretical and experimental data can be noted. For example, the Gd4d spectra exhibit two most intense lines that seem to resemble in shape a doublet caused by the spin-orbit coupling of these electrons (see Fig. 17). Therefore, in the study,⁹⁹ these components in the Gd4d spectrum of metallic gadolinium and Gd₂O₃ were misattributed to the Gd3d_{5/2, 3/2} components of the doublet. In reality, these are two components of the multiplet structure largely associated with the ⁹D and ⁷D final states.⁹⁶ For the Eu atom⁹⁸ and EuO₂ (see Ref. 44), the corresponding peaks in the Eu4d spectrum were also unreasonably ascribed to a doublet. This multiplet spectral structure is typical of particular lanthanide fluorides and in some cases, it can be used to determine the oxidation and spin states of lanthanide ions.

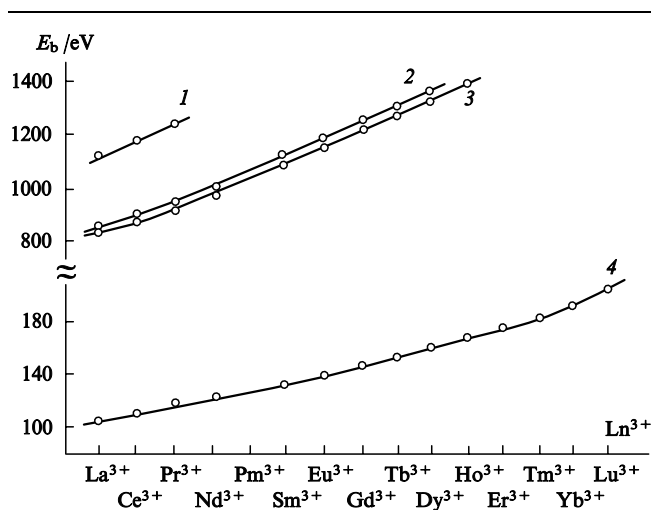


Figure 18. Binding energies (E_b) of the Ln3p_{3/2} (1), Ln3d_{3/2} (2), Ln3d_{5/2} (3) and Ln4d_{5/2} electrons (4) of lanthanide trifluorides vs. the metal atomic number in the La–Lu series.⁵ The Ln4d_{5/2} binding energies were determined for the most intense peaks; the error in the determination of the electron binding energies is ± 0.2 eV.

As the lanthanide atomic number increases, the most intense component in the $\text{Ln}4d$ spectrum shifts regularly towards higher binding energies. This component can formally be matched to the $\text{Ln}4d_{5/2}$ electrons. Figure 18 shows the variation of the binding energies of these components vs. the lanthanide atomic number; the pattern of variation is the same as observed for the core electrons.²² The energies of the $\text{Ln}4d_{3/2}$ electrons can be estimated taking into account the fact that the spin–orbit splitting $\Delta E_{\text{so}}(\text{Ln}4d)$ gradually increases, as noted above, along the lanthanide row (La to Lu) from 3.1 to 10.0 eV.

c. The spectra of the $\text{Ln}4p$ and $\text{Ln}3p$ electrons

The binding energy range corresponding to the $\text{Ln}4p$ electrons in the spectra of lanthanide trifluorides may contain, besides the $\text{Cl}1s$ line caused by the hydrocarbon molecules absorbed on the sample surface, lines related to the Auger electrons.²⁰ These lines are broad and often reflect a whole series of Auger transitions (Fig. 19). For example, the increase in the intensity which starts at 350 eV in the $\text{Dy}4p$ spectrum of dysprosium trifluoride may be due, to an extent, to the electrons of the M_5NO type Auger transitions.⁹² In the $\text{Ho}4p$ spectrum, the Auger lines caused by the M_5NO transitions at $E_b > 310$ eV are so intense that the electronic structure of the XPS spectrum can hardly be observed. The broad band at 400 eV occurring in the $\text{Tm}4p$ spectrum is attributable to the $M_5N_3O_3$ (395.2 eV), $M_5N_4N_5$ (391.1 eV) and $M_5N_4N_4$ (403.2 eV) Auger transitions. The Auger electrons of the $M_5N_2O_2$ (385.8 eV) and $M_5N_1N_7$ (421.7 eV) transitions can be manifested in the $\text{Yb}4p$ and $\text{Lu}4p$ spectra, respectively.

Apart from the lines of the Auger electrons, low-intensity shake-up satellites occur at higher binding energies (by 4–16 eV) than the basic spin doublet lines. In this range of the electron binding energies of lanthanide trifluorides containing unpaired $\text{Ln}4f$ electrons, multiplet splitting can also be observed. Since the LaF_3 and LuF_3 molecules contain no unpaired $\text{Ln}4f$ electrons, the complex structure arising in the spectra of their $\text{Ln}4p$ electrons cannot be attributed to this splitting. The $\text{Ln}4p_{1/2}$ component in these spectra is diffuse; in the case of the $\text{La}4p_{1/2}$ line, the diffusion is pronounced, whereas the $\text{Lu}4p_{1/2}$ spectrum deviates to a lesser extent from the expected one.

Comparison of the $\text{Ln}4p$ and $\text{Ln}4d$ binding energies (see Table 1) shows that the approximate equality $E_b(\text{Ln}4p) \approx 2E_b(\text{Ln}4d)$ holds satisfactorily for the whole lanthanide row. This fact and the presence of a complex structure in the $\text{Ln}4p$ spectrum of lanthanum trifluoride suggest that the significant complication of the $\text{Ln}4p$ spectra for LnF_3 is due to the dynamic effect, which leads to the formation of several final states, $\text{Ln}4p^54d^{10}4f^n \leftrightarrow \text{Ln}4p^64d^84f^{n+1}$ (see Ref. 20). In the case of LuF_3 in which $\text{Lu}4f$ is fully occupied, the giant Coster-Kronig transition of an electron from the $\text{Lu}4d$ shell to the vacant shell next in energy can take place. The probability of such a transition is lower than that of the transition to the $\text{Ln}4f$ shell; therefore, the structural changes in the $\text{Lu}4p$ spectrum caused by the dynamic effect are less pronounced than those in the case of the $\text{La}4p$ spectrum.

The $\text{Ln}3p_{3/2}$ spectra for lanthanum, cerium and praseodymium can be analysed in a similar way (Fig. 20). In these spectral ranges, Auger lines can show up.⁹² Thus, the $\text{Ln}3p_{3/2}$ spectra can be superimposed by the Auger lines of the $M_5N_1N_3$ transitions (1125.6, 1132.0 eV). The Auger transitions of the M_3NO (1184.5 eV), M_3NN (1184.5 eV) and $M_5N_1N_1$ (1202.3 eV) types may be manifested in the $\text{Ce}3p_{3/2}$ range in the spectrum of cerium trifluoride; among other factors, this can be responsible for the intense peak observed at 1200 eV in its XPS spectrum. The Auger electrons of the M_3NN (1175.4 eV) and M_5NN_1 transitions (1184.6 eV) may be a reason for the appearance of the intense broad band at 1226 eV in the $\text{Pr}3p_{3/2}$ spectrum of praseodymium trifluoride.

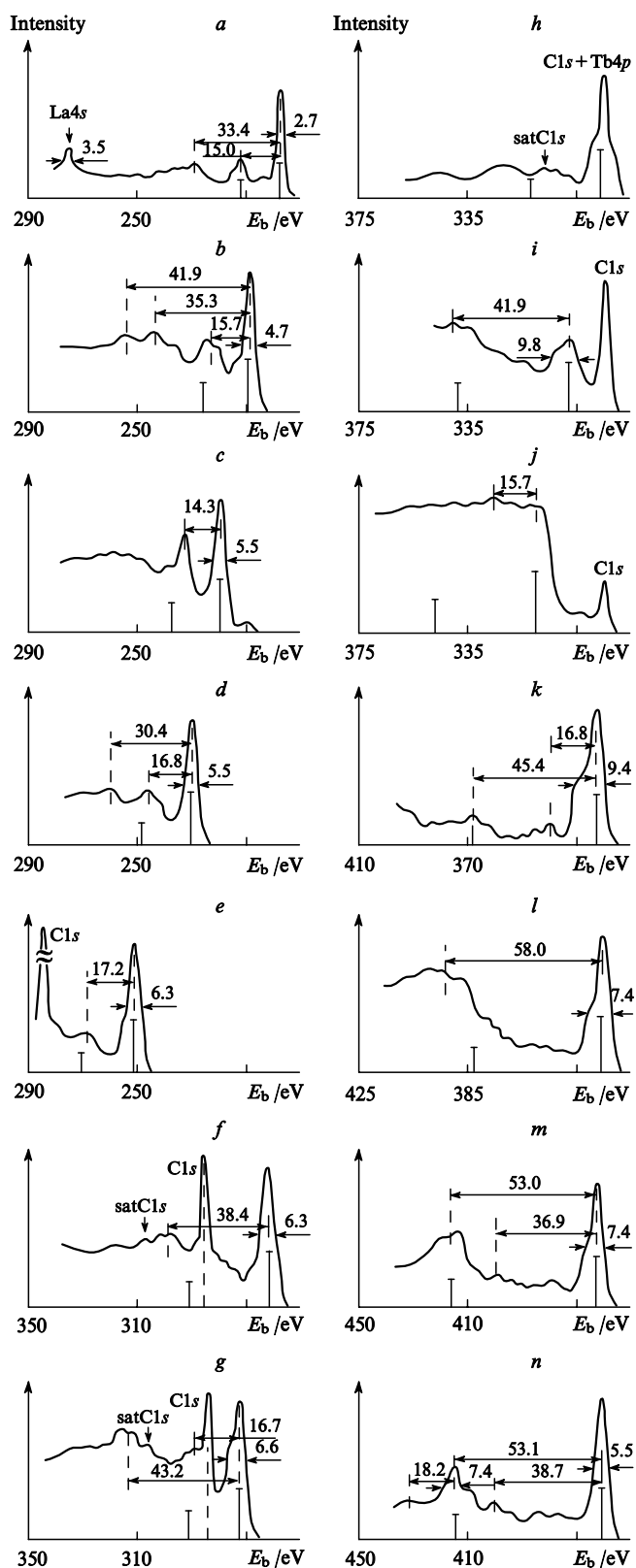


Figure 19. XPS spectra of lanthanide trifluorides in the $\text{Ln}4p$ binding energy range. (a) LaF_3 , (b) CeF_3 , (c) PrF_3 , (d) NdF_3 , (e) SmF_3 , (f) EuF_3 , (g) GdF_3 , (h) TbF_3 , (i) DyF_3 , (j) HoF_3 , (k) ErF_3 , (l) TmF_3 , (m) YbF_3 , (n) LuF_3 .²⁰ Vertical segments show the expected energies for the atomic components of the $\text{Ln}4p_{3/2, 1/2}$ electrons;²² sat is satellite.

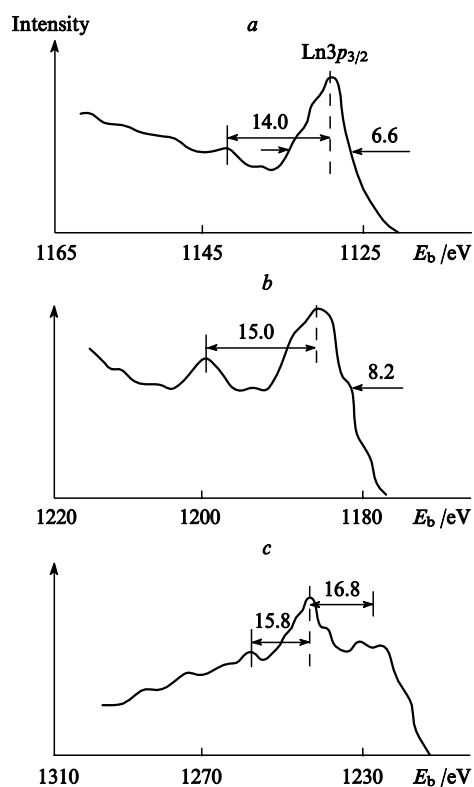


Figure 20. XPS spectra of lanthanum (a), cerium (b), and praseodymium (c) trifluorides in the $\text{Ln}3p_{3/2}$ binding energy range.⁵²

In these spectra, the peaks located at higher (by 14–16 eV) binding energies than the basic lines may be due to many-body perturbation. Since the approximate equality

$$E_b(\text{Ln}3p) \approx E_b(\text{Ln}3d) + E_b(\text{Ln}4s),$$

is obeyed, a structure related to the dynamic effect, giving rise to the $\text{Ln}3p^5 3d^{10} 4s^2 4f^n \leftrightarrow \text{Ln}3p^6 3d^9 4s^1 4f^{n+1}$ final states, should be expected in the $\text{Ln}3p$ spectra. By using a different excitation source, the structure due to a dynamic effect can be separated from the Auger lines. However, apart from $\text{AlK}_{\alpha 1,2}$ radiation (1486.6 eV), only $\text{MgK}_{\alpha 1,2}$ radiation (1253.6 eV) is currently available but its energy is not sufficient for recording these spectra. In this case, a synchrotron radiation source with variable energy is required. The dependence of the $\text{Ln}3p_{3/2}$ binding energy on the lanthanide atomic number for three fluorides is shown in Fig. 18 (curve 1). The $\text{Ln}4p$ and $\text{Ln}3p$ spectra of lanthanide trifluorides are typical of individual compounds and can be used for identification.

d. The structure of the spectra of the $\text{Ln}3d$ electrons

In X-ray photoelectron spectroscopy, determination of the oxidation states of elements from the chemical shifts of their core energy levels is normally done using the most intense single lines corresponding to the ground final state of the ion resulting from electron photoemission. In the case of lanthanide compounds, this procedure is faced with problems, because, as noted above, virtually all the spectral lines situated in the binding energy range normally employed in XPS are structured. As a rule, $\text{Ln}3d$ lines are used for this purpose whenever possible. However, the spectra of these electrons for light lanthanides also have a clear-cut fine structure, while in the case of heavier REE, due to high $\text{Ln}3d$ binding energies, the relevant lines are highly broadened or cannot be observed at all without using the synchrotron radiation (Fig. 21). The structure of the $\text{Ln}3d$ spectra of REE related to the spin–orbit splitting has been considered theoretically.¹⁰⁰

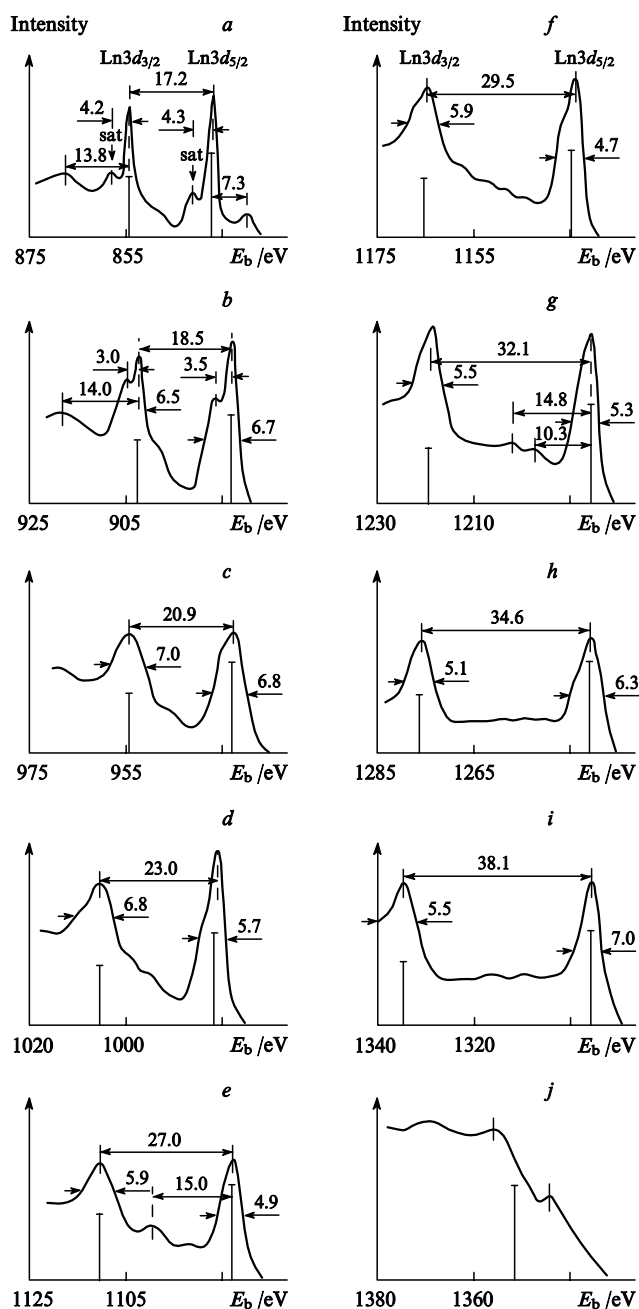


Figure 21. XPS spectra of lanthanide trifluorides in the $\text{Ln}3d$ binding energy range.⁴² (a) LaF_3 , (b) CeF_3 , (c) PrF_3 , (d) NdF_3 , (e) SmF_3 , (f) EuF_3 , (g) GdF_3 , (h) TbF_3 , (i) DyF_3 , (j) HoF_3 . Vertical segments show the lines of the lanthanide atomic spectra.²²

The need for determination of the $\text{Ln}3d$ binding energies in lanthanide compounds has stimulated investigations into the nature of the fine structure observed in these spectra.^{41, 46, 75, 101–109} It is worth noting that some Auger electron lines can also occur in this spectral region.⁹² Thus the $\text{Ln}3d$ spectra for lanthanum and cerium exhibit peaks associated with Auger electrons of the $M_5N_3O_3$ (865.6 eV) and $M_5N_1O_2$ (918.3 eV) transitions, respectively (see Fig. 21). The shoulder on the higher binding energy side with respect to the $\text{Nd}3d_{3/2}$ line can be partly due to the Auger electrons of the $M_2N_2N_2$ transition (1012.1 eV). Broadening of the $\text{Sm}3d_{3/2}$ line can also be related to the superimposition of the Auger line of the M_5N_1N transition (1118.6 eV) onto this spectrum. Due to the Auger N_3OO transition (1341.0 eV), the $\text{Ho}3d_{5/2}$ spectrum virtually cannot be observed. A similar complex structure, except for the Auger lines, shows

itself in the binding energy range of Ln3d electrons in the spectra of LaF₃ and CeF₃ recorded with MgK_{α1,2} excitation (1253.6 eV).⁴⁶ Hence, the intense extra structure in the spectra of these electrons is not related to Auger transitions.

Comparison of the binding energy of low-energy electrons [$E_b \leq E_b(\text{Ln}3d)$] suggests that the structure caused by the dynamic effect is unlikely in the Ln3d spectra. The dependence of the FWHM value (Γ) in the Ln3d_{5/2} spectra on the lanthanide atomic number ($58 \leq Z \leq 66$) suggests that the multiplet splitting does not play a crucial role in the appearance of the extra structure or line broadening (Fig. 22). If this broadening were largely related to the multiplet splitting, as has been noted in some publications,^{101–103} the maximum line width over the Ce³⁺–Gd³⁺ series would be expected for the Gd3d_{5/2} electrons; this does not agree with the $\Gamma(Z)$ dependence found experimentally (see Fig. 22).

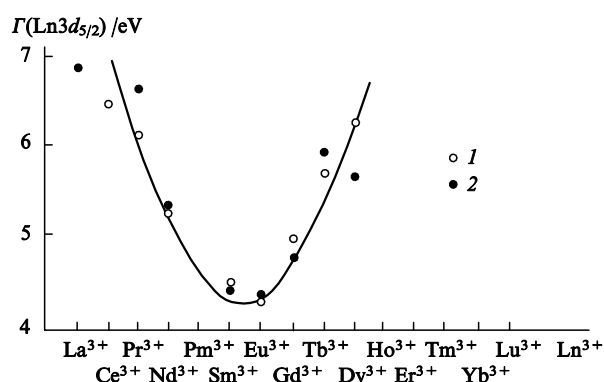


Figure 22. Dependence of the width (Γ) of the Ln3d_{5/2} line on the lanthanide atomic number in the La–Lu series.⁴² (1) LnF₃, (2) Ln₂O₃. The Γ values are referred to $\Gamma(\text{Cl}1s) = 1.3$ eV.

The Ln3d spectra of lanthanide trifluorides exhibit low-intensity shake-up satellites located at a higher binding energy (by 14–16 eV) than the most intense Ln3d_{5/2} lines. The researchers' opinions concerning the nature of the low-energy spectral structure in the vicinity of the basic lines vary. While admitting that for light lanthanides such as La, Ce and so on, the spectral structure in the Ln3d binding energy range is mainly due to many-body perturbation, some researchers believe that these extra lines are shake-up satellites,^{45, 104–107} while others consider them to be shake-down satellites.^{75, 108, 109} A fundamental difference between the two above standpoints is that the line located at a lower binding energy, in the Ln3d_{5/2} range is interpreted as either the basic line or a satellite caused by the many-body perturbation. It is noteworthy that the binding energy of the Ln3d electrons of the ground state has to be known for the solution of many problems.

The presumptive mechanism of the appearance of the Ln3d satellites in the XPS spectra can be illustrated by means of diagrams shown in Fig. 23. They are based on the results of X_α-SW (scattered wave) calculations for the LaF₃, CeF₃, CeF₃⁺ and YbF₃ (D_{3h} symmetry) clusters in which $R(\text{La}–\text{F}) = 0.246$ nm, $R(\text{Ce}–\text{F}) = 0.241$ nm and $R(\text{Yb}–\text{F}) = 0.226$ nm.^{47, 48} The calculations of the electronic structures of these clusters before and after photoemission of an Ln3d electron were performed and MO occupancies in these clusters were analysed. On the basis of these data and using the two-level Larsson's model (see Refs 47 and 110 and references therein), the satellite intensities and energies were estimated with respect to the basic spectral lines in the sudden approximation.^{111, 112} These results have enabled some qualitative conclusions.⁴⁷

For example, for the LaF₃ cluster (D_{3h} symmetry), the removal of an Ln3d electron was found to reduce substantially the energy difference between the system of occupied bonding a'_1 , e' , e'' , a'_2 , a'_2 and e' OVMO, which mainly consist of F2p AO, and

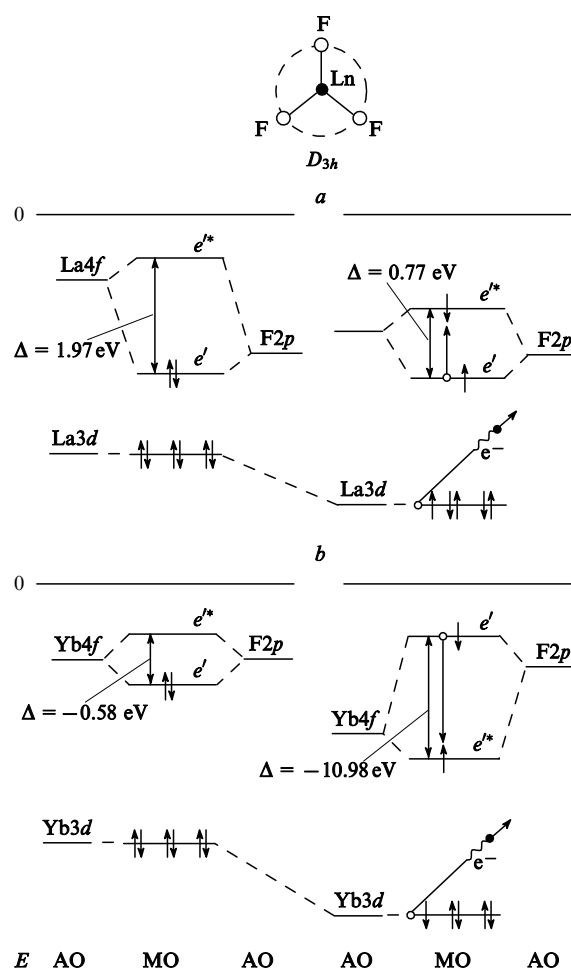


Figure 23. Diagrams illustrating the mechanisms of formation of shake-up (a) and shake-down satellites (b) in the XPS spectra of Ln3d electrons constructed with allowance for the results of X_α-SW calculations for the LnF₃ clusters (D_{3h} symmetry).⁴⁷ The left-hand part of the figure presents the initial states of the systems, while the right-hand part shows the final states after electron photoemission.

the system of vacant antibonding e'' , a'_2 , e'^* , a'_2 and a'_1 OVMO, which include the Ln4f AO. This is due to the fact that the OVMO containing the Ln4f AO respond more efficiently to the appearance of a hole in the lanthanum atom than the OVMO containing the F2p AO. This is reflected in the diagram for the e' and e'^* OVMO couple in lanthanide trifluorides (see Fig. 23 a). In this case, the energy difference (Δ) between these MO decreases from 1.97 to 0.77 eV. Therefore, photoemission of an Ln3d electron can induce electron subexcitation within the considered OVMO, reflecting transition from the e' to e'^* OVMO. Since the e' OVMO energy is greater in magnitude than the e'^* OVMO energy, this transition corresponds to a shake-up process. In the Ln3d spectrum, the corresponding satellites should occur at higher energies than the basic lines. These results show that most intense low-energy lines observed in the La3d spectrum of lanthanum trifluoride should be assigned to the ground final state with a hole in the La3d level. The theoretical values for the satellite energy and its intensity with respect to the basic lines $\Delta E_{\text{sat}} = 1.1$ eV and $I_{\text{sat}}/I_0 = 0.42$ (I_{sat} and I_0 are the satellite and basic line intensities, respectively) differ substantially from the experimental values (4.3 eV and 0.30).⁴² Similar results were obtained for the CeF₃⁺ ($\Delta E_{\text{sat}} = 1.1$ eV, $I_{\text{sat}}/I_0 = 0.23$) and CeF₃ (1.1 eV and 0.37, respectively) clusters. The experimental ΔE_{sat} and I_{sat}/I_0 values for CeF₃ are 3.5 eV and 0.58.⁴²

For the YbF₃ cluster (D_{3h} symmetry), the calculations imply that the MO related to the Yb4f/AO are comparable in energy with

the OVMO caused by the F2p AO.⁴⁷ The removal of two Yb3d electrons entails a very pronounced increase in the energies of these two groups of MO; the energies of the OVMO composed of the Yb4f AO are appreciably increased, and the energy levels of these MO become lower than those of the OVMO formed by the F2p AO. For instance, for the e'^* and e' OVMO couple shown in Fig. 23 b, the energy difference reaches 10.98 eV in magnitude. In this case, transition of an electron from a higher OVMO, for example, e' , to the lower e'^* MO can occur simultaneously with the Yb3d photoemission. Since the e' MO energy is lower than the e'^* MO energy, this transition, as noted above, is referred to as a shake-down process and the spectral structure caused by this transition is a shake-down satellite. In particular, it follows from the results of calculations⁴⁷ that the shake-down satellites in the Yb3d spectrum are expected to occur at lower binding energies than the basic lines ($\Delta E_{\text{sat}} = -16.0$ eV), their intensity being about 5 times as high as the basic line intensity ($I_{\text{sat}}/I_0 = 4.81$). It is noteworthy that no experimental data for this electron energy range for ytterbium compounds are available to date for the reasons noted above.

On the basis of the calculation results, it was concluded⁴⁷ that an increase in the number of Ln4f electrons in the lanthanide fluoride brings about displacement of the satellites in the Ln3d spectra from left to right with respect to the basic doublet components. It remains unknown in which lanthanide spectrum in the La–Lu series the sign of the ΔE_{sat} changes.

It is noteworthy that some suggestions concerning the reasons for the appearance of satellites in the Ln3d spectra based on the results of theoretical calculations do not contradict the available experimental data. Thus an insignificant shift should be expected for the line of the OVMO formed mainly by the F2p AO of fluorides (see Fig. 3) because the F1s binding energy (E_b) changes slightly with an increase in the lanthanide number (Z). In the case of LaF₃, the OVMO line is observed at 8.1 eV (see Table 1, Fig. 1). In the LnF₃ spectra, the centre of gravity of the structure caused by the Ln4f electrons shifts from the level taken as the reference point toward higher binding energies. Due to this shift, the OVMO related to the Ln4f AO and those related to the F2p AO can become equal in energy at some Z , which agrees with the theoretical results (see Fig. 3). Hence, on photoemission of an Ln3d electron, the Ln4f electronic level is expected to be located lower than the corresponding F2p electronic levels. This should favour a shake-down electronic transition (see Fig. 23).

As the atomic number of lanthanide increases, at least, in the case of transition from LaF₃ to PrF₃, the Ln3d spectra show a decrease in the difference between the electron binding energies of the basic and satellite lines (ΔE_{sat}). Furthermore, with the assumption that one reason for the substantial broadening of the Ln3d spectral components is the formation of satellites, the change in the Ln3d_{5/2} FWHM upon an increase in Z (see Fig. 22) can be attributed to migration of the satellite from left to right on passing from La to Lu, as has been suggested on the basis of calculations. In this case, the change in the sign of ΔE_{sat} is to be expected at about $Z = 63$ (Eu) (see Fig. 22).

For identification of lines in the Ln3d spectra of the trifluorides of light lanthanides, Teterin and Baev⁵ have proposed comparing the differences between the electron binding energies of different shells found for metallic lanthanides and for lanthanide compounds. The following values were found for LaF₃: $\Delta E_b(\text{La}5p_{3/2} - \text{Ln}3d_{5/2}) = 818.4$ (823.0) eV, $\Delta E_b(\text{La}5p_{3/2} - \text{La}4d_{5/2}) = 85.8$ eV and $\Delta E_b(\text{La}4d_{5/2} - \text{La}3d_{5/2}) = 732.6$ (737.2) eV (the energies for weaker lines or shoulders are given in parentheses; see Table 1). The corresponding differences between the electron binding energies for metallic lanthanum are 818.2, 86.0 and 732.2 eV. The value $\Delta E_b(\text{La}5p_{3/2} - \text{La}3d_{5/2}) = 818.2$ eV coincides within the error of measurement with a value of 818.6 eV, found by Schlappach and Scherrer.⁹¹

If one assumes that after the IVMO formation from the La5p and F2s AO in lanthanum trifluoride, the spectrum in the La5p_{3/2} region does not differ much from the atomic spectrum (see

Table 1), the comparison of the ΔE_b values leads to the conclusion that the basic La3d line in the spectrum of LaF₃ is located at lower electron binding energies. The satellites recorded at higher (by 4.3 eV) binding energies with respect to the basic lines are due to the shake-up process.

The results of comparison of the binding energy differences $\Delta E_b(\text{Ce}5p_{3/2} - \text{Ce}3d_{5/2})$ for CeF₃ (865.3, 868.8 eV) (see Table 1) and for metallic cerium (866.3 eV),¹¹³ at least, do not contradict the statement that the satellites in the Ce3d spectra are shake-up satellites observed at higher binding energies than the basic lines. The theoretical data do not disprove this either.¹¹⁴ Comparison of the results of calculations for YbF₃ with the experimental spectra is difficult due to the fact that the Yb3d_{5/2} binding energy ($E_b = 1527$ eV) is beyond the range accessible for measurements as long as X-ray AlK _{α} 1,2 excitation is used (1486.6 eV).

The dependence of the Ln3d binding energy on the lanthanide atomic number is shown in Fig. 18. On the basis of the binding energies of these electrons, one can draw conclusions concerning the oxidation state of lanthanides from La to Ho. Note that the use of synchrotron radiation provides the possibility of an XPS study of the Ln3d electrons and compounds of heavier lanthanides.

III. Lanthanide oxides

Lanthanide oxides are the REE compounds most abundant in nature. They serve as the main raw materials for the production of various technologically important lanthanide compounds. Therefore, despite difficulties associated with experimental and theoretical investigations of the electronic structures of lanthanide oxides, this problem attracts increasing attention. These difficulties are related to the complexity of the lanthanide electronic configurations, low symmetry of the close environment of metal atoms in the crystal lattices, and to the presence of Ln ions in different oxidation states in some oxides. Thus praseodymium and terbium oxides are known¹ to have complex stoichiometric compositions (Pr₂O₃·4PrO₂ and Tb₄O₇). The oxidation state of cerium in the cerium oxide is still open to question. According to data obtained by different researchers, this oxide is either described by the general formula CeO₂ (see Ref. 1), or contains a CeO₂· n Ce₂O₃ mixture on the surface,¹¹⁵ or contains variable-valence cerium.¹¹⁶ The other lanthanide oxides may have a stoichiometric composition corresponding to Ln₂O₃.

In recent years, the XPS method has been widely used in the study of REE oxides^{27, 39, 41, 42, 50, 80, 99, 108, 115, 117–127} and some other oxygen-containing compounds.^{19, 28–30, 41, 53, 78, 79, 84, 128} Important information concerning the electronic structures of these oxides can also be drawn from X-ray emission spectra,^{129, 130} however, in most cases, studies are carried out for oxide films and separate electronic shells of metals. In a number of publications,^{5, 18, 20, 37, 68} lanthanide (except for Pm) oxides were studied as bulk samples (pressed powders). Attention was concentrated on elucidation of the mechanisms of formation of fine structure in the spectra of these compounds and the dependence of the spectral structure on the physicochemical properties and on the nature of chemical bonding in lanthanide oxides. For this purpose, the spectra over the whole energy range accessible for measurements were analysed. The binding energies of various electron shells in the ~0–1350 eV range for the oxides under study are presented in Table 3. In all cases, two lines of O1s electrons were observed. The component located at a lower binding energy is attributable to the oxide oxygen,^{33, 41} while the less intense line at higher binding energies should be ascribed to impurities containing carbonate or hydroxy groups.^{19, 131} It has been noted^{5, 42} that successful interpretation of the mechanism of appearance of the fine spectral structure requires that the data for the whole REE row be obtained using the same XPS spectrometer under the same conditions. The results of experimental studies that comply with this requirement^{20, 37, 68, 79, 132–136} are of special interest.

Table 3. Electron binding energies (E_b /eV) for lanthanide oxides.^{5, 59}

Compound	OVMO	IVMO ^a				Ln4 <i>d</i> _{5/2, 3/2}	Ln4 <i>p</i> _{3/2, 1/2}	Ln4 <i>s</i>	Ln3 <i>d</i> _{5/2} (see ^b)	O1 <i>s</i> (see ^b)
		Ln5 <i>p</i> _{3/2}	Ln5 <i>p</i> _{1/2}	O2 <i>s</i>	Ln5 <i>s</i>					
La ₂ O ₃	4.9	17.7	19.4	—; 24.0	35.0	102.8; 105.8	196.3; 199.4; 206.4	274.9	835.1; (888.6)	528.9; (531.4)
CeO ₂ (see ^c)	5.0	18.0	unknown	unknown	36.8	108.5; 112.0; 114.4	207.1; 214.1	288.8	832.3; (888.8)	529.5; (531.8)
Pr ₂ O ₃ (see ^c)	3.7; 5.9	19.3	22.9	—; 24.0	37.4; 38.4	114.0; 116.8; 119.8; 128.2; 131.0	218.5	303.9; 305.9	(929.5); 933.5	528.9; (531.8)
Nd ₂ O ₃	5.3; 9.0	19.4	23.0	—; 24.1	39.1; 40.6	122.0; 125.0	226.4; 229.7; 243.5	319.0; 321.5	(978.0); 981.9	529.4; (531.1)
Sm ₂ O ₃	5.7; 8.2	20.4	24.4	unknown	40.8; 43.3	132.7; 135.1	250.4	348.8; 353.3	1083.1	529.2; (531.6)
Eu ₂ O ₃	—; 7.3	21.5	25.7	the same	43.3; 46.2	136.5; 142.0; 166.4	261.2; 264.2	364.3; 369.8	1134.6	529.2; (531.6)
Gd ₂ O ₃	5.7; 9.0	22.3	27.4	"	44.3; 48.0	142.8; 147.9; 171.8	270.6; 272.6	378.8; 386.7	1187.3	529.3; (531.7)
Tb ₂ O ₃ (see ^c)	3.0; 7.6; 9.8	23.0	28.1	19.4	46.2; 48.8	150.1; —; 178.2	284.0; 323.0	unknown	1241.1	529.2; (531.4)
Dy ₂ O ₃	3.4; 6.0; 9.1	23.4	28.5	19.7	47.0; 49.5	154.8; 156.0; 176.5; 178.9; 184.0	292.6; 294.3; 335.5	413.7; 419.6	1296.0	529.1; (531.7)
Ho ₂ O ₃	7.1; 9.7	24.7	30.4	19.5; 21.5	49.0; 50.7	161.9; 167.4; 776.6; 189.0; 198.0	308.2; 314.2	433.8; 438.2	1352.5	529.3; (531.8)
Er ₂ O ₃	6.3; 9.5	25.3	31.1	20.5; 22.5	51.3; 52.8	169.1; 175.0; 163.4; 191.7; 196.0	320.3; 326.1; 362.9	449.5; 453.0	unknown	529.4; (531.3)
Tm ₂ O ₃	6.0; 7.2; 9.1; 10.9	26.0	32.4	20.5; 23.0	53.5; 54.6	176.8; 180.0; 189.7; 192.2; 201.3	333.0; 337.0	468.8; 470.5	the same	529.4; (531.7)
Yb ₂ O ₃	7.6; 11.1	26.7	33.6	21.5; 23.8	55.4; 56.1	185.1; 188.4; 193.2; 199.3; 205.3	346.4; 399.6	488.0; 489.0	"	529.6; (531.8)
Lu ₂ O ₃	7.8; 9.0	27.5	33.9	21.6; 23.5	57.0	196.5; 206.3	359.3; 412.5	506.7	"	529.6; (531.6)
HfO ₂	5.7; 7.4; 17.4; 18.4	32.8	40.1	unknown	unknown	213.4; 223.9	unknown	"	"	530.7
Y ₂ O ₃	4.3; 5.6	25.0 ^d		20.0	45.4 ^e	156.7; 158.5 ^f	299.8; 312.0 ^g	394.0 ^h	"	530.8; (532.2)
Sc ₂ O ₃	6.0	31.5 ⁱ		21.9	53.4 ^j	unknown	401.9; 406.4 ^k	501.0 ^l	"	530.1; (531.8)

Note. The E_b values are presented for the peaks relative to the C1*s* binding energy for hydrocarbons on the sample surface [$E_b(\text{C1s}) = 285.0$ eV]. ^a The given energies correspond to IVMO electrons exhibited in the spectral ranges of the valence AO electrons. ^b The values in parentheses are the electron energies for less intense lines or shoulders. ^c The E_b values are given for Ln³⁺ in complex oxides (Ln₂O₃ · *n* LnO₂). ^d The Y4*p* line. ^e The Y4*s* lines. ^f The Y3*d*_{5/2, 3/2} lines. ^g The Y3*p*_{3/2, 1/2} lines. ^h The Y3*s* line. ⁱ The Sc3*p* line. ^j The Sc3*s* line. ^k The Sc2*p*_{3/2, 1/2} lines. ^l The Sc2*s* line.

1. Structure of the spectra of low binding energy electrons

The spectra of low binding energy electrons of lanthanide oxides exhibit two groups of lines with binding energies of ~ 0 –15 and ~ 15 –50 eV, attributable to the OVMO and IVMO electrons, respectively (Fig. 24, see Table 3). In the case of lanthanum oxide, the OVMO binding energy range, besides the line at 5.6 eV, mainly due to the $\text{La}5d$, $\text{La}6s$ and $\text{O}2p$ electrons, can display two weak maxima at $E_b = 11$ eV; these are due to some impurities containing presumably the CO_3^{2-} group (this is also valid for other Ln_2O_3). The corresponding $\text{C}1s$ line is located at $E_b = 290.8$ eV. In the spectra of lanthanide oxides containing $\text{Ln}4f$ electrons, the intensity of the corresponding lines gradually increases with an increase in the atomic number (Z) of the metal. The pattern of $\text{Ln}4f$ spectra of lanthanide oxides generally resembles the corresponding structure of the spectra of $\text{Ln}4f$ electrons in lanthanide trifluorides (see Fig. 2). The difference lies in the fact that the OVMO line reflecting mainly the $\text{O}2p$ AO in the XPS spectra of REE oxides is located at binding energies lower in magnitude than the $\text{F}2p$ line in the lanthanide fluoride spectra. For convenience of the comparison of the OVMO and $\text{Ln}4f$ binding energies in REE oxides with the corresponding characteristics of lanthanide fluorides, the absolute E_b values for lanthanide oxides were increased by 1.6 eV (see Fig. 3). This is the shift of the XPS lines of lanthanum trifluoride with respect to the lines of La_2O_3 (see Tables 1, 3). Considerations concerning the origin of the structure of the $\text{Ln}4f$ lines presented above for REE fluorides are also valid for the spectra of these electrons in lanthanide oxides (see Section II). However, the overlap of the OVMO and $\text{Ln}4f$ lines in the XPS spectra of lanthanide oxides starts at a smaller Z than in the case of LnF_3 (see Fig. 3).

The experimental dependence of the $\text{Ln}4f$ line intensity (I_{exp}) on the number n_{4f} of electrons in the Ln^{3+} ion found as the ratio of the total intensity $I[(\text{Ln}4f) + (\sum \text{OVMO})]$ in the binding energy range of 0–15.5 eV to the total intensity $I(\sum \text{IVMO})$, except for the $\text{Ln}5s$ lines, is shown in Fig. 25. Using the least-squares method, this dependence for lanthanide oxides was shown to be linear

$$I_{\text{exp}} = 0.12n_{4f} + 0.25. \quad (6)$$

By analogy with expression (5) corresponding to LnF_3 , the following theoretical dependence was derived for Ln_2O_3 :

$$I_{\text{theor}} = 0.01n_{4f}^{2.24} + 0.18. \quad (7)$$

It can be seen that, as for lanthanide trifluorides (see Fig. 5), in this case, too, the experimental and theoretical plots for the intensity vs. n_{4f} [see Eqns (6), (7) and Fig. 25] are appreciably different.

On passing from Lu_2O_3 to HfO_2 , the metal atomic number increases by unity, the number of the $\text{M}4f$ electrons (14) remains the same, and the intensity of the line under consideration increases jumpwise tending to the corresponding theoretical value (see Fig. 25). The $\text{Hf}4f_{7/2}$ -electron binding energy, equal to 17.4 eV, also markedly (by 9.6 eV) exceeds the binding energy of the OVMO electrons in lutetium (see Table 3). It follows from these data that the $\text{Lu}4f$ electrons, which can be regarded in a certain approximation as inner valence electrons, differ markedly in spectral characteristics from the $\text{Hf}4f$ electrons, which acquire some features of core electrons.

In the $\text{Ln}5p$ and $\text{O}2s$ spectral range, fine structure is observed. The structure becomes most intricate by the middle of the row of lanthanide oxides (see Fig. 24). Among other reasons, complication of the spectral structure may be due to the presence of lanthanide ions in different oxidation states in some lanthanide oxides. In this connection it should be noted that, as shown on the basis of analysis of the spectral structure of core electrons, REE oxides, except for cerium, praseodymium and terbium, contain Ln^{3+} ions. In praseodymium and terbium oxides, Pr and Tb in higher oxidation states occur as impurities, their concentrations being not higher than 5%.⁵ The spectral structure observed for cerium oxide is more complicated. If one assumes that the additional lines in the $\text{Ce}3d$ spectrum (36%) are due to Ce^{4+} ions, the

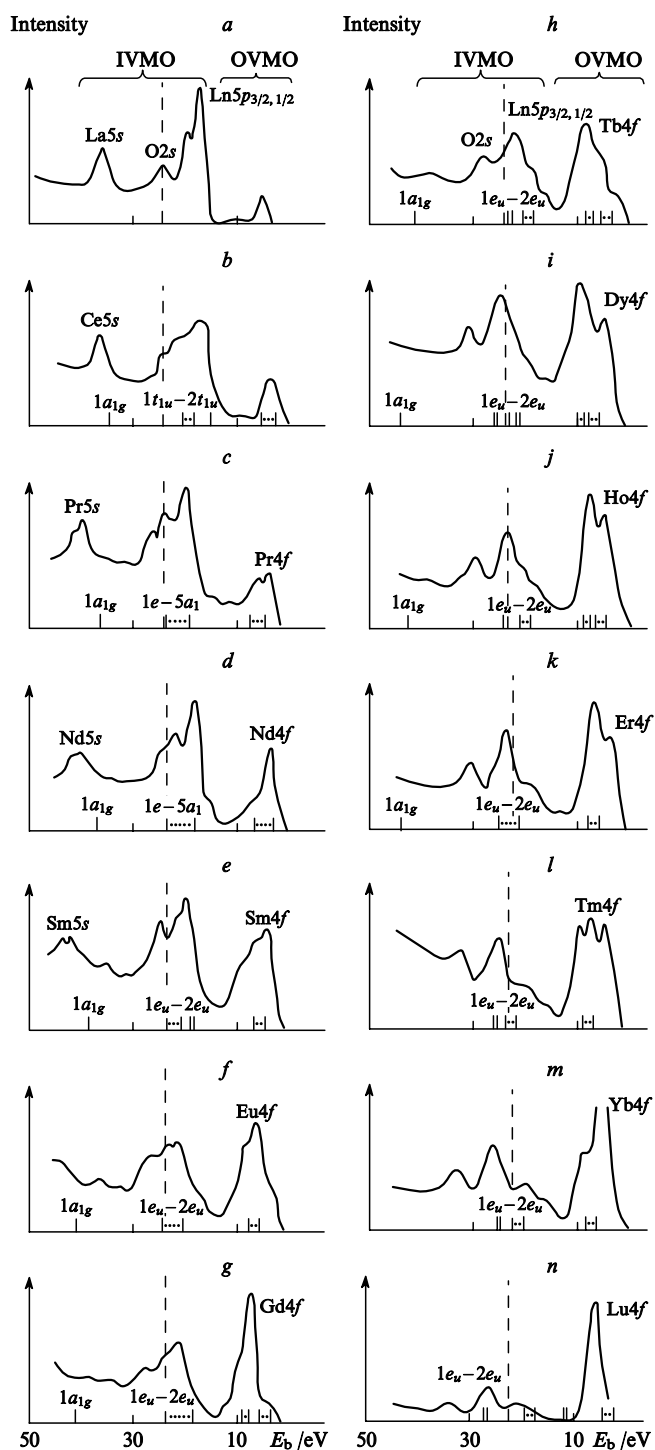


Figure 24. XPS spectra of low binding energy electrons in lanthanide oxides.¹³² (a) La_2O_3 , (b) CeO_2 , (c) Pr_2O_3 , (d) Nd_2O_3 , (e) Sm_2O_3 , (f) Eu_2O_3 , (g) Gd_2O_3 , (h) Tb_2O_3 , (i) Dy_2O_3 , (j) Ho_2O_3 , (k) Er_2O_3 , (l) Tm_2O_3 , (m) Yb_2O_3 , (n) Lu_2O_3 . Vertical segments show the results of calculations (SCF NR X_a -DVM) of the electronic structure of CeO_8^{12-} (O_h symmetry), PrO_7^{11-} and NdO_7^{11-} (C_2 symmetry), and LnO_6^{3-} (D_{3d} symmetry) for other oxides.^{57, 58}

contents of Ce^{4+} and Ce^{3+} ions on the surface of the cerium oxide studied should be 36% and 64%, respectively; this would complicate significantly the considered spectral structure (see Fig. 24). Teterin *et al.*^{137, 138} believe that the additional structure (36%) is caused by many-body perturbation involving the $\text{Ce}5s$ electrons and does not complicate the structures of the $\text{Ce}5p$ and $\text{O}2s$ spectra. Since the $\text{O}1s$ spectra of the studied REE oxides exhibit in

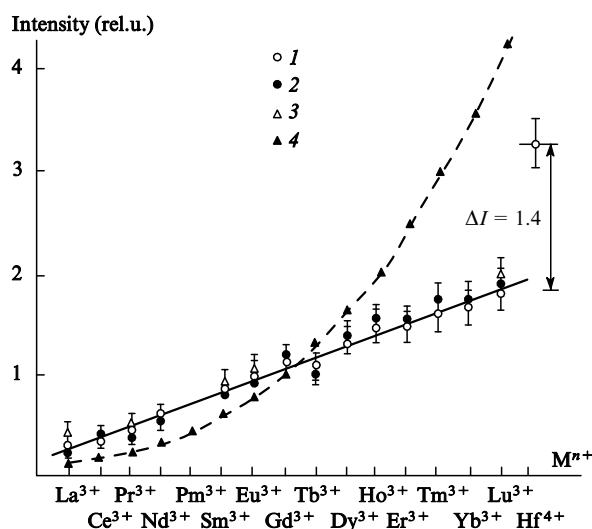


Figure 25. Relative intensity of the XPS lines of the $\text{Ln}4f$ electrons vs. the number of these electrons in lanthanide oxides (1, 2)¹³⁴ and orthoniobates LnNbO_4 (3)¹³³ and the corresponding theoretical dependence (4) [see Eqn (7)]. Two series of oxide samples were used, one provided by the Russian Research Centre ‘Kurchatov Institute’ (1) and one by the Saratov State University (2). For comparison, data for HfO_2 are given ($n_{4f} = 14$).

some cases two lines for oxygen, the $\text{O}2s$ spectrum should also contain two lines. This would complicate the spectral structure in the $\text{Ln}5p$ and $\text{O}2s$ binding energy range.

In the $\text{Ln}5p$ spectra of the oxides of light lanthanides, in particular, lanthanum, the many-body perturbation should be more pronounced than in the spectra of the corresponding fluorides. This suggestion relies on the fact that the $\text{Ln}3d$ spectra recorded for oxides exhibit more intense satellites than the corresponding spectra of fluorides. The influence of the multiplet splitting and the dynamic effect on the $\text{Ln}5p$ spectral structure should not be more pronounced in the case of REE oxides than in the case of REE fluorides and should not result in substantial complication of the spectral structure.

Since the E_b value for the $\text{O}2s$ spectra falls in the middle of the range in which the $\text{Ln}5p$ binding energy varies with an increase in the lanthanide atomic number, the formation of the inner valence MO may be a reason for the appearance of the fine spectral structure in the $\text{Ln}5p$ and $\text{O}2s$ binding energy ranges.^{55–59, 61, 62, 78, 79, 83, 84} These IVMO are largely composed of the $\text{Ln}5p$ and $\text{O}2s$ AO.^{18, 133, 135}

Lanthanide oxides have a complex geometric structure (Fig. 26),^{57–59} which accounts for complication of their electronic structures and, hence, of the XPS spectral structure for low-energy electrons and also complicates the corresponding theoretical calculations. The XPS spectra are often interpreted by referring to the results of quantum-chemical calculations for the electronic structures of lanthanide oxides.^{55, 59, 79, 84} In particular, theoretical

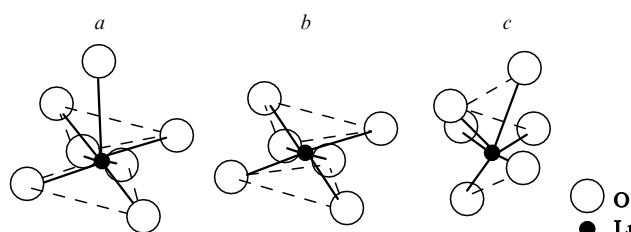


Figure 26. Model clusters of lanthanide oxides in which the structure of the local environment is taken into account.⁵⁹ (a) LnO_7^{11-} (C_2 symmetry) for La–Nd oxides; (b) LnO_6^{9-} (D_{3d} symmetry); (c) LnO_6^{9-} (C_2 symmetry) for Sm–Lu oxides.

investigation of the PrO_7^{11-} and NdO_7^{11-} clusters (C_2 symmetry), two series of LnO_6^{9-} clusters ($\text{Ln} = \text{Sm}–\text{Lu}$) (D_{3d} and C_2 groups of symmetry) and the CeO_8^{12-} complex (O_h symmetry) have been carried out in the spin-polarised approximation of the NR X_α -DV method.^{57–59} The energy levels found by these calculations are shown in Fig. 24 as vertical segments in the low-energy spectral range. Figures 27, 28 show the MO diagrams for the PrO_7^{11-} (C_2 symmetry) and TbO_6^{9-} (D_{3d} symmetry) clusters.

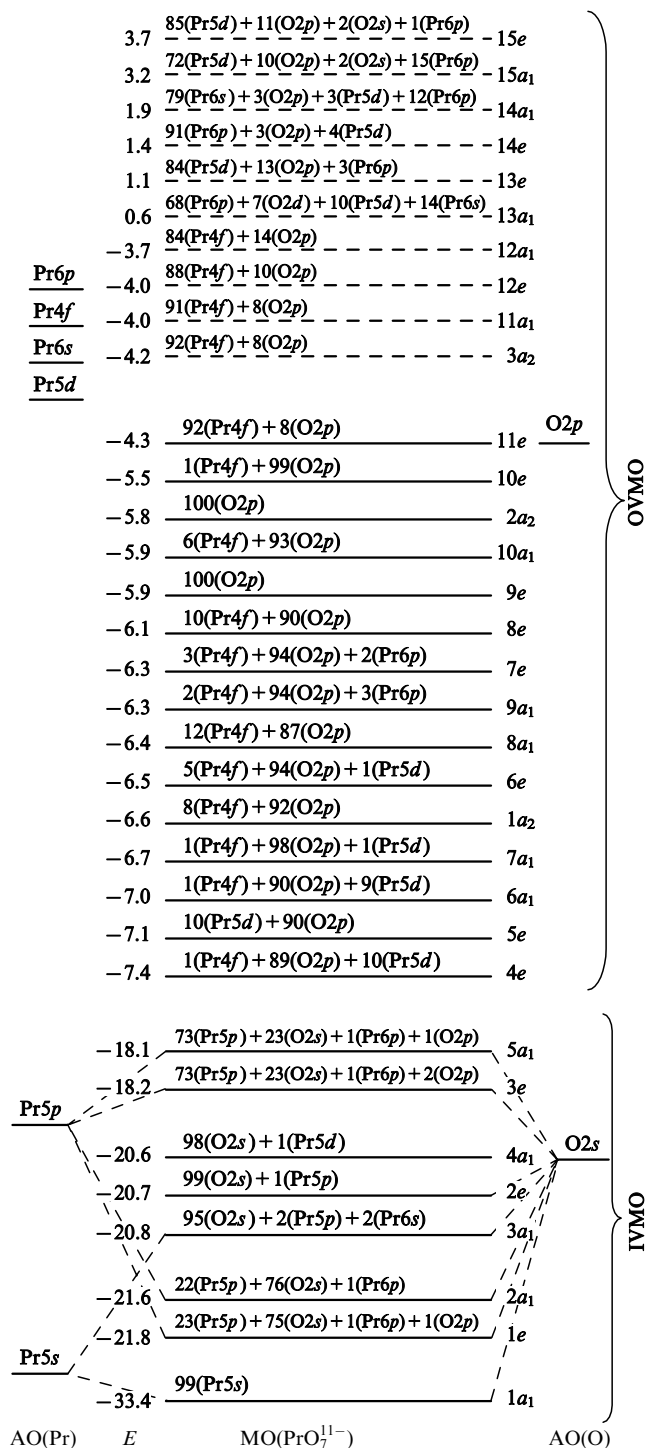


Figure 27. Diagram of the MO of the PrO_7^{11-} cluster [C_2 symmetry, $R(\text{Pr}–\text{O}) = 0.237$ nm, $R'(\text{Pr}–\text{O}) = 0.262$ nm] determined by the SCF NR X_α -DVM calculations for $\alpha(\uparrow)$.⁵⁷ MO energies (eV) and compositions (%) are given (the diagram is not scaled). Unoccupied energy levels are shown by dashed lines.

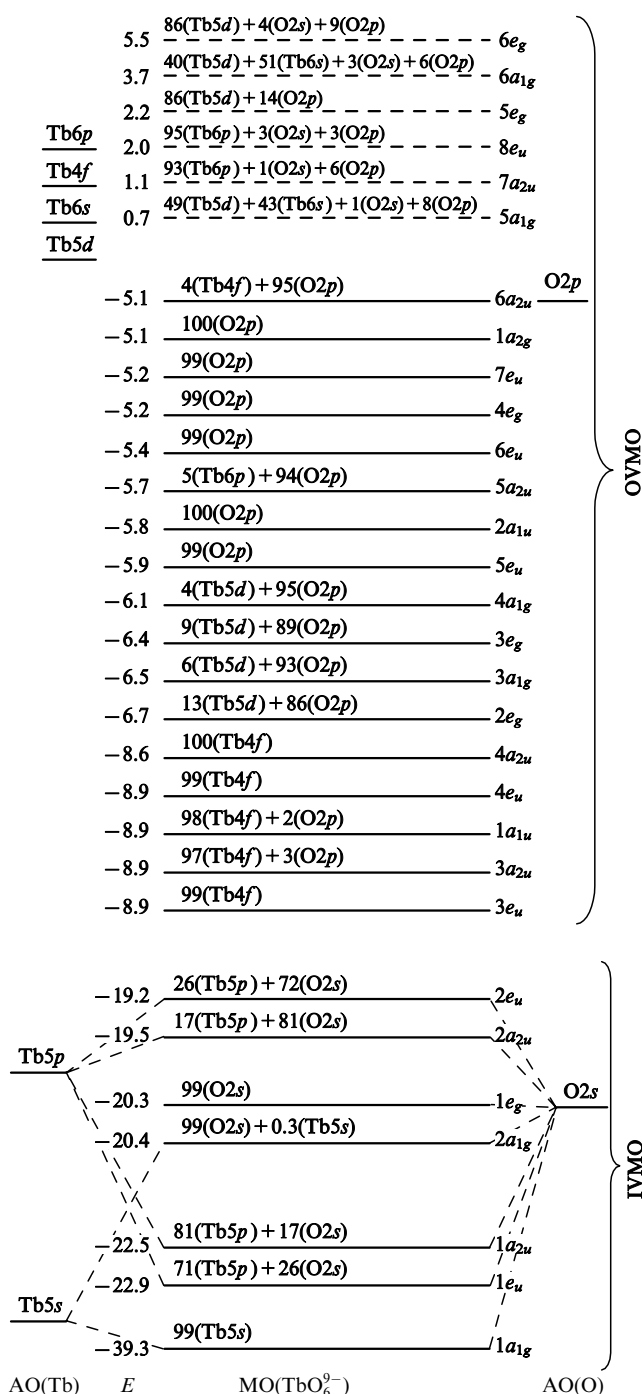


Figure 28. Diagram of the MO for the TbO_6^{9-} cluster [D_{3d} symmetry, $R(\text{Tb}-\text{O}) = 0.230 \text{ nm}$] determined by the SCF NR X_α -DVM calculations for $\alpha(\uparrow)$.⁵⁸ MO energies (eV) and compositions (%) are given (the diagram is not scaled). Unoccupied energy levels are shown by dashed lines.

As follows from the results of calculations, the PrO_7^{11-} cluster (C_2) has two groups of MO consisting of 4e–15e OVMO and 1a₁–5a₁ IVMO type orbitals (see Fig. 27). On the basis of calculations and the relevant XPS parameters, the conclusion concerning the involvement of the Ln4f AO in the formation of OVMO in the lanthanide compounds has been drawn in a number of publications.^{56–59, 68, 78, 79, 83, 84, 132}

The inner valence MO (1a₁–5a₁) of the PrO_7^{11-} cluster (C_2 symmetry) mainly consist of low-energy occupied AO of the neighbouring praseodymium and oxygen atoms. The greatest mixing of the Pr5p and O2s AO is found for the 1e, 2a₁, 3e and

5a₁ IVMO (see Fig. 27). The inner valence Pr5s AO do not participate significantly in the IVMO formation. These results indicate that a substantial overlap of the Pr5p and O2s AO, favourable for the IVMO formation, takes place in the PrO_7^{11-} cluster.

As the lanthanide atomic number increases, the energy of the Ln5p electrons approaches the O2s energy or becomes even higher for relatively large Z values; therefore, for the first half of the lanthanide row, the degree of mixing of the Ln5p and O2s AO increases upon IVMO formation, while on further increase in Z, this degree of mixing gradually decreases.

To illustrate the arrangement of the MO energy levels and the MO composition, the local environments found in the oxides formed by elements of the second half of the lanthanide row were taken into account in the simulation of the structure of the LnO_6^{9-} clusters (D_{3d} symmetry). Figure 28 shows the MO diagram based on the results of the spin-polarised NR X_α -DV calculations of the electronic structure of the TbO_6^{9-} cluster (D_{3d} symmetry).^{58, 59} The occupied 3e_u–6a_{2u} OVMO of this cluster, like those in PrO_7^{11-} , are formed by participation of the 4f AO. However, in this case, unlike PrO_7^{11-} , the molecular orbitals containing the Tb4f AO are lower in energy than the OVMO consisting mostly of the O2p AO. This is a consequence of the lower position of the Tb4f energy level compared to the Pr4f level with respect to O2p (see Fig. 3).

The IVMO in the TbO_6^{9-} cluster (D_{3d} symmetry) differ in structure from the IVMO of the PrO_7^{11-} cluster (C_2 symmetry). This is due to the different structures of these two clusters. However, in the terbium cluster, as in the praseodymium one, substantial mixing of the Tb5p and O2s AO takes place in the IVMO formation (see Fig. 28). As the lanthanide atomic number increases, the degree of participation of the Ln5p AO in, for example, the 2e_u IVMO of these clusters decreases; for LuO_6^{9-} (D_{3d} symmetry), it is as low as 4%.

According to calculations, an increase in the atomic number (Z) of lanthanides in the oxides should entail the displacement of MO energy levels caused by Ln4f electrons towards higher values, which is observed in experimental spectra (see Figs 3, 24). Indeed, the structure of the experimental spectra of Ln_2O_3 in the Ln5p and O2s binding energy ranges becomes much more complicated on approaching the center of the lanthanide row, while the spectral pattern observed for the oxides of elements situated at either the beginning or the end of the row, for example, La_2O_3 and Lu_2O_3 , is close to the sum of the atomic spectra of lanthanides and oxygen (see Fig. 24).

The similar energies of the Ln4f and O2p levels and the relatively short distances between the neighbouring lanthanide and oxygen atoms in the considered oxides may promote an increase in the degree of mixing of the Ln4f and O2p AO giving the OVMO. It is noteworthy that the involvement of the Ln5p and O2s AO in the formation of the IVMO is one of the reasons for the appearance of the fine structure in the Ln5p and O2s spectral range for lanthanide oxides.

2. The core electron spectra of lanthanide oxides

a. The Ln_2O_3 oxides

The spectral structure of the core electrons of lanthanide oxides has much in common with the spectra of the same electrons in lanthanide trifluorides provided that the lanthanide oxidation states in these compounds are equal. The formation mechanisms for the fine structure of these oxides can also be considered in the ionic approximation. Thus the spectra of the Ln5s and Ln4s electrons in Ln_2O_3 , like the spectra of the corresponding electrons in LnF_3 , exhibit multiplet splitting characterising the lanthanide spin state in oxides and fluorides (Fig. 29, see also Fig. 16). In some cases, these data can be used to determine the lanthanide oxidation state. For example, comparison of the multiplet splittings for Ln4s and Ln5s electrons in individual lanthanides and in the oxides indicates that the most pronounced discrepancy is observed between europium and Eu_2O_3 (see Fig. 29). The multiplet splitting ΔE_{ms} for the Eu4s electrons in the XPS spectra of

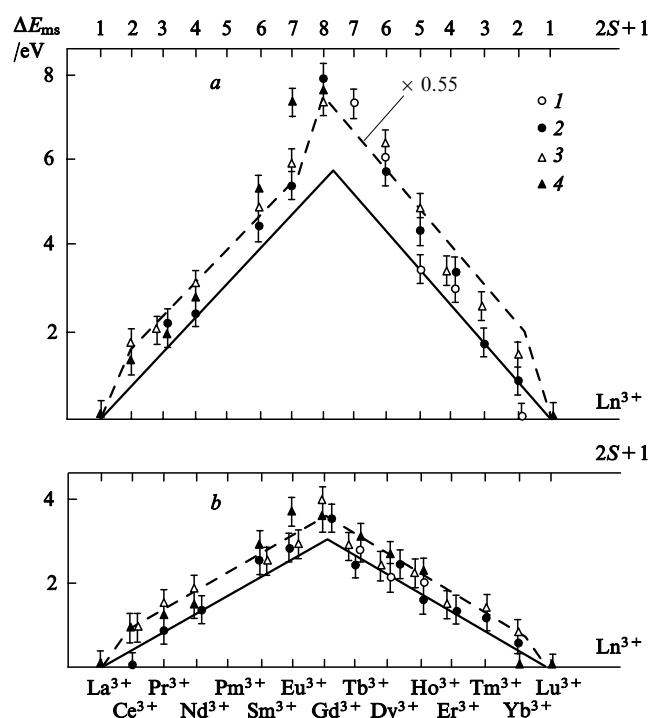


Figure 29. Multiplet splitting (ΔE_{ms}) of the $Ln4s$ (a) and $Ln5s$ lines (b) in the XPS spectra of oxygen-containing compounds of lanthanides and individual metals; (1) surface oxides;⁸⁰ (2) Ln_2O_3 oxides; (3) LnL_3 (L is the *o*-methoxybenzoic acid residue);⁵ (4) individual metals;⁹³ the continuous line shows the results of SCF NR X_α -DVM calculations;⁶⁹ the dashed line corresponds to the results of *ab initio* calculations;^{44,93} the dependence of ΔE_{ms} on the multiplicity ($2S+1$) of the $Ln4s$ electrons was multiplied by 0.55.⁹³

europium metal [$\Delta E_{ms}(Eu) = 7.4 \pm 0.2$ eV] differs considerably from the corresponding value for the oxide [$\Delta E_{ms}(Eu_2O_3) = 5.5 \pm 0.2$ eV] and is approximately equal to the multiplet splitting observed in the spectrum of gadolinium oxide [$\Delta E_{ms}(Gd_2O_3) = 7.8 \pm 0.2$ eV]. These results are attributable to the fact that the number n_{4f} of unpaired $Eu4f$ electrons in europium atoms is greater in the metal than in the oxide and is equal to the number of these electrons in the gadolinium contained in the oxide. In terms of the ionic approximation, this implies that europium metal contains Eu^{2+} ions, which is a known fact, while the oxide contains Eu^{3+} atoms.

The multiplet splitting in the $Ln4d$ spectra of the Ln_2O_3 oxides for $58 \leq Z \leq 70$ has a more complicated pattern than that in the $Ln4s$ and $Ln5s$ spectra of the same compounds, the structure caused by this splitting being mainly consistent with the corresponding structure observed in the spectra of the $Ln4d$ electrons in LnF_3 (Fig. 30, see also Fig. 17). As an example, Fig. 30 shows the spectrum of the $Tm4d$ electrons in Tm_2O_3 . Whereas the complex structure in the spectrum of Tm_2O_3 is mainly related to the multiplet splitting, this splitting is missing from the $Ln4d$ spectra of La_2O_3 and Lu_2O_3 , because La^{3+} and Lu^{3+} ions in the oxides contain no unpaired $Ln4f$ electrons. Indeed, the spectra of these electrons in lanthanum and lutetium oxides contain mainly doublets caused by the spin-orbit splitting: $\Delta E_{so}(La4d) = 3.0 \pm 0.1$ eV and $\Delta E_{so}(Lu4d) = 9.8 \pm 0.1$ eV. These values are in good agreement with analogous values for LaF_3 and LuF_3 (3.1 ± 0.1 and 10.0 ± 0.1 eV, respectively; see Figs 17, 30 and Tables 1, 3). The observed violation of the intensity ratio of the $La4d_{5/2}$ and $La4d_{3/2}$ doublet components in La_2O_3 can be related, as has been noted, for example for $La(OH)_3$ ^{139,140} and La_2O_3 ,⁵⁰ to the superposition of the shake-up satellite from the $La4d_{5/2}$ line on the $La4d_{3/2}$ doublet component. The structures of the $Ln4d$ spectra for other Ln_2O_3 oxides in which the lanthanide ions have

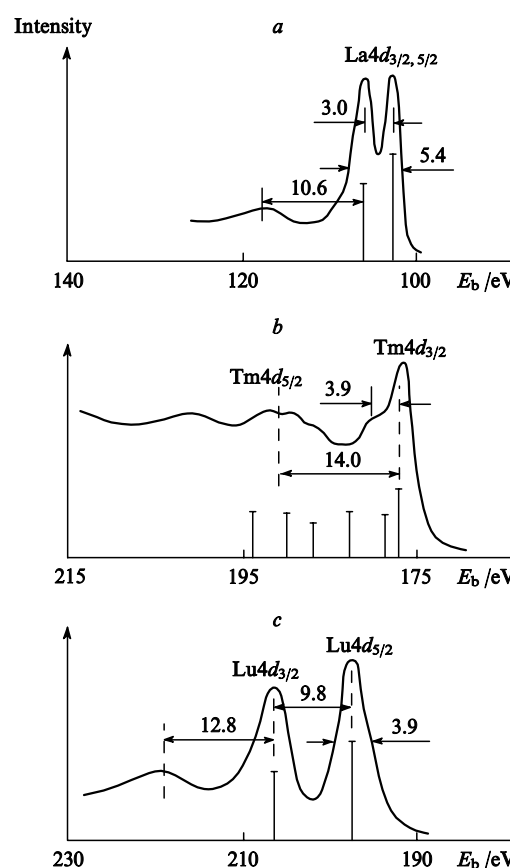


Figure 30. XPS of lanthanum (a), tulium (b), and lutetium (c) oxides in the $Ln4d$ binding energy range. The intensity of the $La4d_{3/2}$ component is increased due to the superposition of the shake-up satellite from the $La4d_{5/2}$ line.⁸³ The vertical segments below the Tm_2O_3 spectrum show the results of calculations with allowance for the multiplet splitting.⁶⁶

electronic configurations with $Ln4f$ electrons are much more complicated than the spin doublet (see Fig. 30). The spectral structures observed for the bulk samples of lanthanide oxides^{5,123} are similar to those in the spectra of surface oxides.^{73,80,118,122}

These results can serve as experimental evidence for the fact that the multiplet splitting in the spectra of $Ln4d$ electrons of lanthanide oxides gives rise to a complex fine structure the main features of which can be considered in the ionic approximation.^{45,66} Replacement of the ligands surrounding the Ln^{3+} ions induces changes in the fine spectral structure, which can be partially due to the many-body perturbation and the dynamic effect in the spectra of these electrons. In other words, fine structure parameters depend on the nature of ligands in lanthanide compounds, *i.e.*, on the type of chemical bonds in them. As a consequence, despite its complexity, the fine structure of the $Ln4d$ spectra is characteristic of a given lanthanide compound and can be used as a 'fingerprint' for compound identification.

The fine structure observed in the spectra of the $Ln4p$ electrons of lanthanide oxides generally resembles the corresponding spectral structure of lanthanide trifluorides (Fig. 31). Instead of the expected doublet related to the spin-orbit splitting, the $Ln4p$ spectra of REE oxides in the series from La to Yb exhibit a structure around the $Ln4p_{3/2}$ line and the component corresponding to the $Ln4p_{1/2}$ electrons is highly smeared.^{20,83} Note that for oxides of elements situated at the end of the lanthanide row, in particular, for Yb_2O_3 , the structure of the $Ln4p$ spectrum is similar to a doublet in shape, while the spectrum of the corresponding electrons of Lu_2O_3 is already mainly a spin doublet (see Fig. 31).

On the basis of the XPS data for lanthanide fluorides, the structure of the $Ln4p$ spectra was suggested to be due to the

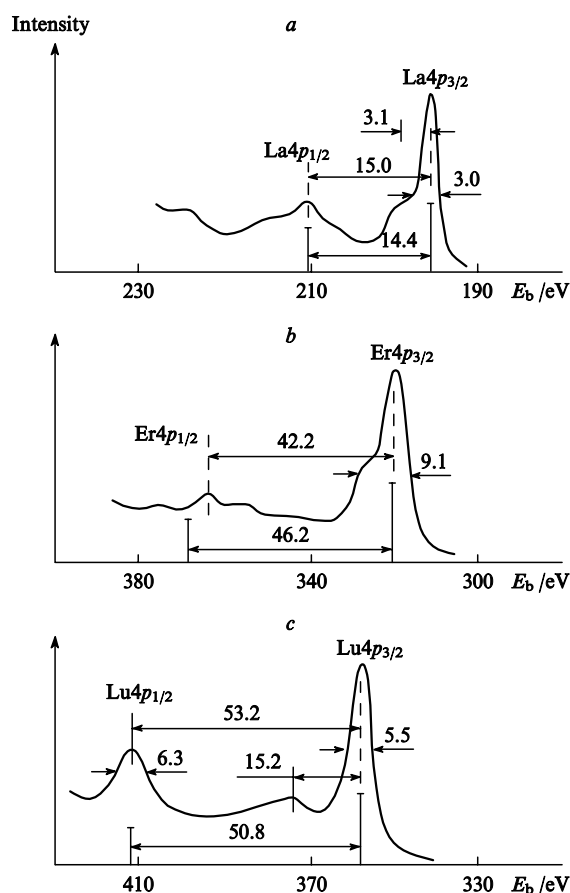


Figure 31. XPS spectra of lanthanum (a), erbium (b) and lutetium (c) oxides in the Ln4*p* binding energy range.²⁰ Vertical segments show the expected atomic spectra without allowance for the dynamic effect.²²

dynamic effect, inducing the formation of the $\text{Ln}4p^5 4d^{10} 4f^n \leftrightarrow \text{Ln}4p^6 4d^8 4f^{n+1}$ type final states after photoemission of the Ln4*p* electron.⁴² The appearance of an additional final state $\text{Ln}4p^6 4d^8 4f^{n+1}$ is possible only in the case where the Ln4*f* shell is not fully occupied. This assumption is in good agreement with the experimental data for REE oxides (see Fig. 31). Indeed, since the electronic configurations of the La^{3+} and Er^{3+} ions are $\text{La}4f^0$ and $\text{Er}4f^{11}$, respectively, the photoemission of an Ln4*p* electron from La_2O_3 and Er_2O_3 may give, in addition to the ground state, $\text{Ln}4p^5 4d^{10} 4f^n$, one more two-hole final state, $\text{Ln}4p^6 4d^8 4f^{n+1}$, which would result in the formation of the fine structure in the La4*p* and Er4*p* spectra of these oxides (see Fig. 31). Photoemission of an Lu4*p* electron from Lu_2O_3 cannot produce this additional final state, and the spectrum of the Lu4*p* electrons exhibits a spin doublet and satellites associated with many-body perturbation. These results can serve as yet further proof of the fact that the XPS fine structure in the spectra of the Ln4*p* electrons of REE compounds is mainly due to the dynamic effect. The considered data²⁰ are at variance with the suggestion⁸⁰ that the Ln4*p* spectral structure of REE oxides is mainly determined by multiplet splitting.

The spectra of the Ln3*d* electrons for light lanthanide oxides exhibit a fine structure the characteristics of which differ appreciably from those of the fine structure of other REE compounds (Fig. 32, see also Fig. 21). As noted above in the discussion of the spectra of the Ln3*d* electrons in lanthanide trifluorides, the spectral fine structure is due to the many-body perturbation. The dependence of the FWHM (Γ) of the Ln3*d*_{5/2} line on the atomic number (*Z*) for lanthanide oxides resembles a similar dependence for LnF_3 (see Fig. 22). As noted previously, the observed change in the line width cannot be explained by multiplet splitting. The

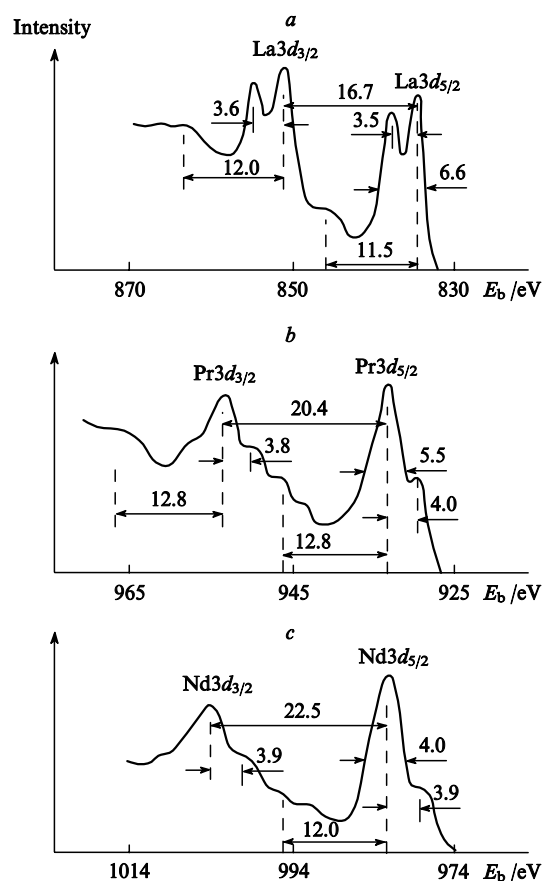


Figure 32. XPS spectra of lanthanum (a), praseodymium (b) and neodymium (c) oxides in the Ln3*d* binding energy range in which many-body perturbation effects are visible.⁸³

decrease in the Γ value (Ln3*d*_{5/2}) for REE oxides for the beginning of the lanthanide row is due, as indicated by the spectra, to a decrease in the intensity of the low-energy component of the structure containing satellites.

It has been shown for 3*d*-metal compounds^{24, 141} that the intensity of satellites in the spectra of electrons of various shells decreases with a decrease in the binding energy. A similar regularity is found in the spectra of La3*d* and La4*d* electrons for LaNbO_4 .¹³³ Therefore, a similar pattern could be expected in the spectra of lanthanide compounds, in particular, oxides. In other words, if the fine structure of the Ln3*d* spectra is caused by many-body perturbation, satellites, although less intense, should also appear in the spectra of other, lower binding energy electrons. Their positions with respect to basic lines are expected to be approximately the same as those in the spectra of Ln3*d* electrons. Indeed, the most clear-cut satellites of this type (with an intensity of 43%) are found in the La4*d* spectrum of La_2O_3 (see Fig. 30); they occur on the higher binding energy side of the basic lines and can be classified as shake-up satellites. A similar satellite is recorded in the La4*p*_{3/2} spectrum (intensity 30%). This serves as experimental evidence for the fact that in the spectra of La3*d* electrons, satellites are located at a higher binding energy than the basic lines.

Comparison of the difference between the core level binding energies for LaF_3 , La_2O_3 and metallic lanthanum also leads to the conclusion that the components located at lower binding energies in the spectrum of La3*d* electrons of lanthanum oxide should be identified as the basic lines. The binding energy differences between the La4*d*_{5/2} and La3*d*_{5/2} electrons $\Delta E_b(\text{La}4d_{5/2} - \text{La}3d_{5/2})$ for metallic lanthanum and its oxide and fluoride found with allowance for the low-energy components of the La3*d*_{5/2}

spectra are equal to 732.2 ± 0.4 ,⁵ 732.3 ± 0.4 and 732.9 ± 0.4 eV, respectively (see Tables 1, 3). These values are in satisfactory agreement with one another within the determined error; meanwhile, the $\Delta E_b(\text{La}4d_{5/2} - \text{La}3d_{5/2})$ values for the $\text{La}3d_{5/2}$ high-energy components for La_2O_3 and LaF_3 are equal to 735.8 ± 0.4 and 737.2 ± 0.4 eV, *i.e.*, they markedly exceed the corresponding energy difference (732.2 ± 0.4 eV) for metallic lanthanum (see Tables 1, 3). It is also worth noting that the spectrum of $\text{La}3d$ electrons for metallic lanthanum exhibits no extra lines^{91, 142–144} comparable to the basic lines in intensity; this contradicts the data of another study¹⁴⁵ in which an intense extra structure has been detected in the spectrum of metallic lanthanum.

The data considered above convincingly demonstrate that the satellites observed in the $\text{La}3d$ spectra of the lanthanum compounds in question are due to a shake-up process which accompanies photoemission of $\text{La}3d$ electron; this is consistent with the results of other publications.^{50, 105, 140}

As noted above, praseodymium and terbium oxides may have a complex stoichiometric composition other than Ln_2O_3 . These oxides are supposed¹ to contain lanthanide ions in different oxidation states, for example, Ln^{3+} and Ln^{4+} . The intensity of the extra structure in the spectra of $\text{Pr}3d$ and $\text{Tb}3d$ electrons, which can be attributed to Pr^{4+} and Tb^{4+} ions, does not exceed 3%–5% of the basic line intensity corresponding to Pr^{3+} and Tb^{3+} ions.⁵ It has been noted¹¹⁷ that on passing from the Eu^{2+} in the metal to the Eu^{3+} in the Eu_2O_3 oxide, the energy levels of the core electrons shift by about 10 eV. Significant changes in the spectral structure of complex lanthanide oxides with respect to the spectra of Ln^{3+} compounds are also found for cerium oxide.^{116, 137}

b. Cerium oxide

In recent years, considerable attention has been devoted to the study of variable valence in lanthanides and their compounds,^{146–148} which may be responsible for the fine structure in the XPS spectra. The extra structure in the spectra of the valence and core electrons of rare earth metals,^{101, 149, 150} intermetallics^{119, 151–156} and lanthanide compounds^{157–165} has been attributed to the presence of lanthanide atoms in variable oxidation states. Theoretical calculations of the XPS spectra of rare earth metals^{166, 167} and their compounds^{116, 168–170} are often carried out using so-called Andersson's impurity model^{38, 39, 171} and its various modifications. In particular, this model has been used to interpret the complex structure of the XPS spectra of core electrons in CeO_2 .^{116, 170}

The structure of the spectrum of the $\text{Ce}3d$ electrons in cerium oxide contains a number of additional lines that are missing from the corresponding spectra of other oxygen-containing compounds and cerium fluoride (Fig. 33, see also Fig. 21).^{137, 138} This extra structure is a doublet the splitting of which ($\Delta E_b = 18.3$ eV) is in good agreement with the spin–orbit splitting of the $\text{Ce}3d$ line [$\Delta E_{so}(\text{Ce}3d) = 18.3$ eV]¹³⁸ and with the data of one more study.¹¹⁹ For example, it was assumed on the basis of the analysis of cerium spectra in intermetallic compounds^{172–174} that the two intense extra lines with $E_b \approx 898.0$ and 916.3 eV are components of a spin doublet corresponding to Ce^{4+} ions, while the low-energy doublet containing a complex structure corresponds to the $\text{Ce}3d$ electrons of the Ce^{3+} ion. It has been suggested that the presence of two types of cerium ions in the oxide may be due either to variable valence exhibited by cerium in chemical¹⁷⁵ and intermetallic compounds,¹⁵⁵ or to the formation of a mixture of oxides on the sample surface.

Thus on the basis of X-ray CeL_{III} absorption spectra and the $\text{Ce}4d$ XPS spectra it was concluded¹⁷⁶ that Ce^{3+} and Ce^{4+} ions are formed on the CeCo_2 surface. The XPS spectra of the CeO_2 oxide and the theoretical data¹⁷⁷ indicate that a variable valence of cerium in the oxide is impossible, the structure observed in the $\text{Ce}3d$ spectrum being due to the $\text{Ce}3d^9 4f^0$ and $\text{Ce}3d^9 4f^1$ configurations of the final state. The results of NR X α -SW calculations suggest¹⁷⁸ that the extra structure in the $\text{Ce}3d$ and $\text{Ce}4d$ spectra of

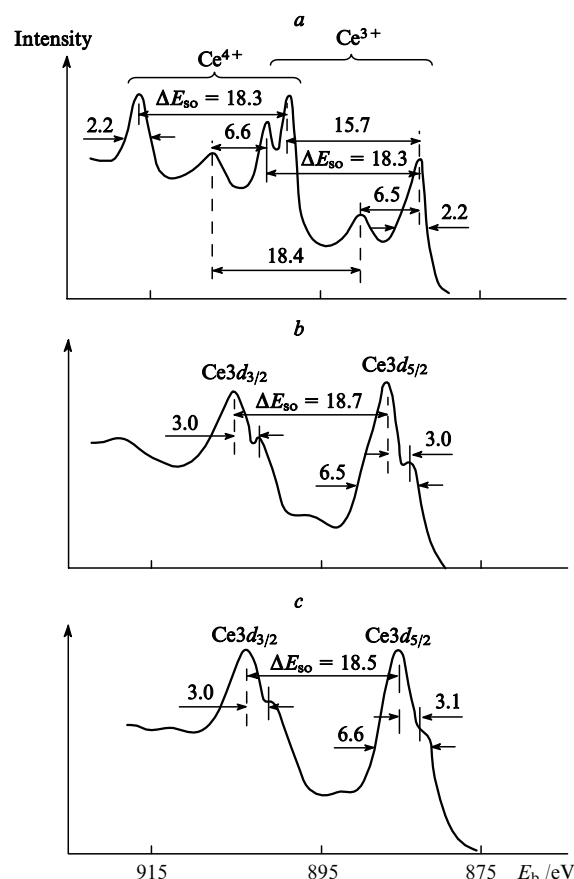


Figure 33. XPS spectra of the $\text{Ce}_2\text{O}_3 \cdot n\text{CeO}_2$ oxide (a) and the CeL_3 (b) and $\text{CeL}_3 \cdot 1.5 \text{H}_2\text{O}$ (c) cerium complexes in the $\text{Ce}3d$ binding energy range (L^1 and L^2 are the residues of *o*-methoxybenzoic and diphenylacetic acids, respectively).¹³⁷

CeO_2 is due to shake-up satellites. These satellites in the spectra of the $\text{Ce}3d$ electrons correspond to the $\text{Ce}3d^9 4f^0$, $\text{Ce}3d^9 4f^1$ and $\text{Ce}3d^9 5p^5(np)$ final states of the cerium ion.

X-Ray photoelectron spectra provide an unambiguous answer to the question as to whether or not the structure of the $\text{Ce}3d$ spectra is related to a complex initial or final state of the cerium ion in compounds.^{137, 138} One of the main suggestions is that the observed spectra of the core electrons of cerium in the oxide result from superposition of the structures related to the $\text{Ce}3d^9 4f^0$, $\text{Ce}3d^9 4f^1$ and $\text{Ce}3d^9 5p^5(np)$ type final states of the cerium ion. [The formation of the unusual final state $\text{Ce}3d^9 5p^5(np)$ is confirmed by the fact that the spectra of the $\text{Ce}5p$ and OVMO electrons do not exhibit the extra structure characteristic of the $\text{Ce}3d$, $\text{Ce}4d$ and $\text{Ce}4p$ spectra.] Indeed, comparison of the spectra of the $\text{Ce}4d$ and $\text{Ce}4p$ electrons for cerium oxide and the CeL_3 complex (L is the *o*-methoxybenzoic acid residue) shows that three groups of lines corresponding to cerium ions in different final states can be distinguished in these spectra as well as in the spectra of the $\text{Ce}3d$ electrons of cerium oxide (Fig. 34). In these spectra, the line corresponding to the Ce^{4+} ion is located 13.2 eV away from the corresponding Ce^{3+} line, which is consistent with the calculation results.¹⁷⁹ The intensity ratio of the lines corresponding to the $\text{Ce}3d$ electrons of cerium ions in different oxidation states indicates that the near-surface layer of the sample studied contained 36% of Ce^{4+} and 64% of Ce^{3+} in the final state.

As expected, the spectrum of $4d$ electrons of the Ce^{4+} ion is a doublet caused by the spin–orbit splitting; $\Delta E_{so}(\text{Ce}4d) = 3.4$ eV (see Fig. 34a,b). This proves experimentally the fact that the complex structure of the $4d$ spectrum of the Ce^{3+} ions with the $\text{Ce}5s^2 5p^6 4f^1$ final state is due to multiplet splitting.

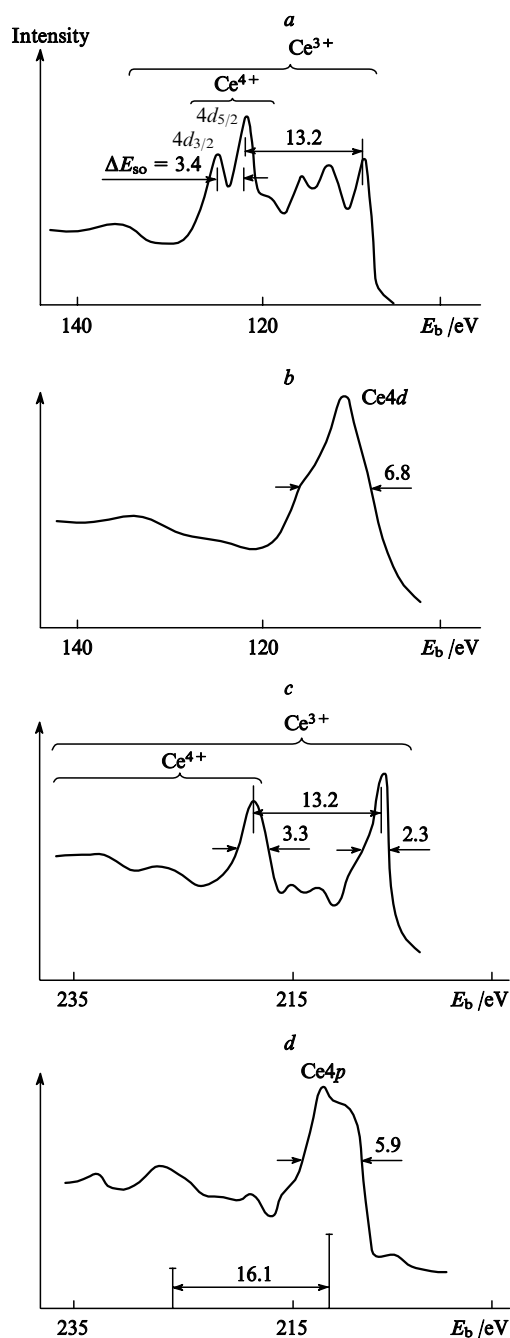


Figure 34. XPS spectra of the $\text{Ce}_2\text{O}_3 \cdot n\text{CeO}_2$ oxide and the CeL_3 complex in the $\text{Ce}4d$ (a,b) and $\text{Ce}4p$ (c,d) binding energy ranges (L is the *o*-methoxybenzoic acid residue).¹³⁸ (a,c) $\text{Ce}_2\text{O}_3 \cdot n\text{CeO}_2$; (b,d) CeL_3 .

The structures of the $\text{Ce}4p$ spectra for Ce^{4+} and Ce^{3+} ions have much in common (see Fig. 34 c,d). Thus in both cases, the component due to the $\text{Ce}4p_{1/2}$ electrons virtually cannot be detected, despite the fact that the electronic configuration of Ce^{4+} is $\text{Ce}4p^5 5s^2 5p^6 4f^0$, i.e., cerium contains no unpaired $4f$ electrons. This proves experimentally the fact that the complex structure in the spectrum of $\text{Ce}4p$ electrons is mainly due to the dynamic effect.

The spectra of the $3d$ and $4d$ electrons of the Ce^{4+} ion consist of two components of a doublet and contain no complex structure, in particular, no satellites (see Figs 33, 34). This allows one to determine the binding energy difference, $\Delta E_b(4d_{5/2} - 3d_{5/2}) = 776.3$ eV. This value is close to the energy difference between the corresponding low-energy components in the $3d_{5/2}$ and $4d_{5/2}$ spectra of the Ce^{3+} ions ($\Delta E_b = 882.3 - 108.5 = 773.8$ eV, see

Table 3). The observed difference between these values ($776.3 - 773.8 = 2.5$ eV) can be due to various reasons. First, the multiplet splitting changes the structure of the $4d$ spectrum of Ce^{3+} ; this may displace the most intense peak with respect to the Ce^{3+} $4d_{5/2}$ component. However, the same difference (2.5 eV) is found between the most intense components of the $\text{Ce}4p$ doublet the structures of which for Ce^{3+} and Ce^{4+} are similar. Second, the chemical shifts of metal ions in different oxidation states are well-known³³ to be different for different energy levels. Comparison of the spectra for the $\text{Ce}3d$ (~ 900 eV), $\text{Ce}4p$ (~ 220 eV) and $\text{Ce}4d$ (~ 120 eV) shells demonstrates that the differences between the electron binding energies corresponding to the most intense lines for individual shells in Ce^{3+} and Ce^{4+} amount to 15.7, 13.2 and 13.2 eV, respectively (see Fig. 33, 34). These data suggest that upon increasing the electron binding energy from 100 to 900 eV, the difference between the chemical shifts of separate levels does not exceed 16%.^{137, 138}

It follows from the results obtained that the most intense low-energy component in the $3d_{5/2}$ spectra of Ce^{3+} may be identified as the basic line and the components next in energy may be considered as shake-up satellites. The most intense satellites are due to the many-body perturbation involving the $\text{Ce}5p$ electrons, which gives rise to an ion with a poorly shielded hole at the $\text{Ce}5p$ level.

The spectra of core electrons also allow the conclusion that the stoichiometric compositions of praseodymium and terbium oxides basically correspond to Ln_2O_3 .

IV. General rules for the formation of the XPS spectral structure of lanthanide compounds

The XPS spectral structures observed for different lanthanide compounds are rather similar if the metal ions contained in them all have the same formal oxidation state equal to three. When the lanthanide oxidation state in a compound differs from three, the structure of their XPS spectra substantially changes.

1. Spectral region of low-energy electrons

In the spectral region corresponding to low-energy electrons of various lanthanide compounds, an increase in the atomic number (Z) and the number of $\text{Ln}4f$ electrons (n_{4f}) entail an increase in line intensity near the Fermi level (see Figs 2, 24). The structure observed in this spectral region for compounds formed by elements of the middle and the end of the lanthanide row is mainly due to $\text{Ln}4f$ electrons because photoionisation cross-sections of these electrons exceed appreciably the corresponding values of the electrons of the outer valence $\text{Ln}5d$, $\text{Ln}6s$ and $\text{L}2p$ AO of the lanthanide and the ligand.⁷⁶ As noted above, the data obtained in recent years using the SCF NR X_α -DV and X_α -SW calculations for the electronic structures of clusters^{56–59} confirm the substantial participation of the $\text{Ln}4f$ AO in the formation of OVMO. Therefore, attempts have been made^{37, 68, 132} to estimate the degree of participation of the $\text{Ln}4f$ electrons in the chemical bond on the basis of spectral parameters or, at least, to estimate the degree to which the $\text{Ln}4f$ electrons can be regarded as outer valence electrons.

On passing from lanthanide oxides to fluorides, the weighted-mean $\text{Ln}4f$ electron binding energies increase. The chemical shifts of these electron levels observed on passing from one compound to another are comparable to the corresponding values for the core levels.

For example, the chemical shift (ΔE_b) of the $\text{Lu}4p_{3/2}$ electron levels in LuF_3 (relative to Lu_2O_3) in which the lutetium ion is formally in the trivalent state amounts to 1.8 eV, and the weighted-mean value for the $\text{Lu}4f$ level, $\Delta \bar{E}_b(\text{Lu}4f)$, equals 1.7 eV. The binding energy differences $\Delta E_b(\text{Lu}4f - \text{Lu}4p_{3/2})$ for lutetium oxide and fluoride coincide within the experimental error and are 350.8 and 350.9 eV for Lu_2O_3 and LuF_3 , respectively. It should be noted that the $\text{Ln}4f$ electrons respond to minor changes in the effective charge of lanthanide nuclei to approximately the

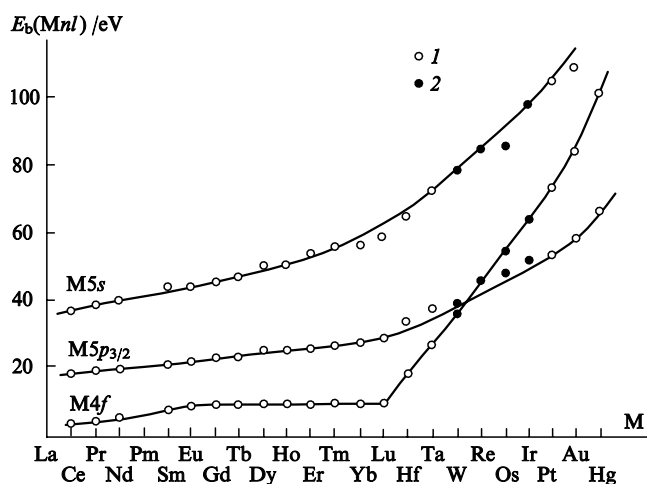


Figure 35. Binding energy of the Mnl electrons [$E_b(Mnl)$] for metal oxides, except for metallic Au and Pt, vs. the metal atomic number in the La–Hg series. (1) The results from Ref. 132; (2) the data from Ref. 22. For $M4f$ and $M5s$ electrons, the weighted-mean values of the binding energy are given, and for the Hf–Hg oxides ($Z > 71$), only the energies of the $M4f_{7/2}$ electrons are given.

same extent as the core electrons. For a separate series of lanthanide compounds, a substantial increase in the metal atomic number in the $58 \leq Z \leq 71$ range causes insignificant variation of the weighted-mean value of the $Ln4f$ binding energy. The increase in the binding energy of these electrons over the lanthanide row is 6.8 eV for fluorides and 4.5 eV for oxides (Fig. 35). On further increase in the atomic number, *i.e.*, on passing from Lu to Hg ($Z = 72$), the binding energy of the $M4f$ electrons sharply increases. The $M5p_{3/2}$ -electron binding energy varies in a similar way, although to a lesser extent. The same trend, even less pronounced, can also be followed for the $M5s$ electrons (see Fig. 35).

The dependence of the $M4f$ binding energy on Z for compounds of lanthanides and heavier metals (see Fig. 35) resembles the corresponding dependences of the Mnd electrons in transition metals and in the subsequent elements.^{22, 132} For example, the weighted-mean binding energy for the $M3d$ electrons in $3d$ -metal oxides, as in the lanthanide oxides, depends only slightly on Z over the $21 < Z \leq 29$ range but starting with zinc, it sharply increases (Fig. 36).

The relative intensity of the $Ln4f$ line in the lanthanide compounds studied follows an almost linear dependence on the metal atomic number in the $57 < Z \leq 71$ range (see Figs 5, 25). A further increase in Z results in a sharp change in the pattern of dependence (Fig. 37). For comparison with the experimental dependence,¹³² Fig. 37 also shows the relevant data obtained using photoionisation cross-sections.⁷⁶ The fundamental qualitative difference between the experimental and theoretical curves cannot be interpreted, for example, by assuming that after photoemission from a substance, the electrons are highly scattered. The extrapolation of the straight section of the theoretical curve to $Z = 57$ (La) shows that the plot for the relative intensity of the $M4f$ line vs. Z is a straight line in the case where all the $Ln4f$ shells are fully occupied. The deviation of the $Ln4f$ line intensity from a linear dependence occurs for Hf and Ta due to the fact that the outer valence $Ln4f$ electrons in these metals become inner electrons. It follows from experimental data that the relative intensity of the $M4f$ line for lanthanide oxides increases in proportion with Z . For the latter half of the lanthanide row, these values remain lower than the theoretical values but in the $71 < Z \leq 78$ range, they rapidly increase and subsequently, they exceed the theoretical values by, on average, 25%–27%; like theoretical values, they also increase with an increase in Z . Thus for Hg ($Z = 82$) in HgO,

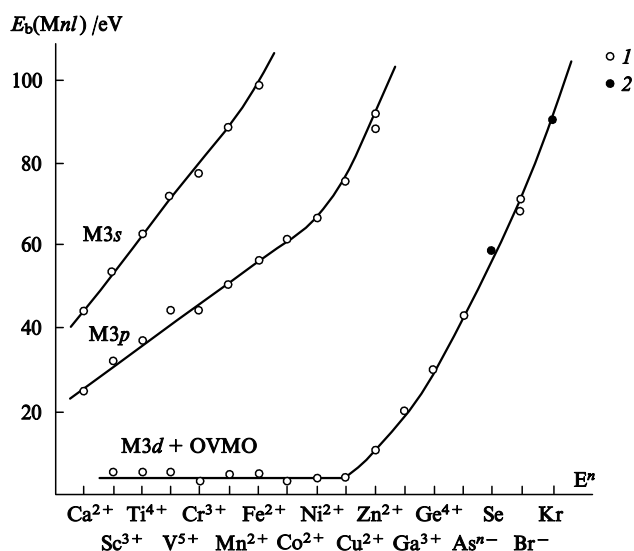


Figure 36. Binding energy (E_b) of the Mnl electrons of CaO , Sc_2O_3 , TiO_2 , V_2O_5 , Cr_2O_3 , MnO , FeO , CoO , NiO , CuO , ZnO , Ga_2O_3 , GeO_2 , and $FeAs_2$, Se, KBr, Kr vs. the element (E) atomic number in the Ca–Kr series. (1) the results from Ref. 5; (2) the data from Ref. 22. For $M3d$ electrons, the weighted-mean values for these OVMO electrons are given, and for Zn, Ga, Ge oxides and for As^{n-} , Se, Br[−] and Kr ($Z \geq 30$), the $M3d$ energies are presented.

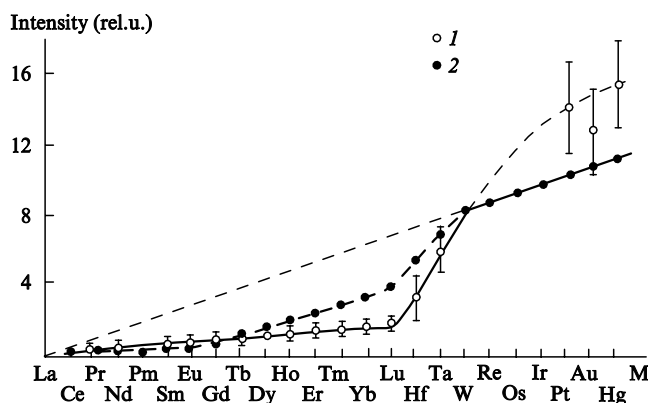


Figure 37. Experimental (1) and theoretical (2) dependences of the relative intensities of the $M4f$ lines for REE and heavier metal oxides, except for metallic Pt and Au, vs. the metal atomic number in the La–Hg series.¹³²

$I_{exp} = 15.6$, $I_{theor} = 11.4$ and $\Delta(I_{theor} - I_{exp}) = 4.2$, while for uranium ($Z = 92$) in $K_4UO_2(CO_3)_3$, $I_{exp} = 22.3$, $I_{theor} = 16.9$ and $\Delta I = 5.4$.

This is exemplified in Fig. 38 which shows for comparison the variations of the relative intensities of the OVMO and $E3d$ lines in the oxides of Period 4 elements (E). The corresponding theoretical intensities were calculated for atoms E using the data obtained by Scofield.⁷⁶ For elements with $Z > 30$, the experimental and theoretical values are presented as the intensity ratios for the lines of $3d$ and $3p$ electrons. This does not introduce a substantial error because the photoionisation cross-sections of the $E3d$ and $E3p$ shells are much greater than those of the $E4s$, $E4p$ or $O2p$ shells. If one takes into account the contribution to the intensity of the $O2p$ electrons of the oxide oxygen atoms for elements with $20 \leq Z \leq 29$, the theoretical intensity value would increase by approximately 10%, which provides a better qualitative agreement with the experimental data (see Fig. 38).

It follows from the obtained results that spectral characteristics of the $Ln4f$ electrons have much in common with those of the Mnd electrons in compounds of nd transition metals, which can

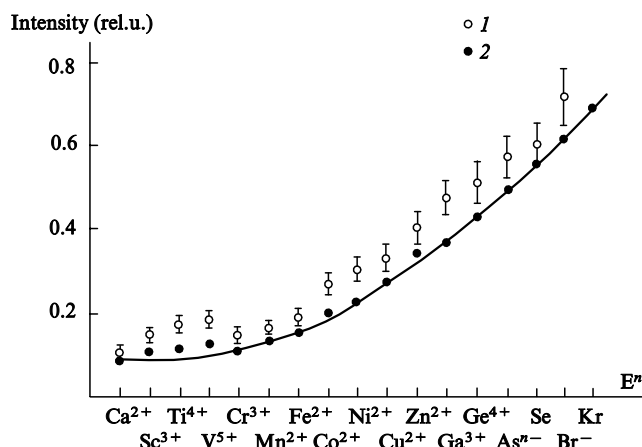


Figure 38. Experimental¹³² (1) and theoretical⁷⁶ (2) dependences of the relative intensities of the E3d and OVMO lines for CaO, Sc₂O₃, TiO₂, V₂O₅, Cr₂O₃, MnO, FeO, CoO, NiO, CuO, ZnO, Ga₂O₃ and GeO₂ oxides and FeAs₂, Se, KBr and Kr on the element (E) atomic number in the Ca–Kr series. For the oxides of elements with $Z \leq 30$ (Ca–Zn), the intensities were found as the ratio of the total intensity of the OVMO and E3d lines to the intensity of the 3p-electron lines, and for $Z > 30$ (Ga–Kr), they were found as the ratio of the 3d to 3p lines.

efficiently participate in the MO formation. In lanthanides, Ln4f is a valence shell, it can be involved in the MO formation in Ln compounds. At least, XPS data do not contradict the assumption, based on calculations, concerning substantial participation of the Ln4f AO in the formation of MO in these compounds.^{56–59, 180} Indeed, the involvement of these electrons in the chemical bond may be the reason for the decrease in the experimental intensity of the Ln4f lines compared to the theoretical intensity for the oxides formed by elements of the second half of the lanthanide row.

2. The spectra of the inner valence MO electrons

In order to elucidate the general features of the IVMO formed from the Ln5p and O2s AO in oxygen-containing lanthanide compounds, model NR SCF X_α-SW calculations both with and without allowance for the electron spin polarisation were carried out for the LnO₃³⁻ clusters (D_{3h} symmetry).^{79, 84} The $R(\text{Ln}–\text{O})$ bond lengths were taken to be equal to the sum of the covalent radii of the lanthanide and oxygen ions.¹ The calculation results are reflected in Fig. 39 and, for the LaO₃³⁻ cluster (D_{3h} symmetry) in which $R(\text{La}–\text{O}) = 0.174$ nm, they are also presented in Table 4. The total partial charges (Q_i^j , electron charge units) for this cluster found using the MT (muffin-tin) approximation of the SCF X_α-SW technique⁷⁹ are presented below (region II is an asymmetric region within the Watson sphere, and region III is situated outside this sphere⁵⁶).

La				O		Regions II, III
s	p	d	f	s	p	
1.6	4.0	0.6	0.8	4.3	10.4	10.3

It follows from the data of Table 4 that the occupied low-energy valence Ln5p and O2s AO can participate substantially in the MO formation in the cluster in question.

Thus in the LaO₃³⁻ cluster (D_{3h} symmetry), the 1a₂^{''} IVMO can be regarded, to a certain approximation, as a quasi-atomic MO composed mainly of the La5p AO. The 1e' and 2e' (1a₁' and 2a₁') IVMO can formally be attributed to the bonding and antibonding orbitals, respectively (see Table 4). The bonding 1a₁' IVMO contains 85% of the La5s AO and 12% of the O2s AO, whereas the antibonding 2a₁' IVMO, 17% of the La5s AO and 80% of O2s AO. In addition, the contributions of the outer valence AO of lanthanum and oxygen to these IVMO couples are quite sub-

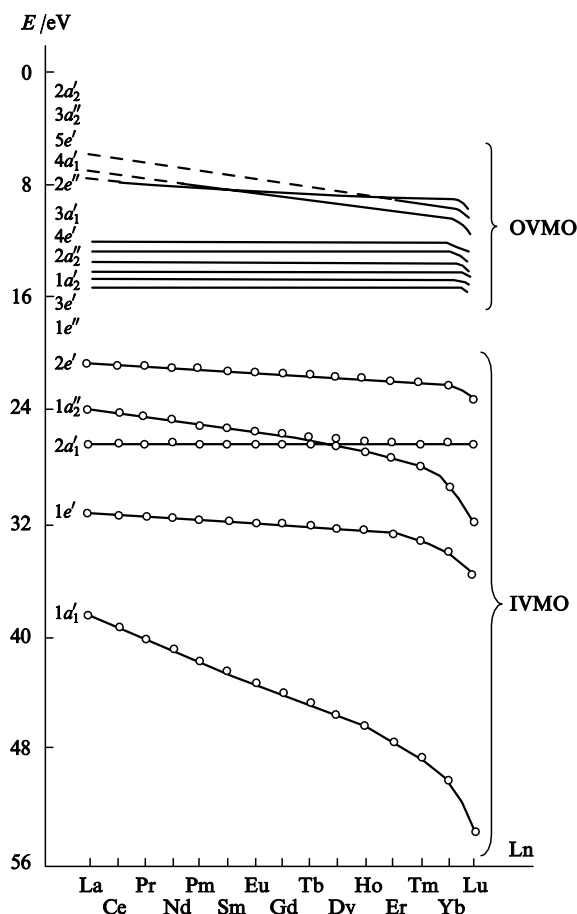


Figure 39. MO energies (E) for the LnO₃³⁻ cluster (D_{3h} symmetry) vs. the lanthanide atomic number in the La–Lu series.⁷⁹ The 4a₁' and 5e' OVMO energies are not given. The dashed lines show unoccupied MO.

stantial but different. For example, whereas the bonding 1e' MO contains only 2.5% of the O2p AO, the antibonding 2e' MO

Table 4. MO energies (E /eV), partial electron contributions (%) to different regions of the LaO₃³⁻ cluster [D_{3h} symmetry, $R(\text{La}–\text{O}) = 0.174$ nm] calculated in the SCF X_α-SW approximation.⁷⁹

MO type	Orbital	–E	La				O		Regions I, II, III
			s	p	d	f	s	p	
OVMO	2a ₂ '	6.25	–	–	–	88.0	–	6.3	5.7
	3a ₂ '	6.91	–	1.1	–	84.9	–	3.3	10.7
	5e'	7.15	–	0.6	1.2	83.0	–	2.7	12.5
	4a ₁ '	7.35	2.0	–	8.4	25.7	–	–	63.9
	2e''	7.38	–	–	2.2	77.9	–	–	19.9
	3a ₁ '	12.29	1.3	–	5.0	15.7	0.3	53.1	24.6
	(see ^a)								
	4e'	12.60	–	7.4	5.3	4.0	–	52.2	41.1
	2a ₂ '	13.51	–	6.2	–	4.2	–	57.0	32.6
	1a ₂ '	14.66	–	–	–	6.8	–	57.6	35.6
IVMO	3e'	14.96	–	2.3	3.0	–	1.5	55.8	37.4
	1e''	15.11	–	–	2.8	1.8	–	53.7	41.7
	2e'	20.67	–	40.0	0.7	0.1	20.4	10.2	28.6
	1a ₂ '	24.03	–	59.6	–	–	–	3.0	37.4
	2a ₁ '	26.50	13.1	–	0.9	1.1	61.8	0.3	22.8
	1e'	31.23	–	18.2	0.9	0.2	49.5	1.8	29.4
	1a ₁ '	38.87	66.0	–	–	0.1	9.3	2.1	22.5

^a The upper fully occupied orbital.

contains 14% of the $O2p$ AO. Such admixtures of the outer valence AO to the IVMO, as noted in a series of studies of molecules of light elements^{18,55,61,86,87} and in another series of studies^{18,55,181–183} of molecules of heavy elements, result in weakening of the antibonding nature of the higher MO, in particular, the $2e'$ IVMO. As a consequence, the contributions of the electrons of IVMO couples such as, for example, the $1e'$ and $2e'$, strengthens the chemical bond between the lanthanum and oxygen atoms.

As the lanthanide atomic number in the LnO_3^{3-} cluster grows, the energies and compositions of their MO change significantly. In constructing the dependence of MO energies of these clusters on Z , the energy of the quasi-atomic $2a'_1$ MO of oxygen was suggested to be constant and equal to 26.5 eV (see Fig. 39).⁷⁹ This energy was chosen as the reference value to compare the results of theoretical calculations with experimental data. Upon an increase in Z , the most pronounced changes in energy are observed for the upper $2e''-2a'_2$ OVMO and the $1a'_2$ and $1a'_1$ IVMO. The compositions of the considered MO substantially change. Thus, with an increase in the atomic number Z , the $2e''-2a'_2$ OVMO group approaches the $O2p$ AO to an increasing extent, while the $1e''-3a'_1$ orbitals become similar to the $Ln4f$ AO. The degree of mixing of $Ln5p$ and $O2p$ AO increases with an increase in Z from 57 to ~ 64 . It follows from these data that the degree of mixing of the $Ln5p$ and $O2s$ AO in the $1e'$ and $2e'$ IVMO in, for example TbO_3^{3-} , is substantially greater than that in LaO_3^{3-} , while the lower $1a'_1$ IVMO becomes a quasi-atomic MO to an increasing extent.

As noted above, the formation of IVMO from the metal $Ln5p$ AO and the ligand $L2s$ AO in lanthanide can complicate the structure of the XPS spectra of these electrons compared to the sum of the atomic spectra (see Fig. 24). The most pronounced

complication of the spectrum in the energy range of these electrons should be expected for the oxygen compounds of lanthanides situated in the middle of the row because for these oxides, the $Ln5p$ and $O2s$ energies are the closest to each other. The degree of participation of the $Ln5p$ and $L2s$ AO in the formation of IVMO can be estimated experimentally using the method of binding energy differences between the core and valence electrons.^{182,183}

The oxygen-containing lanthanide compounds have a rather complex structure. The metal atoms are surrounded by a large number of oxygen atoms. However, there is no strong anisotropy for the $R(Ln-O)$ bond lengths in these compounds. Therefore, the IVMO of the ML_8^{n-} and ML_8^{n-} type clusters (O_h group of symmetry) can be used in qualitative considerations (see Fig. 8*b,c*). The correlation schemes of these IVMO imply that upon the formation of IVMO of the t_{1u}^* type in lanthanide compounds, their energies shift to lower (in magnitude) values with respect to the core levels. In this case, the Δ_1 value (see Fig. 8), which characterises the degree of participation of the $Ln5p$ and $L2s$ AO in the formation of the t_{1u}^* IVMO, can be estimated experimentally. The $\Delta E_3(Ln5p_{3/2}-Ln3d_{5/2})$ values reflecting the difference between the $Ln3d_{5/2}$ and the t_{1u}^* MO binding energies for various lanthanide compounds are presented in Table 5. To estimate Δ_1 (see Fig. 8), the experimental values for the corresponding energy differences for metallic lanthanides are also presented. If, as has been suggested,^{50,140} the basic line in the $Ln3d$ spectra of light lanthanide compounds occurs at higher binding energies, comparison of these data indicates that the Δ_1 value for lanthanum oxygen-containing compounds reaches 2.3 eV, that for cerium, 4.5 eV, and that for praseodymium, 0.6 eV (for the oxide) (see Table 5).

Table 5. Binding energies (E_b , eV) and binding energy differences (ΔE_i /eV) for the electrons of lanthanides and ligands in compounds.⁵

Compound ^a	$-E_b(Ln5p_{3/2})$	$\Delta E_1(Ln5p_{3/2}-Ln5p_{1/2})$	$-E_b(Ln3d_{5/2})^b$	$\Delta E_2(Ln3d_{5/2})$	$\Delta E_3(Ln5p_{3/2}-Ln3d_{5/2})$	$\Delta E_4(X2s-X1s)^c$
LaF ₃	18.6	2.2	837.3 (1.00); 841.6 (0.30)	4.3	818.7; 823.0	655.8
La ₂ O ₃	17.7	1.7	835.1 (1.00); 838.6 (0.83)	3.5	817.4; 820.9	507.4
LaL ₃ ¹	18.3	2.1	835.7 (0.76); 838.8 (1.00)	3.1	817.4; 820.5	—
LaL ₃ ² · 1.5 H ₂ O	18.3	—	836.0 (1.00); 838.8 (1.00)	2.8	817.7; 820.5	506.8
La ₂ Ti ₂ O ₇	17.3	2.0	834.6 (1.00); 838.8 (0.91)	4.2	817.3; 821.5	507.9
LaNbO ₄	17.2	—	834.8 (1.00); 838.8 (0.72)	4.0	817.6; 821.6	508.2
LaH ₃ (see d) ⁹¹	19.3	2.4	835.5 (0.48); 839.2 (1.00)	3.7	816.2; 819.9	—
La (see d) ⁹¹	17.7	2.3	—; 836.3	—	—; 818.6	—
CeF ₃	19.4	3.0	884.7 (1.00); 888.2 (0.58)	3.5	865.3; 868.3	655.9
CeO ₂	18.0	—	882.3 (1.00); 888.8 (0.68)	6.5	864.3; 870.8	—
CeL ₃ ¹	18.7	3.0	882.8 (0.32); 885.8 (1.00)	3.0	864.1; 867.1	—
CeL ₃ ² · 1.5 H ₂ O	19.3	2.2	882.3 (0.30); 885.4 (1.00)	3.1	863.0; 866.1	506.6
CeH ₃ (see d) ¹¹³	19.2	2.6	882.4 (0.36); 886.4 (1.00)	4.0	863.2; 867.2	—
Ce (see d) ¹¹³	18.0	2.9	—; 884.3	—	—; 866.3	—
PrF ₃	20.1	3.7	—; 934.4	—	—; 914.3	655.7
Pr ₂ O ₃ (see c)	19.3	3.6	929.5 (0.32); 933.5 (1.00)	4.0	910.2; 914.2	—
PrL ₃ ¹	19.7	2.5	929.0 (0.22); 932.8 (1.00)	3.8	909.3; 913.1	—
PrL ₃ ² · 1.5 H ₂ O	20.2	2.8	929.9 (0.24); 934.1 (1.00)	4.2	909.7; 913.9	506.1
PrNbO ₄	18.9	—	929.2 (0.25); 933.2 (1.00)	4.0	910.3; 914.3	507.9
PrH ₃ (see d) ¹⁰⁹	20.2	—	930.4 (0.21); 934.6 (1.00)	4.2	910.2; 914.4	—
Pr (see d) ¹⁰⁹	18.8	—	—; 932.4	—	—; 913.6	—
NdF ₃	20.7	3.7	—; 982.6	—	—; 961.9	655.7
Nd ₂ O ₃	19.4	3.6	978.0 (0.29); 981.9 (1.00)	3.9	958.6; 962.5	507.0
NdL ₃ ¹	20.3	3.9	978.8 (0.37); 982.8 (1.00)	4.0	958.5; 962.5	—
NdL ₃ ² · 1.5 H ₂ O	20.7	4.2	979.0 (0.35); 982.9 (1.00)	3.9	958.3; 962.2	505.7
NdPc ₂	20.3	3.0	978.1 (0.35); 982.1 (1.00)	4.0	957.8; 961.8	381.6
NdPct ₂	19.9	3.9	978.6 (0.38); 982.4 (1.00)	3.8	958.7; 962.5	381.7
Nd (see d) ¹⁴²	—	—	—; 981.2	—	—	—
SmF ₃	22.1	4.3	1084.4	—	1062.3	655.5
Sm ₂ O ₃	20.4	4.0	1083.1	—	1062.7	—

Table 5 (continued).

Compound ^a	$-E_b(\text{Ln}5p_{3/2})$	$\Delta E_1(\text{Ln}5p_{3/2} - \text{Ln}5p_{1/2})$	$-E_b(\text{Ln}3d_{5/2})$ ^b	$\Delta E_2(\text{Ln}3d_{5/2})$	$\Delta E_3(\text{Ln}5p_{3/2} - \text{Ln}3d_{5/2})$	$\Delta E_4(X2s - X1s)$ ^c
SmL ₃ ¹	20.8	—	1083.8	—	1063.0	—
SmL ₃ ² · 1.5 H ₂ O	21.3	4.4	1084.5	—	1063.2	505.7
SmNbO ₄	20.0	4.5	1080.1 (0.18); 1083.1 (1.00)	3.0	1060.1; 1063.1	509.2
EuF ₃	22.4	—	1135.3	—	1112.9	655.8
Eu ₂ O ₃	21.5	4.2	1134.6	—	1113.1	—
EuL ₃ ¹	22.0	—	1135.2	—	1113.2	—
EuL ₃ ² · 1.5 H ₂ O	22.6	4.7	1135.3	—	1112.7	507.0
EuNbO ₄	21.3	—	1134.8	—	1113.5	—
GdF ₃	22.9	—	1187.7	—	1164.8	655.6
Gd ₂ O ₃	22.3	5.1	1187.3	—	1165.0	—
GgL ₃ ¹	22.7	5.0	1187.3	—	1164.6	—
GdL ₃ ² · 1.5 H ₂ O	23.3	4.3	—	—	—	506.7
LuF ₃	28.4	7.3	197.3 ^f	—	168.9 ^g	—
Lu ₂ O ₃	27.5	6.4	196.5 ^f	—	169.0 ^g	508.1
LuL ₃ ¹	29.0	6.4	197.6 ^f	—	168.6 ^g	—
LuL ₃ ² · 2 H ₂ O	28.5	6.4	197.7 ^f	—	169.2 ^g	—
LuNbO ₄	27.4	—	196.4 ^f	—	169.0 ^g	508.8
Lu ₂ O ₃ (see ^d) ⁸⁰	27.7	—	196.7 ^f	—	169.0 ^g	—
Oxide adsorbed on metallic Lu (see ⁸⁰)	27.8	6.4	197.4 ^f	—	169.6 ^g	—
Lu (see ^d) ⁸⁰	26.6	7.0	196.3 ^f	—	169.7 ^g	—

^a L¹ is the diphenylacetic acid residue, L² is the *o*-methoxybenzoic acid residue, Pc is the unsubstituted diphthalocyanine residue, Pct is the 4-*tert*-butyldiphthalocyanine residue. ^b The intensities of one of the Ln3d_{5/2} lines referred to the line whose intensity is taken to be unity are given in parentheses. ^c X = O, F, N; the binding energy differences are given for those compounds for which the X1s spectrum is a single line. ^d The binding energies are referred to the electron binding energy for carbon in adsorbed hydrocarbons, $E_b(\text{C}1s) = 285.0$ eV [at $E_b(\text{Au}4f_{7/2}) = 83.8$ eV for the standard gold plate, $E_b(\text{C}1s) = 284.4$ eV]. ^e The E_b values are given for Ln³⁺. ^f The Lu4d_{5/2} binding energy. ^g The $\Delta E_3(\text{Lu}5p_{3/2} - \text{Lu}4d_{5/2})$ values.

The data considered lead to the conclusion that IVMO are actually formed in these compounds, the upper orbitals being antibonding. If the basic lines in the Ln3d spectra of light lanthanides occur at lower binding energies, as shown for the Ln compounds studied in a number of publications,^{5,50,140} the Δ_1 value (see Fig. 8) changes its sign, while its magnitude $|\Delta_1|$ for lanthanum oxygen compounds reaches 1.3 eV (see Table 5). These results confirm the formation of IVMO in these compounds. In addition, they indicate that the upper IVMO is a bonding orbital in this case.

The same conclusion can be drawn by considering the $\Delta E_b(\text{Ln}5p_{3/2} - \text{Ln}4d_{5/2})$ energy differences for lanthanide compounds. The values for LaF₃, La₂O₃, LaL₃¹, LaL₃² · 1.5 H₂O, La₂Ti₂O₇, LaNbO₄ and metallic lanthanum amount to 85.8, 85.1, 85.4, 86.0, 85.0, 85.7 and 86.1 eV, respectively. These data confirm once again the fact that in the La3d spectra of the lanthanide compounds studied, the basic lines are located in the lower binding energy region.

On passing from light to heavy lanthanides, the Ln5p_{3/2} energy level is lowered. In the case of lutetium, it is located below the O2s level; thus, the Δ_1 value for the lutetium compounds (see Fig. 8) should change the sign. In other words, the ΔE_3 difference (see Table 5) for oxygen compounds of lutetium should become smaller in magnitude than that for metallic Lu. Indeed, it follows from the data of Table 5 that in some cases, $\Delta E_3(\text{Ln}5p_{3/2} - \text{Ln}4d_{5/2})$ for atomic lutetium is 1.1 eV higher than these values for Lu in compounds ($\Delta_1 = -1.1$ eV).

It has been noted¹⁸⁴ that the emission spectra¹⁸⁵ of Eu₂O₃ and other 'sesquialteral' lanthanide oxides exhibit peaks related to the Ln5p and O2s hybrid orbitals. The X-ray SL_{II,III} emission spectra of some sesquialteral REE sulfides¹⁸⁶ and lanthanide monosulfides¹⁸⁷ also contain peaks due to the formation of IVMO consisting of the Ln5s, Ln5p and S3s AO.

3. Multiplet splitting

Multiplet splitting shows itself most clearly in the case of the Ln4s, Ln4d and Ln5s electrons in lanthanide compounds. In the XPS spectra of Ln4s and Ln5s electrons, this splitting gives rise to two components the distance between which is correlated, along the energy scale, with the number n_{4f} of unpaired Ln4f electrons (see Figs 16, 29). These results are in satisfactory agreement with theoretical data,^{44,69,93} and the multiplet splitting value can be used as a parameter in determining the spin and oxidation states of REE ions in compounds.

The XPS spectra of compounds of lanthanides containing unpaired Ln4f electrons in the Ln4d binding energy region are due to multiplet splitting and exhibit a complex structure (see Fig. 17, 30). Instead of the expected doublets characterised by a spin-orbit splitting energy not exceeding 10 eV even for heavy lanthanides, the spectrum of these electrons exhibits a fine structure in the energy range of up to ~40 eV. The results of theoretical calculations^{45,66} carried out in the ionic approximation are in satisfactory agreement with experimental data. The fine structure of the XPS spectra of the Ln4d electrons is typical of particular REE in compounds and can be used for identification and for determination of the oxidation state of the lanthanide ion. For example, this structure allows one to make the conclusion that the cerium oxidation state in all the compounds studied, except for the oxide, is close to Ce³⁺. Apparently, in the oxide, cerium forms specific clusters, photoemission of a core electron from which gives rise to three final states including the unusual two-hole Ce3d⁹5p⁵(np) state (see Figs 33, 34). The presence of one unpaired Ce4f electron in Ce³⁺ results in a pronounced disturbance of the structure of the spin doublet present in the Ce4d spectra of the Ce⁴⁺ ion, which does not contain this Ce4f electron. The structure of the Yb4d spectra leads to the conclusion that ytterbium exists as Yb³⁺ in all the compounds studied. The Yb³⁺ electronic configuration is 4f¹³, which markedly complicates the expected spectral structure. The spectrum of the Yb4d electrons of the Yb²⁺ with the 4f¹⁴ configuration (in the YbCu₂Ge₂ intermetallic com-

pound¹⁵⁶ and metallic ytterbium^{71, 96, 188}) contains a doublet caused by the spin – orbit splitting.

4. Splitting resulting from the induced charge

Charge inducing on the centres regarded previously as diamagnetic (Ti^{4+}) in the double oxides of the FeTiO_3 type was first observed by X-ray emission spectroscopy.¹⁸⁹ The excess electron density on the titanium ion contained in complex oxides of the MTiO_3 type arises in the case where the second coordination sphere contains paramagnetic metal ions (M). Analysis of the X-ray emission spectra shows^{189–191} that, for example, on passing from TiO_2 to FeTiO_3 and, possibly, to $\text{Ln}_2\text{Ti}_2\text{O}_7$,^{28, 192, 193} the titanium ions, which are expected to be diamagnetic, are actually paramagnetic. This results in splitting of the emission lines of the titanium ions. A similar situation is also found for niobium compounds. This line splitting is a specific case of multiplet splitting, which is an indirect consequence of the presence of paramagnetic ions connected to the metal ion in question *via* an oxygen bridge.

By using a procedure for recording high-resolution XPS spectra of dielectric materials, Teterin and co-workers^{133–136, 194, 195} were able to measure the relative line widths of the spectra and the electron binding energies with an accuracy higher than ~ 0.1 eV. Thus, it became possible to detect, with a relatively high accuracy, slight changes in the unpaired electron density ($\Delta\rho$) on a metal ion in a dielectric material and to estimate semi-quantitatively the $\Delta\rho$ value using the XPS method. An increase in the number of unpaired electrons in a 3d-metal or lanthanide ion in a compound by one electron ($\Delta\rho = 1e^-$) is known^{44, 93, 94, 196} to increase the splitting of the $\text{M}3s$ or $\text{Ln}4s$ line by approximately 1 eV (see, for example, Fig. 29). Since the binding energies and the line widths for core levels can be measured with an accuracy higher than ± 0.1 eV, the change in the $\Delta\rho$ value by $0.1e^-$ can be detected by XPS. Using results reported by Teterin *et al.*,¹⁹⁴ the $\Delta\rho$ value for Ti in FeTiO_3 was found to be $\sim 0.5e^-$, while that for Nb in SmNbO_4 was found to exceed $1e^-$.

This phenomenon has been studied in more detail by XPS^{133, 134, 136} in relation to lanthanide (except for Pm and Tm) orthoniobates. On passing from niobium oxide ($\alpha\text{-Nb}_2\text{O}_5$) to orthoniobates (LnNbO_4) containing Ln^{3+} paramagnetic ions, characteristics of the XPS spectra of the core electrons of niobium change. Thus the line widths in the $\text{Nb}3p_{3/2}$, $\text{Nb}4s$ and $\text{Nb}4p$ spectra for LnNbO_4 containing lanthanides of the middle of the row are much greater than the corresponding values for the $\alpha\text{-Nb}_2\text{O}_5$ oxide. The broadening of the $\text{Nb}4s$ line becomes so pronounced that at least two components of the complex structure are clearly manifested. The observed line broadening is assumed to be mainly due to charge induction ($\Delta\rho$) onto the Nb^{5+} ion, and, on passing from $\alpha\text{-Nb}_2\text{O}_5$ to LnNbO_4 (Ln are lanthanides from the medium of the row), the Nb^{5+} ion electronic configuration changes appreciably from $\{4d\}$ to $\{4d^{\Delta\rho}\}$. It has been noted^{44, 93, 94, 196} that the multiplet splitting arises with the highest probability in the spectra of core electrons having the same principal quantum number as the unpaired electrons. In this case, the most pronounced multiplet splitting should be expected in the spectra of the $\text{Nb}4s$ electrons. This was actually observed in experiments. However, Lebedev *et al.*¹³⁶ do not rule out the possibility that the dynamic effect may also be manifested in these spectra, although it is less pronounced than the multiplet splitting.

The excess unpaired electron density ($\Delta\rho$) has been estimated^{133, 134, 136} using data on the multiplet splitting of the $\text{Ln}4s$ lines for Ln_2O_3 oxides,⁸⁰ which indicate that the presence of one unpaired 4f electron in a lanthanide ion induces splitting of the $\text{Ln}4s$ line by $\Delta E_{\text{ms}}(\text{Ln}4s) \approx 1.1$ eV. In this case, for GdNbO_4 , it was found that $\Delta\rho_1 > 1e^-$. The appearance of the extra electron density $\Delta\rho$ on the niobium ion on passing from $\alpha\text{-Nb}_2\text{O}_5$ $\{4d^0\}$ to GdNbO_4 $\{4d^{\Delta\rho}\}$ results in a shift of the core electron lines towards low binding energies; for example, for the $\text{Nb}3p_{3/2}$ electrons, this

shift is $\Delta E_b(\text{Nb}3p_{3/2}) = 0.8$ eV. Since a change in the formal oxidation state of a metal in compounds by unity results in a change of the chemical shift of the core levels by approximately one electron-volt (see, for example, Ref. 33), the excess electron density ($\Delta\rho_2$) found from the chemical shift of the $\text{Nb}3p_{3/2}$ level is smaller than the $\Delta\rho_1$ value determined from splitting of the $\text{Nb}4s$ lines, and equals $\sim 0.8e^-$. This difference between the considered values may be due, in particular, to the fact that $\Delta\rho_1$ is the sum of two contributions ($\Delta\rho_1 = \Delta\rho_2 + \Delta\rho_3$), one of them ($\Delta\rho_2$) being due to the excess charge directly on the $\text{Nb}^{\Delta\rho_2}$ ion and the other ($\Delta\rho_3$) being related to polarisation (for example, polarisation of the valence-shell electrons).

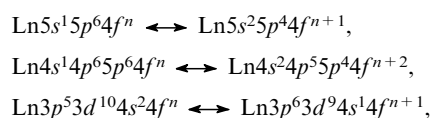
The results obtained represent one of the first steps in the study of the appearance of excess unpaired electron density on the ionic centres that have previously been considered diamagnetic. Since double oxides possess ferroelectric (LnNbO_4), antiferromagnetic (FeTiO_3) and other important physical properties, further investigation of the charge induction mechanism may shed light on the nature of these phenomena and favour the development of methods for the preparation of substances with *a priori* specified useful properties. The use of characteristics of the spectral fine structure allows efficient utilisation of the XPS method in a study of charge induction caused by indirect exchange interaction between metal ions in valuable complex materials.

5. Dynamic effect

Experimental data show that the fine structure associated with the dynamic effect is manifested most clearly in the spectra of those atomic levels the energies of which are divisible by the energies of the nearest upper levels (see above). This shows itself as an individual structure in the spectra of the $\text{Ln}4p$ electrons for all lanthanide compounds that obey most closely the approximate equality $E_b(\text{Ln}4p) \approx 2 E_b(\text{Ln}4d)$ (see Figs 19, 31, 34). Common features of the spectra of these electrons in various lanthanide compounds are that the $\text{Ln}4p_{3/2}$ component has a fine structure and that the intensity of the $\text{Ln}4p_{1/2}$ component is most often substantially suppressed.

The structure of the $\text{Ln}4p$ spectra of lutetium compounds is much less complicated. This led to the suggestion that^{5, 20} one of the possible final configurations of lanthanide ions resulting from photoemission of the $\text{Ln}4p$ electron is due to the $\text{Ln}4d$ -to- $\text{Ln}4f$ electron migration: $4p^5 4d^{10} 4f^n \leftrightarrow 4p^6 4d^8 4f^{n+1}$. The resulting data contradict the suggestion made by Padalia *et al.*⁸⁰ that the structure of the $\text{Ln}4p$ spectra is due to multiplet splitting but are consistent with the results of a calculation for X-ray $\text{LnL}\gamma_{\text{II, III}}$ emission spectra¹⁹⁷ and other X-ray spectra of lanthanides.^{198, 199}

The structure caused by the dynamic effect giving rise to the final states of the type



can markedly complicate the $\text{Ln}5s$, $\text{Ln}4s$ and $\text{Ln}3p$ spectra of lanthanides in compounds.^{5, 200}

Study of the nature of generation of the XPS spectral structure associated with the dynamic effect may clarify the role of the secondary electron processes that accompany the photoemission of electrons from individual shells. In particular, analysis of the XPS spectra stimulates the theoretical investigation of these processes,^{168, 200} while the spectra can serve as a criterion for the validity of the models chosen for calculations.

6. Many-body perturbation

When manifested to a substantial extent, many-body perturbation gives rise to satellites in the spectra of electrons of various shells. As shown for 3d transition metal^{23, 122} and lanthanide^{44, 48, 135} compounds, the most intense satellites should be manifested in the spectra of low-lying electron levels because these electrons possess a relatively low kinetic energy after photoemission. For com-

pounds of light lanthanides, the problem of the mechanism of satellite formation is especially acute for several reasons.

As noted in the Introduction, in the binding energy range used normally in investigations, virtually all the XPS spectra of various electron shells in lanthanide compounds exhibit complex structures. The structure present in the spectra of core electrons hampers the measurement of binding energies, which are traditionally used to determine the relative oxidation states of lanthanides in compounds. In the case of light lanthanides, one component of the $\text{Ln}3d_{5/2, 3/2}$ spin doublet is considered to be suitable for this purpose. However, both the $\text{Ln}3d_{5/2}$ and $\text{Ln}3d_{3/2}$ spectra in lanthanide compounds can contain at least two intense lines. Study of the reasons for the appearance of complex structures in the spectra of $\text{Ln}3d$ electrons of rare earth metals²⁰¹ and light lanthanide compounds¹⁷⁷ has attracted considerable attention.

An important problem arising in the analysis of the $\text{Ln}3d$ spectral structure in lanthanide compounds is to find out which of the two lines reflects the main final state with the hole in the $\text{Ln}3d$ level formed upon photoemission of an electron. On the one hand, clarification of this item is needed for measuring the relative binding energies of these electrons and, on the other hand, this would enable the use of the method of binding energy difference between the core and valence MO when analysing the nature of individual MO.

In a number of studies,^{45, 50, 105, 178} it has been suggested that the spectral structure of the $\text{Ln}3d$ electrons in lanthanide compounds is due to many-body perturbation giving rise to shake-up satellites, which can be more intense than the basic lines. The results obtained for individual light lanthanides^{108, 109, 155, 201} indicate that the $\text{Ln}3d$ spectra do not exhibit the highly intense satellites observed by Shabanova *et al.*¹²⁶ The low-intensity extra lines ($\sim 10\text{--}2\%$) observed in the $\text{Ln}3d$ spectra of metallic lanthanides on the lower binding energy side of the basic lines may be due to a shake-down process.²⁰¹ By analogy, it has been suggested^{75, 108, 109} that the intense extra lines recorded in the $\text{Ln}3d$ spectra of light lanthanide hydrides, oxides and hydroxides are also due to many-body perturbation with the formation of shake-down satellites. In other words, the lines in the spectra of $\text{Ln}3d$ electrons that have previously^{45, 50, 178} been classified as satellites have also been proposed^{75, 108, 109} to be basic lines. These lines should occur at higher binding energies than satellites (see Figs 21, 33).

As an argument supporting the formation of shake-down satellites in the spectra of the $\text{Ln}3d$ electrons of light REE, the researchers^{108, 109} proposed the fact that the electron binding energy corresponding to the high-energy component of lanthanide compounds is greater than the $\text{Ln}3d$ energy in individual metals (see Table 5). However, to measure the $\text{Ln}3d$ binding energy in lanthanide compounds more rigorously, one should take into account the whole structure of the spectrum of these electrons.²⁰² In this case, the $\text{Ln}3d$ binding energy can be determined using the weighted-mean value found from the complex spectrum. Moreover, if the extra structure in the spectra of these electrons is due to shake-down satellites, similar satellites (although less intense) should also occur in the spectra of electrons characterised by lower binding energies than the $\text{Ln}3d$ electrons. Unfortunately, in none of the studies^{75, 108, 109} in which a shake-down process has been proposed to interpret the $\text{Ln}3d$ spectral structure, was such an analysis performed.

In elucidation of the reasons for the appearance of highly intense satellites in the $\text{Ln}3d$ spectra of light lanthanides,^{51, 64, 135} three spectral parameters have been used: (i) the chemical shift of the electronic energy level corresponding to the considered component relative to the $\text{Ln}3d$ energy level in the metal; (ii) the presence of satellites in the spectra of other electronic energy levels; (iii) binding energy differences between lanthanides in compounds and in metals for various electrons the spectra of which exhibit no intense satellites of this type.

When considering the spectral structure for the $\text{La}3d$ electrons in lanthanum compounds from this standpoint, one can detect shake-up satellites. Indeed, the weighted-mean values of the $\text{La}3d$ binding energies in lanthanum compounds are about 0.3 eV higher than the corresponding values for metallic lanthanum, $E_b(\text{La}3d_{5/2}) = 836.6$ eV (see Table 5). The spectra of other electrons of lanthanum compounds also display satellites at higher binding energies relative to the basic lines, the satellite intensity decreasing with a decrease in the binding energies of these electrons (Table 6). This statement is also in agreement with the relationship between the binding energy difference $\Delta E_3(5p_{3/2} - 3d_{5/2})$ in the lanthanum compounds and metallic La. For example, the increase in ΔE_3 for the high-energy component of the spectrum by 4.4 eV on passing from metallic lanthanum to the trifluoride can hardly be explained by the assumption that the basic line for the $\text{La}3d$ electrons occurs in the spectrum at higher electron binding energies (see Table 5). Meanwhile, the concomitant increase in ΔE_3 for the low-energy component by 0.1 eV can be easily explained by the fact that the upper IVMO in the formation of the $\text{La}-\text{F}$ bond is an antibonding orbital. The slight participation of the $\text{La}5p$ and $\text{F}2s$ AO in the formation of IVMO in LaF_3 is also confirmed by calculations (see Fig. 12). However, to estimate more rigorously the character of the IVMO on the basis of binding energy differences, it is necessary to use the $\text{La}3d$ binding energies found as the weighted-mean ΔE_b values for the electrons reflecting the whole spectral structure.

Table 6. Intensities of the shake-up satellites $I = I_{\text{sat}}/I_0$ (%) and their energies (ΔE_{sat} , eV) relative to the basic lines in the XPS spectra of various lanthanum shells in compounds.^{20, 79, 84, 135}

Compound ^a	$I(3d_{5/2})$	$\Delta E_{\text{sat}}(3d_{5/2})$	$I(4p_{3/2})$	$I(4d_{5/2})$
LaF_3	30	4.3	18	13
LaNbO_4	72	4.2	34	27
La_2O_3	83	3.5	29	22
$\text{La}_2\text{Ti}_2\text{O}_7$	91	4.2	27	—
$\text{LaL}_3^2 \cdot 1.5\text{H}_2\text{O}$	100	2.8	—	24
LaL_3^1	132	3.1	—	55

Note. The errors in the determination of I values are $\pm 10\%$, ΔE_{sat} is ± 0.2 .
^a L^1 is the diphenylacetic acid residue, L^2 is the *o*-methoxybenzoic acid residue.

This assumption is in good agreement with the results of the study¹⁴⁰ which illustrates the formation of shake-down satellites in the spectra of the $\text{La}3d$ electrons for metallic lanthanum and shake-up satellites in the spectra of these electrons in the dielectric $\text{La}(\text{OH})_3$ (Fig. 40). Upon the formation of a hole in a core level of lanthanum, the energy of the empty $\text{La}4f$ AO levels decreases. In a metal, these levels can be filled due to transition of an electron from the conduction band, which corresponds to a shake-down process. In a dielectric having the valence band rather than the conduction band at a higher binding energy, these $4f$ levels can be occupied due to transition of an electron from this band, which implies a shake-up process.

In reality, the satellite formation is a more complex process.^{41, 203, 204} The structure and intensity of these satellites are highly sensitive to the variation of a stoichiometric composition of the substance and the nature of the ligands surrounding the lanthanide. Thus it has been noted^{45, 46} that an increase in the covalent nature of the bond, for example, in the series of lanthanum halides LaF_3 , LaCl_3 , LaBr_3 , entails a decrease in the binding energies of shake-up satellites relative to the $\text{La}3d$ basic lines, while the satellite intensity markedly increases. Hence, the spectral characteristics of the satellites may allow one to estimate the degree of ionicity (covalence) of the $\text{La}-\text{L}$ chemical bonds in lanthanum compounds. For example, it follows from XPS spectra that the ionic type of the $\text{La}-\text{O}$ bond markedly increases over the series LaL_3^1 , $\text{LaL}_3^2 \cdot 1.5\text{H}_2\text{O}$, La_2O_3 (see Table 6). Similar consid-

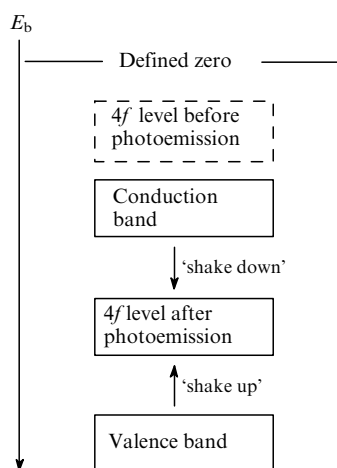


Figure 40. Diagram representing the positions of the 4f energy level in compounds of the light lanthanides before and after photoemission of a core electron.¹⁴⁰ The conduction band in a dielectric, for example, in La_2O_3 , is empty.

erations concerning the nature of satellites are also valid for cerium compounds.^{137, 138, 205} However, it follows from the low-energy spectra in which the $\text{Ln}4f$ states are shifted relative to the OVMO energy and from the pattern of variation of the $\text{Ln}3d_{5/2}$ FWHM for lanthanide trifluorides following an increase in the Ln atomic number (see Figs 23, 22) that shake-down satellites may be expected in the spectra of compounds formed by heavier elements.²⁰⁶ This is also consistent with the results of theoretical calculations.^{47, 114}

The data considered above make it possible to draw the conclusion that determination of the lanthanide oxidation state based on the $\text{Ln}3d$ XPS spectral characteristics of lanthanide compounds should be done using the weighted-mean value for the binding energy found with allowance for the whole complex structure of the spectrum.

V. Conclusion

The variation of the binding energy and the relative line intensity for the $\text{Ln}4f$ electrons vs. the atomic number of lanthanide in lanthanide oxides shows that the $\text{Ln}4f$ electrons largely resemble in spectral characteristics the Mnd electrons of nd transition metals. These data are consistent with the results of theoretical calculations pointing to a substantial participation of the $\text{Ln}4f$ AO in the formation of MO in lanthanide compounds. In all the studied compounds of scandium, yttrium and lanthanides, IVMO are efficiently formed by participation of occupied $\text{Sc}3p$, $\text{Y}4p$, $\text{Ln}5p$ and $\text{L}2s$ AO; this is supported by the results of theoretical calculations. This allows experimental evaluation of the type (either bonding or antibonding) of some IVMO.

The dependences on the multiplet splitting (ΔE_{ms}) of the $\text{Ln}4s$ and $\text{Ln}5s$ lines of lanthanide trifluorides, oxides and other compounds on the number of unpaired $\text{Ln}4f$ electrons have been established; they make it possible to determine spin population on the Ln atom in compounds. It was found that, due to the multiplet splitting, the spectrum of $\text{Ln}4d$ electrons for lanthanide compounds extends over a range of ~ 40 eV, which is several times greater than the spin-orbit splitting of the lines of these electrons. The mechanism of satellite formation in the spectra of $\text{Ln}3d$ electrons was analysed. For LnF_3 and Ln_2O_3 , the theoretical concept concerning the change of the sign of the binding energy difference $\Delta E_{\text{sat}} = |E_{\text{sat}}| - |E_0|$ between the satellite and the basic line (from 'plus' to 'minus') with an increase in the atomic number (Z) over the lanthanide row was confirmed experimentally. It was shown that the structure of the $\text{Ln}4p$ spectra and, in

some cases, the $\text{Ln}3p$ spectra is largely determined by the dynamic effect, resulting in the $\text{Ln}4p^5 4d^{10} 4f^n \leftrightarrow \text{Ln}4p^6 4d^8 4f^{n+1}$ and $\text{Ln}3p^5 3d^{10} 4s^2 4f^n \leftrightarrow \text{Ln}3p^6 3d^9 4s^1 4f^{n+1}$ final states, respectively.

The electron density induction on ions previously considered diamagnetic has been studied by X-ray electron spectroscopy in relation to the lanthanide-containing titanium and niobium double oxides.

Interpretation of the reasons for the formation of fine structure in the XPS spectra of lanthanides and elucidation of the relationships between the structure parameters and the physico-chemical properties of these compounds markedly extends the scope of application of the XPS method for the investigations of these compounds. In this case, X-ray electron spectroscopy becomes the most adequate method for determination of the elemental and ionic composition of lanthanide compounds, electronic configurations and magnetic characteristics of lanthanide ions, for investigations into the nature of the chemical bond and secondary electronic processes that accompany photoemission of electrons, and for determining the structure of the local environment of metal ions.

This provides the possibility of more efficient use of expensive advanced equipment and synchrotron radiation in diverse investigations of compounds of lanthanides and other elements.

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High-temperature superconductors based on complex layered copper oxyfluorides[†]

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Abstract. Chemical aspects of the synthesis of complex layered copper oxyfluorides possessing superconducting properties or serving as structural matrices for the preparation of new superconductors are discussed. Primary attention is given to fluorination of layered cuprates. Different ways of inserting fluorine into complex copper oxides and the corresponding synthetic approaches are surveyed. The influence of the synthesis conditions on the fluorination pathway, which involves either the incorporation of fluorine or partial replacement of oxygen with fluorine, is analysed. The advantages of xenon difluoride over other fluorinating agents are considered. Fluorination of complex copper oxides often leads to structural changes as exemplified by fluorine-containing phases obtained with the use of both XeF₂ and other fluorinating agents. The bibliography includes 104 references.

I. Introduction

Superconducting materials possess unique properties. The high practical potential of a new generation of high-temperature superconductors, *viz.*, complex copper oxides, gave impetus to comprehensive studies of their physical and chemical properties, structural characteristics and ‘chemical composition–properties–structure–synthesis conditions’ relationships.

The data on the relationships between the composition, structure and properties of numerous copper-containing high-temperature superconducting (HTSC) oxides made it possible to state the following structural and chemical criteria for the appearance of superconductivity:¹

- the existence of a layered structure composed of weakly distorted or planar superconducting CuO₂ layers, which occur as an infinite network of vertex-sharing CuO₄ squares;

- the presence of optimum interatomic Cu–O distances (ranging from 1.90 to 1.97 Å) in the plane of the conducting layer, which ensure overlapping of the 3d_{x²–y²}-orbitals of copper

and the 2p_{x,y}-orbitals of oxygen to form delocalised states in the σ* band;

- the optimum concentration of charge carriers in the conducting CuO₂ layers must correspond to the ranges of the formal oxidation state of copper from +2.05 to +2.25 and from +1.8 to +1.9 for *p*- and *n*-type superconductors, respectively.

In the structures satisfying these criteria, the negative charge of the CuO₂ layers (if these layers are considered as composed of the Cu²⁺ cations and O^{2–} anions) is compensated by the positive charge of the adjacent nonconducting cationic-anionic charge-reservoir blocks, which offer a means of changing the oxidation state of copper in the CuO₂ layers. By varying the positive charge of these blocks, for example, through either the heterovalent cation substitution or a change in the oxygen content, the required concentration of charge carriers in the conduction band can be achieved. Another way of changing the concentration of charge carriers is to replace a portion of oxygen in the anion sublattice of complex cuprate by fluorine or to insert the fluorine atoms into the structure.

The oxygen and fluorine anions have similar ionic radii (*r*_{F[–]} = 1.29 Å and *r*_{O^{2–}} = 1.35 Å; for the coordination number of 2; see Ref. 2). Many oxides have structures analogous to those of fluorides and oxyfluorides (for example, CaO and NaF, LaOF and CaF₂, La₂CuO₄ and K₂CuF₄, *etc.*). Consequently, the incorporation of fluorine into complex layered copper oxides can give rise to oxyfluorides structurally similar to these oxides. Fluorine atoms can occupy the anion vacancies or replace oxygen atoms. In both cases, the formal oxidation state of copper is changed. If this incorporation does not lead to destruction or deformation of the CuO₂ layers, the resulting complex oxyfluoride would be expected to exhibit superconducting properties. The superconducting transition critical temperatures (*T*_c) of some complex copper oxyfluorides are even higher than those of their oxygen analogues (Table 1). Hence, complex layered copper oxyfluorides can be considered as a promising class of compounds for constructing high-temperature superconductors.

Fluorination of complex cuprates not only enables one to achieve the optimum concentration of charge carriers but also offers additional possibilities of searching for new layered compounds. The requirements for the retention of the charge balance and compatibility of interatomic distances in structural fragments (commensurability) impose limitations on the choice of cations involved in nonconducting blocks, which compensate the negative charge of the CuO₂ layers. The replacement of O^{2–} with F[–],

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[†] The review is dedicated to the blessed memory of Professor L M Kovba.

Low-temperature fluorination afforded fluorine derivatives of layered cuprates, *viz.*, $\text{YBa}_2\text{Cu}_3\text{O}_{6+\delta}$,^{22, 23} La_2CuO_4 ,²⁴ $\text{M}_{2-x}\text{A}_{1+x}\text{Cu}_2\text{O}_{6-\delta}$ ($\text{M} = \text{La}$ or Nd ; $\text{A} = \text{Ca}$ or Sr),²⁵ $\text{Pb}_2\text{Sr}_2\text{YCu}_3\text{O}_8$,²⁶ *etc.* Fluorine derivatives of complex cuprates decompose upon heating to form thermodynamically stable products. Their stability is determined primarily by high crystal lattice energies of fluorine-like alkaline-earth fluorides and rare-earth oxyfluorides.

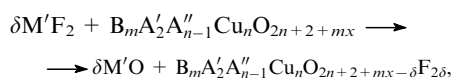
3. Fluorinating agents for the synthesis of fluorine-containing high-temperature superconductors

Low-temperature syntheses of complex copper oxyfluorides were carried out with the use of various fluorinating agents, *viz.*, gaseous fluorine (pure^{22, 27} or in mixtures with other gases^{19, 24}), NF_3 ,²³ NH_4F ,^{28–31} NH_4HF_2 ,^{32, 33} transition-metal fluorides (ZnF_2 , CuF_2 , NiF_2 , AgF_2)^{34–38} and ClF_3 .^{39, 40}

Xenon difluoride, which offers promise as a fluorinating agent, was first proposed for fluorination of HTSC cuprates in the study.¹⁷ This reagent has advantages over other reagents. At room temperature, XeF_2 is a solid compound, which enables one to use it in precise amounts and, hence, to attain the required degree of fluorination and the desired oxidation state of copper. Xenon difluoride is much less aggressive than gaseous fluorine due to which no expensive bulky apparatus is required. In addition, xenon difluoride does not generate by-products that contaminate the sample synthesised.

Xenon difluoride serves as an oxidising agent, unlike ammonium fluoride, which creates reductive conditions and leads to an increase in the oxidation state of copper only in the reactions performed in the presence oxygen^{18, 30} or through disproportionation of the reaction products to form oxidised and reduced phases.²⁰

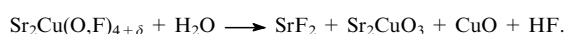
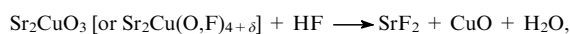
Many transition-metal fluorides $\text{M}'\text{F}_2$ ($\text{M}' = \text{Hg}$ or Ag), like XeF_2 , are oxidising fluorinating agents. However, the reactions with the use of these compounds not only lead to fluorine incorporation but can also be accompanied by anion substitution, the probability of the latter being increased as the reaction temperature is raised. Fluorination with $\text{M}'\text{F}_2$ ($\text{M}' = \text{Zn}$, Cu or Ni) proceeds predominantly according to the reaction



In this case, the oxidation state of copper remains unchanged. When the exchange reactions are performed by direct mixing of $\text{M}'\text{F}_2$ with the compound to be fluorinated rather than being carried out in the gas phase, impurities of metal oxide contaminate the resulting sample.

4. Use of XeF_2 as a fluorinating agent in the synthesis of fluorine-containing high-temperature superconductors

Trace amounts of water, which are, for example, adsorbed on the powdered starting compounds, contaminate fluorination products due to pyrohydrolysis. Hydrogen fluoride, which is evolved in the reactions of XeF_2 or oxyfluoride that formed with water, reacts with the starting oxide or oxyfluoride with elimination of water. The latter is again involved in pyrohydrolysis.¹⁷ For example,



Fluorination at high temperatures must be carried out in hermetically sealed containers resistant to fluorine because it is necessary, first, to exclude exposure to water vapour and, second, to prevent leakage of xenon difluoride that has high volatility. We developed an original procedure for fluorination. According to this procedure, the reactions are carried out in a sealed nitrogen-filled copper tube in which a nickel crucible containing a mixture of the starting compound and XeF_2 is placed. (All operations

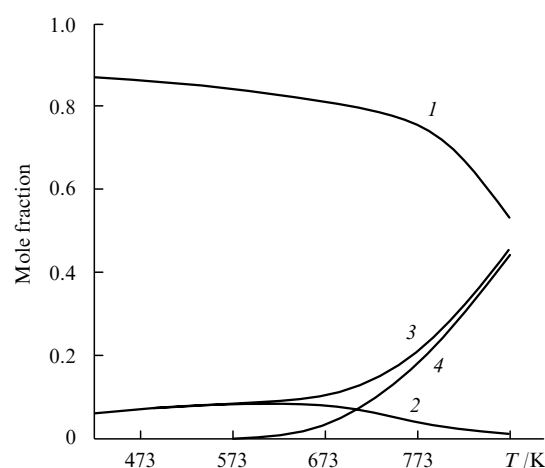
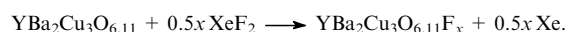


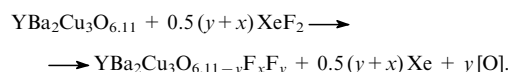
Figure 1. Temperature dependence of the equilibrium composition of the gas mixture containing one mole of XeF_2 at 1 atm.⁴¹ (1) XeF_2 , (2) XeF_4 , (3) Xe , (4) F_2 .

associated with the preparation of samples must be performed in a dry chamber.) In the temperature range of 423–673 K, XeF_2 exists predominantly in the gas phase and reacts with complex oxides through a gas–solid mechanism. Calculations of the temperature dependence of the equilibrium composition of the gas mixture (using the database⁴¹) containing one mole of XeF_2 at 1 atm (Fig. 1) demonstrated that at temperatures below 673 K this mixture is composed of Xe , XeF_2 and XeF_4 as the major components, the last two compounds serving as fluorinating agents. Xenon tetrafluoride surpasses xenon difluoride in oxidising activity^{42, 43} but its concentration in the gas mixture at $T < 673$ K is much lower than the concentration of XeF_2 . At reaction temperature higher than 673 K, dissociation of XeF_2 into F_2 and Xe becomes noticeable.

Fluorination with xenon difluoride in different temperature ranges involves the following main reactions. It was demonstrated⁴⁴ that the incorporation of fluorine into the structure of complex cuprate was the major process in the case of fluorination of $\text{YBa}_2\text{Cu}_3\text{O}_{6.11}$ (Y123 phase) in the temperature range from 423 to 573 K



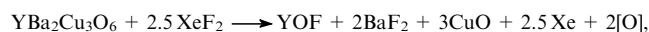
This reaction led to an increase in the formal oxidation state of copper from +1.74 in the starting strongly reduced phase $\text{YBa}_2\text{Cu}_3\text{O}_{6.11}$ to +2.03–+2.14 in the fluorinated samples. When the temperature was increased to 673 K, competitive anion exchange took place, *i.e.*, oxygen atoms were partially replaced by fluorine atoms. The anion exchange causes partial reduction of copper cations because the formation of the fluorinated phase is accompanied by the replacement of one O^{2-} anion with one F^- anion. It is impossible to distinguish unambiguously the temperature ranges in which the fluorine incorporation and anion exchange proceed autonomously. Both competitive processes occur simultaneously



It can only be noted that the anion exchange is enhanced as the temperature is increased and finally dominates over fluorine incorporation. Thus, the reaction of the oxidised phase $\text{YBa}_2\text{Cu}_3\text{O}_{6.95}$ with XeF_2 at 623 K led to a decrease in the oxidation state of copper from +2.30 to +2.22, which is indicative of the formation of a more reduced phase, *i.e.*, of the partial replacement of oxygen with fluorine. Oxygen evolved in the course of this process is absorbed by the walls of a copper tube to form Cu_2O due to which it cannot act as an oxidiser. At 603 K,

the partial pressure of oxygen in the tube [$\ln P_{O_2} = -22.2$ (atm)], which corresponds to the equilibrium pressure of oxygen over a mixture of Cu and Cu_2O at this temperature, is comparable to the partial pressure of oxygen over the strongly reduced phase $YBa_2Cu_3O_{6.1}$ [$\ln P_{O_2} = -21.1$ (atm)] at the same temperature.⁴⁴

Nevertheless, the process can be forced to occur predominantly either by fluorine incorporation or anion exchange by changing the temperature range. This can be used for choosing the method of doping to create *p*- or *n*-type superconductors. The final step of the anion exchange involves the destruction of the structure of complex copper oxide (in the temperature range of 673–773 K) under the action of xenon difluoride or fluorine generated upon decomposition of the former:



III. Structural transformations upon fluorination of complex cuprates

As mentioned above, oxygen and fluorine have similar ionic radii and the simple replacement of oxygen atoms by an equivalent amount of fluorine atoms would not lead to substantial structural changes of complex oxyfluoride copper compared to that of complex oxide but must be accompanied by a decrease in the formal oxidation state of copper. As an example, we refer to the $Nd_2CuO_{4-x}F_x$ solid solutions, which have tetragonal structures of the T' phase (Nd_2CuO_4) (Fig. 2). An increase in the degree of replacement of O atoms by F atoms is accompanied by an increase in the unit cell parameter *a* because a reduction in the formal oxidation state of copper leads to an increase in the occupancy of the antibonding σ^* band and elongation of the equatorial Cu–O_{eq} bond. Simultaneously, the structure is slightly contracted along the *c* axis, which is probably associated with the difference in the ionic radii of oxygen and fluorine.^{4, 28}

Studies of fluorinated samples by near-edge X-ray absorption fine structure (NEXAFS) spectroscopy demonstrated that fluorine atoms replace oxygen atoms in the tetrahedrally coordinated positions of the fluorite-like Nd_2O_2 block.⁴⁵ Distortions of the crystal structures of the $Nd_2CuO_{4-x}F_x$ and $Nd_{2-x}Ce_xCuO_4$ solid solutions were examined by the electron diffraction method and high-resolution transmission electron microscopy (HRTEM).⁴⁶ The observed various superstructures of fluorine-containing compounds were identical with those of cerium-substituted compounds. These superstructures resulted, apparently, from

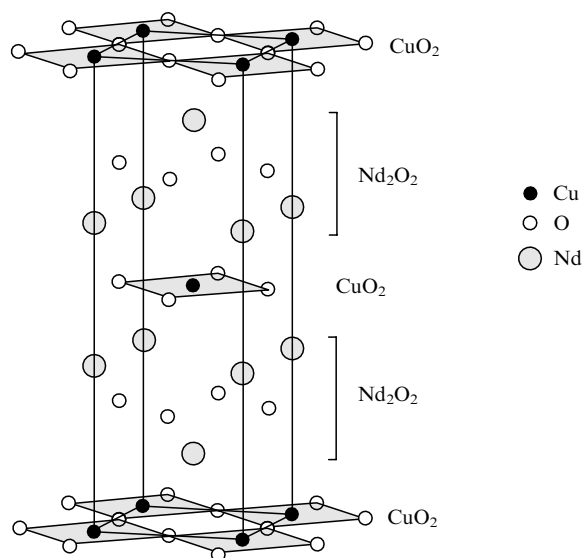


Figure 2. Crystal structure of Nd_2CuO_4 .

ordering of the anions and anion vacancies, which were generated upon annealing of the samples at 523–1023 K *in vacuo*, rather than were associated with the replacement of oxygen by fluorine. The examination of the superconducting $Nd_2CuO_{3.8}F_{0.2}$ sample by the HRTEM method did not reveal a superstructure for this compound.⁴

The appearance of hyperstoichiometric anions in the structure due to fluorine incorporation or the replacement of O^{2-} anions with a double amount of F^- ions can lead to structural transformations involving changes in the coordination polyhedra, interatomic distances and space symmetry up to the complete rearrangement of the crystal structure. For example, strontium cuprate Sr_2CuO_3 is structurally similar to La_2CuO_4 . However, unlike the crystal structure of the latter, which consists of the CuO_2 layers, the crystal structure of Sr_2CuO_3 is composed of chains of the vertex-sharing CuO_4 squares (Fig. 3a) due to ordering of the oxygen atoms and anion vacancies. Hence, the composition of the layer can be written as $CuO\Box$. Fluorination of Sr_2CuO_3 caused the rearrangement of the oxygen atoms and their migration from the Sr_2O_2 block to the equatorial coordination environment about the copper atoms.^{19, 47} As a consequence, complex oxyfluoride $Sr_2CuO_2F_{2+\delta}$ contains the conducting CuO_2 layers (Fig. 3b). As a result of incorporation of additional fluorine atoms into the tetrahedral cavities of the Sr_2O_2 block, the concentration of holes in the conduction band became higher than the optimum value. However, the required doping level was achieved upon subsequent reductive annealing and the compound was transformed into the superconducting state at 46 K. The partial replacement of strontium with barium to form the $Sr_{2-x}Ba_xCuO_2F_{2+\delta}$ solid solution made it possible to increase T_c to 64 K ($x = 0.6$).²⁰ Calculations of the energy of Coulombic interactions^{19, 47} suggested that the driving force for the anionic rearrangement is the difference between the lattice energy of the compound which contains fluorine atoms in the axial vertices of the octahedra about the copper atoms and the lattice energy of the same compound which contains the fluorine atoms in the equatorial positions to form the $CuOF$ layers.

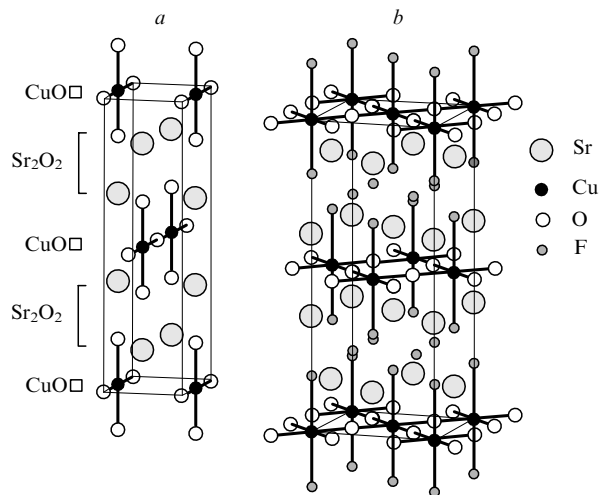


Figure 3. Crystal structures of Sr_2CuO_3 (a) and $Sr_2CuO_2F_{2+\delta}$ (b).

The incorporation of additional anions into vacancies of the anion sublattice of the $B_mA_2A'_{n-1}Cu_nO_{2n+2+m\delta}$ compounds leads to an increase in the coordination number of the B cations, which was initially smaller than 6. If these cations are Cu^{2+} , the completion of their coordination environment to an octahedron must lead to deformation of the crystal structure accompanied by an increase in the distance between the layer containing the copper cations and the adjacent layers containing the A cations. The $Cu(O,F)_6$ octahedron is tetrahedrally distorted due to the

Jahn–Teller effect resulting from the unsymmetrical occupancy of the e_g level ($3d_{z^2}^2 3d_{x^2-y^2}^1$). As a consequence, the Cu–O_{ax} distance becomes substantially larger than the Cu–O_{eq} distance resulting in an increase in the interlayer distances in the structure. Thus, the formation of an octahedron about the copper atoms in Sr₂CuO₂F_{2+δ} leads to a substantial increase in the unit cell parameter c ($c = 13.468$ Å)¹⁹ as compared to that observed in the initial compound Sr₂CuO₃ ($a = 12.716$ Å).⁴⁸

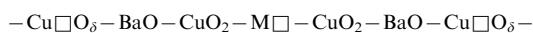
If the B sublattice contains cations whose stable coordination number is smaller than 6, for example, the Ga³⁺ cations in the tetrahedral environment in the Ga1201 (MACuGaO₅, M = La, Pr or Nd; A = Ca or Sr)^{49, 50} and Ga1212 (Y_{0.6}Ca_{0.4}Sr₂Cu₂GaO₇) phases,⁵¹ the crystal structures, including the CuO₂ layers, may be distorted due to ordering of the oxygen atoms and anion vacancies in the B(O,□)₂ layers. Deformation of the structure may be responsible for the absence of superconducting properties. The filling of vacancies with additional anions upon fluorination leads to a reduction in deformations up to the formation of a structure characterised by a higher space symmetry group and undeformed conducting layers. The same effect would be expected to occur when fluorination causes changes in the sizes of the structural blocks in the plane of the CuO₂ layers, which are favourable for the establishment of their commensurability and removal of structural distortions appearing upon adaptation of the structural blocks to each other. The incorporation of fluorine atoms into the interlayer cavities of the structure with the completed anion sublattice would, most probably, lead to lowering of the symmetry due to displacement of the atoms from the ideal positions, thus minimising Coulombic repulsions between the anions in the interlayer cavities and the anions in the adjacent atomic layers.

Hence, the superconducting properties of complex copper oxyfluorides are determined not only by the character of changes in the oxidation state of copper through different mechanisms of fluorination but also by possible structural transformations.

IV. Structures, synthesis and superconducting properties of different classes of copper oxyfluorides

1. Fluorination of the MBa₂Cu₃O_{6+δ} (M = Y, Dy, Ho, Tm) and Y₂Ba₄Cu₇O_{14+δ} phases

The perovskite-like anion-deficient structures of the MBa₂Cu₃O_{6+δ} phases (M123 phase) with unit cell parameters $a \approx b \approx a_p$, $c \approx 3a_p$, where a_p is the parameters of the perovskite sublattice (Fig. 4a), involve the following layer sequence



(□ is the anion vacancy).

The anion positions in the Cu□O_δ layer (Cu1 layer) can be completely vacant at $\delta = 0$, which corresponds to the structure of the tetragonal strongly reduced M123 phase. The latter does not possess superconducting properties (the formal oxidation state of copper is +1.67). The Cu1 atoms (see Fig. 4a) have a dumbbell-like coordination typical of the Cu⁺ cations. At $\delta \approx 1$, the oxygen atoms occupy half of the vacancies in the Cu1 layer in an ordered fashion thus completing the coordination environment about the copper atoms to a square. The chains of the vertex-sharing CuO₄ squares are oriented along the b axis resulting in an orthorhombic distortion of the structure. The hole concentration in the compounds with $\delta \approx 1$ is close to the optimum value and these compounds have the highest superconducting transition temperatures ($T_c = 92$ – 94 K) of all MBa₂Cu₃O_{6+δ} compounds.

The Y₂Ba₄Cu₇O_{14+δ} compound (Y247 phase) is structurally related to YBa₂Cu₃O_{6+δ} (Y123) with the difference that the former structure contains chains consisting of the doubled copper–oxygen squares (see Fig. 4b). In the structures of both phases, the fluorine atoms can occupy the anion positions of the Cu1 layer instead of the oxygen atoms. Fluorination of samples of

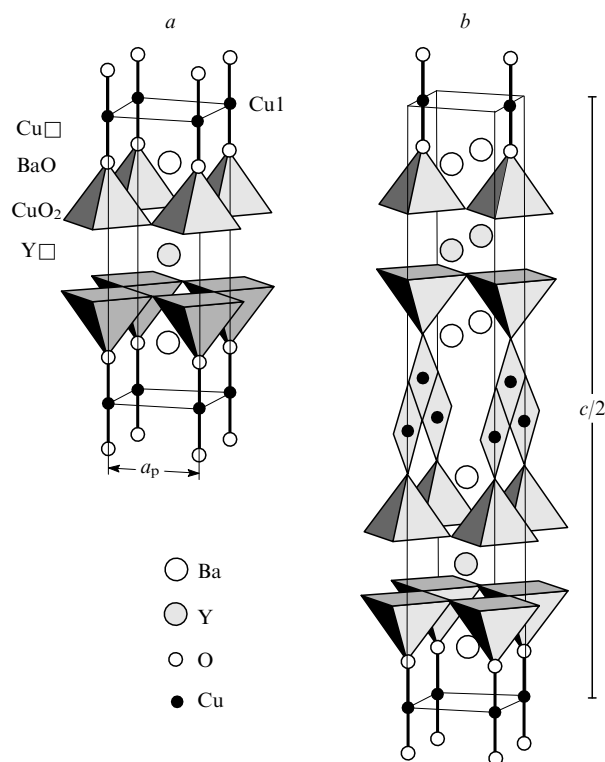


Figure 4. Crystal structures of YBa₂Cu₃O₆ (a) and Y₂Ba₄Cu₇O₁₄ (b).

the Y123 phase characterised by different oxygen contents was examined in numerous studies. The results of these investigations are briefly summarised below.

Fluorine is incorporated into the structures of partially reduced or completely oxidised YBa₂Cu₃O_{6+δ} samples ($\delta \geq 0.65$) and occupy vacancies in the Cu1 layer both along the a and b directions of the orthorhombic unit cell. The positions are occupied successively. In the case of a low degree of fluorination, the fluorine atoms occupy predominantly the position (0, 1/2, 0). Powder neutron-diffraction studies demonstrated⁵² that once the occupancy of this position reached 80%, the incorporation of the fluorine atoms into the position (1/2, 0, 0) started. This scheme of filling the positions is consistent with the fact that the orthorhombic distortion of the unit cell was enhanced for YBa₂Cu₃O_{6.7}F_{0.15} and was subsequently reduced for YBa₂Cu₃O_{6.7}F_{0.3}. Fluorination of YBa₂Cu₃O_{6.7} led to an increase of T_c from 65 to 90 K.

Fluorination of a strongly reduced YBa₂Cu₃O_{6.2} sample by the electrochemical method caused the orthorhombic distortion of its tetragonal structure.⁵³ The fluorine incorporation gave rise to a blurred superconducting transition with $T_c = 55$ – 60 K, which is similar to T_c for YBa₂Cu₃O_{6.5}.

In most cases, fluorination of the strongly oxidised YBa₂Cu₃O_{6+δ} phase with δ nearly-unity allows one to prepare compounds possessing T_c no higher than that achieved for the optimally oxygen-doped sample.^{22, 23, 53, 54} However, it was reported that the treatment of YBa₂Cu₃O_{6+δ} with a mixture of nitrogen and fluorine led to an increase of T_c from 92 to 96 K.⁵⁵

An increase in the degree of fluorination of the starting phase Y123 gave rise to a fluorinated phase with a tetragonal unit cell regardless of the hyperstoichiometric oxygen content.^{53, 56} Fluorination, like the oxygen incorporation, was accompanied by the contraction of the structure along the c axis. This indicates that the copper atoms in the fluorinated and oxygen-doped Y123 phases have similar coordination environments and that anion vacancies are abundant in the Cu1 layer, which is retained even in the case of a high degree of fluorination. As exemplified by the YBa₂Cu₃O_{6.65} sample treated with NF₃,⁵⁶ tetragonal symmetry occurs due to the

fact that the positions $(1/2, 0, 0)$ and $(0, 1/2, 0)$ are statistically occupied by the anions (the occupancies of the positions are 68%).

Kistenmacher predicted⁵⁷ the existence of complex oxyfluoride $\text{YBa}_2\text{Cu}_3\text{O}_6\text{F}_2$. In the structure of this compound, the anion vacancies in the Cu1 layer are completely filled with fluorine atoms. In this compound, the oxidation state of copper must be equal to +2.33, which is identical to that observed in $\text{YBa}_2\text{Cu}_3\text{O}_7$ (oxygen-doped Y123 phase). Oxyfluoride would be expected to have tetragonal symmetry (due to the replacement of the copper–oxygen chains with the two-dimensional CuF_2 layers) and exhibit superconducting properties. Evidently, the parameter c of the tetragonal unit cell of complex oxyfluoride $\text{YBa}_2\text{Cu}_3\text{O}_6\text{F}_2$ must be substantially larger than the analogous parameter of the oxide phase due to manifestation of the Jahn–Teller effect in the CuO_2F_4 octahedra.

For complex oxyfluoride $\text{YBa}_2\text{Cu}_3\text{O}_6\text{F}_2$ to be formed, the Cu1 layers in the starting compound must contain as few oxygen atoms as possible. Fluorination of the reduced nonsuperconducting $\text{YBa}_2\text{Cu}_3\text{O}_{6.11}$ compound led to substantial changes in the X-ray diffraction pattern, an increase in the oxidation state of copper to +2.14 and the manifestation of superconductivity at 94 K (the volume of the superconducting phase was ~25%). The X-ray diffraction pattern of the fluorinated compound is characterised by the presence of sharp intense reflections with the Miller indices hkl . The general reflections hkl are virtually absent. Relying on these data, only the parameter $a = 3.869 \text{ \AA}$ of the tetragonal unit cell of the fluorinated compound was determined, the existence of strong disorder was proposed and the occurrence of numerous defects along the c direction was suggested.⁴⁴

The structure of the fluorinated sample was examined by the HRTEM method in combination with electron probe X-ray analysis, which confirmed the presence of fluorine in crystallites. The electron diffraction pattern and images obtained by the HRTEM method (Fig. 5) are unambiguously indicative of the formation of a new compound with unit cell parameters $a \approx 3.87 \text{ \AA}$ and $c \approx 13 \text{ \AA}$.⁵⁸

In the crystallites, the domains of this compound (F2 phase) or extended defects alternate with the domains of the starting structure (F1 phase). Electron probe X-ray analysis demonstrated that the fluorine content in the F2 phase is much higher than that in the F1 phase (the precise fluorine content is impossible to

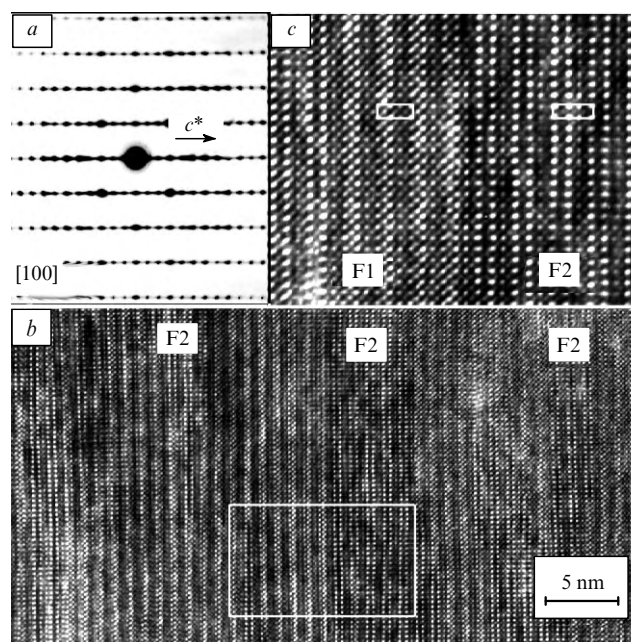


Figure 5. Images along the $[100]$ direction obtained by electron diffraction (a) and HRTEM (b, c) methods. The sample was prepared by the treatment of $\text{YBa}_2\text{Cu}_3\text{O}_{6.11}$ with xenon difluoride at 623 K for 50 h.

determine by this method). Substantial broadening and a decrease in the intensities of the lines with the non-zero Miller indices l in X-ray diffraction experiments are accounted for by small sizes of the domains along the $[001]$ direction. A comparison of the experimentally observed contrast in the images obtained by the HRTEM method with the results of calculations using different structural models allowed the conclusion that an increase in the parameter c for the F2 phase is associated with an increase in the distance between the BaO and Cu1 layers (but not in the distance between the CuO_2 and $\text{Y}\square$ layers). On this basis, it was suggested that the fluorine atoms are incorporated into the anion vacancies

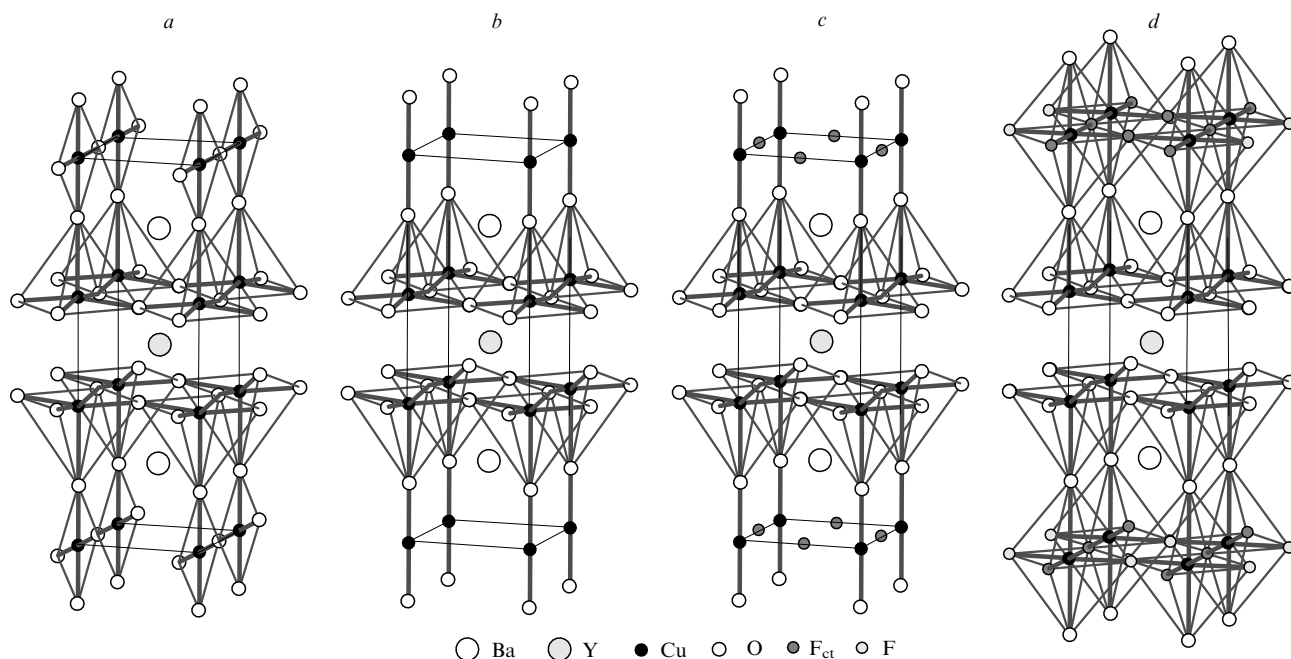


Figure 6. Scheme of the structural transformations in the Y123 phase upon oxygen and fluorine incorporation. (a) $\text{YBa}_2\text{Cu}_3\text{O}_7$; (b) $\text{YBa}_2\text{Cu}_3\text{O}_6$; (c) $\text{YBa}_2\text{Cu}_3\text{O}_6\text{F}$; (d) $\text{YBa}_2\text{Cu}_3\text{O}_6\text{F}_2$.

in the Cu1 layer, which is accompanied by the formation of the distorted CuO_2F_4 octahedra. According to the proposed structural model, elongation of the axial Cu–O distance from 1.85 Å in the initial compound $\text{YBa}_2\text{Cu}_3\text{O}_{6.11}$ to 2.3–2.5 Å in the fluorinated sample must lead to the parameter c of 12.8–13.2 Å in the $\text{YBa}_2\text{Cu}_3\text{O}_6\text{F}_2$ structure. The results of an electron microscopic study confirmed this suggestion and provided support for the fact that new superconducting oxyfluoride with composition $\text{YBa}_2\text{Cu}_3\text{O}_6\text{F}_2$ was synthesised. The scheme of the structural transformations caused by the incorporation of the oxygen and fluorine atoms into the tetragonal $\text{YBa}_2\text{Cu}_3\text{O}_6$ structure is shown in Fig. 6.

Upon fluorination, the properties of the $\text{Y}_2\text{Ba}_4\text{Cu}_7\text{O}_{14+\delta}$ (Y247 phase) compound are changed in much the same manner. The incorporation of fluorine atoms into the structure of strongly reduced oxide $\text{Y}_2\text{Ba}_4\text{Cu}_7\text{O}_{14.09}$ led to a rise in T_c from 30 to 62 K and an increase in the unit cell parameter c from 50.6 to 53.5 Å.⁵⁹ The fluorinated Y247 phase, unlike the fluorinated Y123 phase, remains orthorhombic because fluorination has no effect on the chains formed by the doubled copper–oxygen CuO_4 squares although the degree of orthorhombic distortion is somewhat lowered.

Investigation by the HRTEM method demonstrated that the incorporation of the fluorine atoms into the Y123 and Y247 phases occurred non-homogeneously. The completely fluorinated phase with composition $\text{YBa}_2\text{Cu}_3\text{O}_6\text{F}_2$ was found as extended domains in a matrix of the partially fluorinated Y123 phase. In the fluorinated Y247 phase, the regions in which the positions in the Cu1 layer are completely occupied by the fluorine atoms occur only as local defects (Fig. 7). An analogous microstructure was found in the fluorinated $\text{MBa}_2\text{Cu}_3\text{O}_{6.12}$ phases (M = Dy, Ho or Tm).⁶⁰ Unlike the Y123 phase, the reactions of the M123 phases with XeF_2 proceed predominantly through a mechanism of anion exchange due to which it is impossible to achieve the oxidation state of copper suitable for the manifestation of superconductivity.

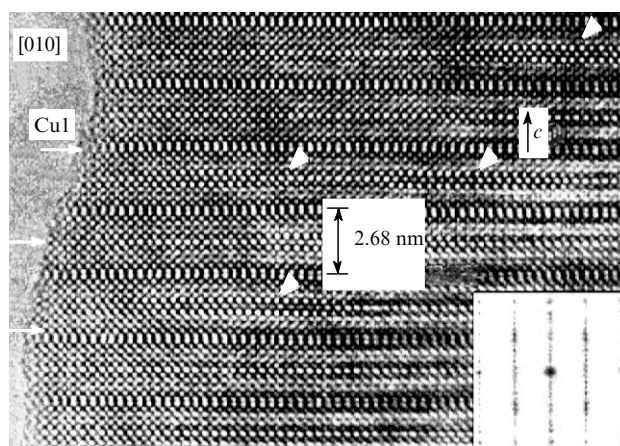


Figure 7. HTREM image of the [010] zone. Local defects, which are inclusions of the $\text{Y}_2\text{Ba}_4\text{Cu}_7\text{O}_{14}\text{F}_2$ phase, are indicated by arrows. The optical-diffraction image is shown in the lower inset at the right of the illustration.

2. Fluorine derivatives of mercury-containing superconducting cuprates $\text{HgBa}_2\text{CuO}_{4+\delta}$ (Hg1201) and $\text{Hg}_{0.8}\text{Ba}_2\text{Ca}_2\text{Cu}_3\text{O}_{8+\delta}$ (Hg1223)

Fluorine atoms incorporated into the Y123 structures and related phases form strong bonds with the copper cations in the Cu1 layers thus changing their coordination environment and inter-atomic distances (Fig. 8). The structures of mercury-containing cuprates are characterised by the presence of the anion position $(1/2, 1/2, 0)$ in the mercury-containing layer. This position can be

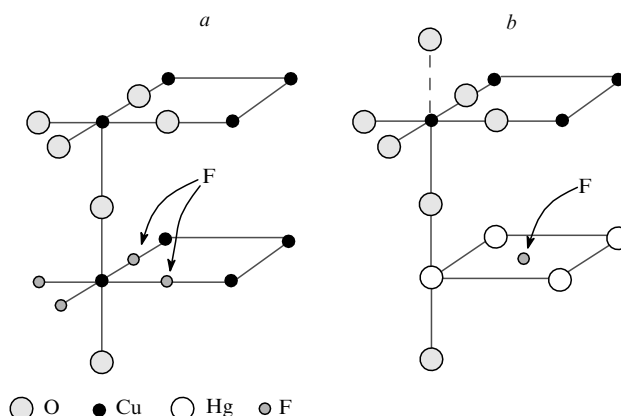
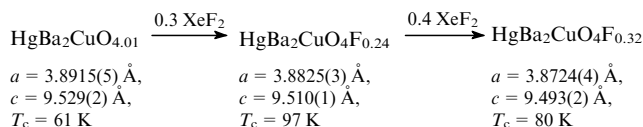


Figure 8. Scheme of incorporation of fluorine atoms into the structures of the phases Y123, Y247 (a) and Hg1201, Hg1223 (b).

partially occupied by oxygen or fluorine atoms, thus changing the hole concentration in the conduction band. The stable dumbbell-like coordination of the Hg^{2+} cations is responsible for the absence of steric hindrances as well as for weak interactions between these anions and the mercury cations. Due to the formation of the long weak Hg–O(F) bond in the plane of the layer, the incorporation of anions into this layer cannot induce substantial structural changes, which were observed in the Y123 and Y247 phases.⁶¹ A comparative analysis of the properties of samples oxidised with fluorine or oxygen (the anion contents, the formal oxidation states of copper, structural parameters and the superconducting transition temperatures were compared) allowed important conclusions about the nature of superconductivity in mercury-containing cuprates.

Early experiments on the synthesis of the fluorinated Hg1212 and Hg1223 phases were performed with the use of BaF_2 (Ref. 62) or CuF_2 (Ref. 63) as a source of fluorine. The experiments were carried out at high temperatures (923–1073 K). These syntheses afforded multiphase samples, which contained superconducting phases with unit cell parameters similar to those of the corresponding phases in oxygen-saturated samples.

The reactions of mercury-containing cuprates with xenon difluoride proceeded at rather low temperatures (423–473 K), which made it possible to perform fluorination predominantly through fluorine incorporation, the probability of anion exchange being substantially decreased. Fluorination of the strongly reduced $\text{HgBa}_2\text{CuO}_{4.01}$ phase with $T_c = 61$ K led to a change in the superconducting transition critical temperature. At low degrees of fluorination, T_c reached maximum value of 97 K and then decreased. In the case of too high oxidation states (overdoping) of copper, the superconductivity can be completely suppressed.⁶⁴ The aforesaid is illustrated by the following example:



The presence of fluorine atoms in the mercury-containing layer was unambiguously established by ^{19}F NMR spectroscopy.^{65,66} The possible distribution of the atoms over the crystallographic positions in these structures can be judged from the temperature dependences of the rates of ^{19}F spin–lattice relaxations for the optimally fluorine-doped and overdoped Hg1201 samples. In the optimally doped compound, the fluorine atoms occupy the position $(1/2, 1/2, 0)$. An increase in the fluorine content leads to the partial replacement of oxygen atoms in the position $(0, 0, \sim 0.21)$ with fluorine atoms (in the axial vertex of the CuO_6 octahedron).⁶⁷ The structures of the optimum fluorine-doped ($T_c = 97$ K) and overdoped ($T_c \approx 80$ K) compounds were

refined by the powder neutron-diffraction method. The refined occupancies of the anion position (1/2, 1/2, 0) in the mercury-containing layer are 0.24(2) and 0.32(2) for two compounds, respectively. These values are substantially larger than the occupancies found for the oxygen-oxidised Hg1201 phases with the similar temperatures T_c [0.124(9) and 0.19(1), respectively].⁶⁸ The plots of T_c versus the fluorine or oxygen content in the mercury-containing layer are dome-shaped. However, the curve for the fluorinated samples is shifted toward larger δ values (Fig. 9). As is evident from Fig. 9, twice as much fluorine as compared to that of oxygen is required for the same T_c values and the corresponding doping level to be attained, which corresponds to the difference in the formal charges of the O^{2-} and F^- anions. This fact provides support for the ionic model of doping of mercury-containing cuprates, *viz.*, an oxygen atom creates twice as many holes in the conduction band as that generated by a fluorine atom.

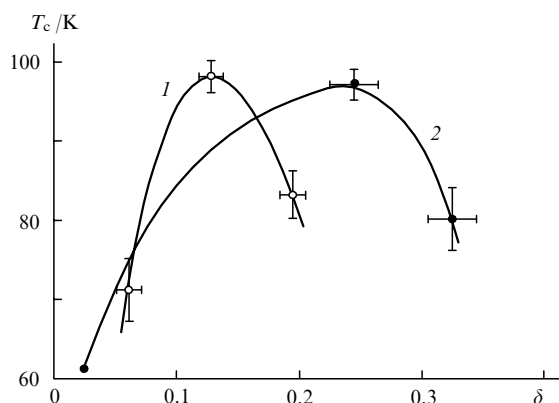


Figure 9. Plot of T_c vs. the excessive oxygen (1) or fluorine (2) contents in the Hg1201 phase.

The dependence of T_c on the unit cell parameter a (or on the interatomic Cu—O_{eq} distance in the plane of the CuO₂ layer) both for the fluorinated and oxygen-oxidised samples can be approximated by a single parabolic curve with a maximum at 97 K and $a = 3.882$ Å (Fig. 10). Hence, the same superconducting transition temperatures in complex mercury-containing cuprates can be achieved not only at the same doping level but also with approximately equal equatorial Cu—O_{eq} bond lengths. If the oxidation state of copper remains constant, the Cu—O_{eq} distances are virtually independent of the amount of hyperstoichiometric anions. In contrast, the Cu—O_{ax} distance changes substantially as the occupancy of the anion position in the mercury-containing layer is varied, *viz.*, the Cu—O_{ax} bond is shortened as the amount

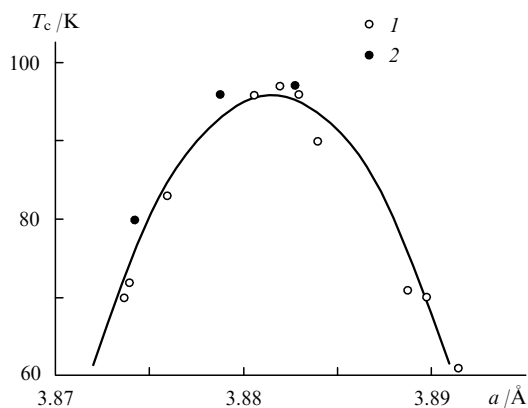


Figure 10. Plot of T_c vs. the unit cell parameter a for oxygen-doped (1) and fluorinated (2) Hg1201 samples.

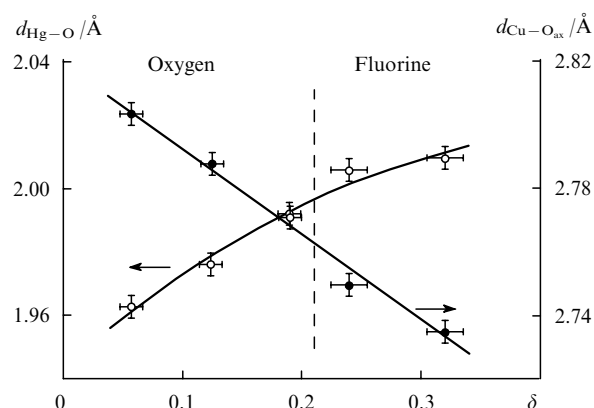


Figure 11. Interatomic Cu—O_{ax} and Hg—O distances vs. the amounts of the oxygen or fluorine atoms in the mercury-containing layer.

of the hyperstoichiometric anions is increased. Figure 11 shows the virtually linear dependence of this distance on the amount of excessive (δ) oxygen or fluorine. In the fluorinated compounds, this bond is substantially shorter than those in oxygen-containing compounds with similar T_c .

Apparently, shortening of the Cu—O_{ax} distances results from extension of the Hg—O dumbbells, which is associated with an increase in the coordination number of the mercury atoms due to incorporation of additional anions in the mercury-containing layer. This leads to the displacement of the O_{ax} atom from mercury to copper accompanied by a noticeable shortening of the Cu—O_{ax} distance, the Cu—O_{eq} bond lengths and T_c remaining virtually constant. This change in the interatomic distances can be considered to be a result of anisotropic contraction of the CuO₆ octahedra under the action of the external pressure (~ 2 GPa) applied along the c axis.⁶⁹ According to $dT_c/dP \approx 2$ K GPa⁻¹ for the optimally oxygen-doped compound,⁷⁰ T_c for the fluorinated sample with $\delta_F \approx \delta_{opt}$ would be expected to increase by ~ 4 K. The fact that the optimally fluorine- and oxygen-doped samples have identical T_c indicates that shortening of the Cu—O_{ax} bond exerts only a slight effect on the increase in T_c in mercury-containing cuprates under the influence of the applied external pressure. The increase in T_c is most probably caused by shortening of the Cu—O_{eq} distances.

This conclusion was confirmed by the results of studies of the fluorinated Hg_{0.8}Ba₂Ca₂Cu_{3.2}O_{8+δ} samples (Hg1223 phase). The reduced Hg1223 sample ($T_c = 100$ K) was divided into two portions one of which was annealed under a stream of oxygen, and the remaining portion was fluorinated. For both samples, T_c was found to be increased, but the transition temperature for the fluorinated sample was 4 K higher (138 K) than that for the oxygen-oxidised sample (134 K).^{71,72} The unit cell parameters a and c of these samples are given below:

Sample	a / Å	c / Å
Hg _{0.8} Ba ₂ Ca ₂ Cu _{3.2} O _{8+δ}	3.8524(4)	15.819(4)
Hg _{0.8} Ba ₂ Ca ₂ Cu _{3.2} O ₈ F _{2δ}	3.8501(2)	15.773(3)

The structure of the fluorinated sample was refined based on the neutron diffraction data.⁷² In this sample, two anion positions in the mercury-containing layer, *viz.*, (1/2, 1/2, 0) and (1/2, 0, 0), are occupied with occupancies of 27(1)% and 10(1)%, respectively, as distinct from the fluorinated Hg1201 sample. Apparently, the fact that the anions occupy the position (1/2, 0, 0) is associated with the partial replacement of the mercury atoms with copper atoms. The total amount of anions in the mercury-containing layer of the fluorinated sample with the maximum T_c value is substantially larger than the amount of hyperstoichiometric oxygen in the optimally oxygen-doped sample [18% and 8% for the positions (1/2, 1/2, 0) and (1/2, 0, 0), respectively].⁷³

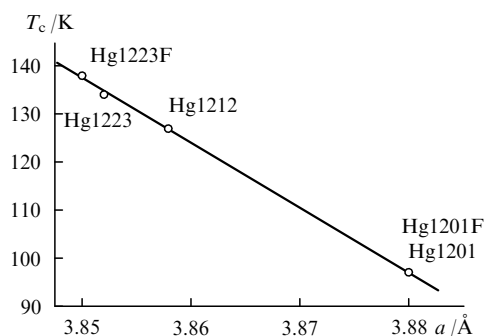


Figure 12. Maximum T_c vs. the unit cell parameter a for oxygen-oxidised and fluorinated mercury-containing cuprates.

The maximum T_c values for the first three members of the homologous series of mercury-containing complex cuprates $\text{HgBa}_2\text{Ca}_{n-1}\text{Cu}_n\text{O}_{2n+2+\delta}$ and the fluorinated Hg1201 and Hg1223 phases depend linearly on the unit cell parameter a ; $dT_c/da \approx 1350 \text{ K } \text{\AA}^{-1}$ (Fig. 12).^{72, 74} It is believed that the T_c for these compounds depends on the degree of contraction of the CuO_2 planes induced by the modification of the chemical composition. The similar value of dT_c/da was also found upon epitaxial contraction of thin single-crystalline films of $\text{La}_{0.9}\text{Sr}_{0.1}\text{CuO}_4$.⁷⁵

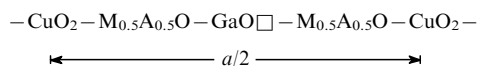
For the fluorinated Hg1223 sample, the absolute value of dT_c/da is almost an order of magnitude larger than dT_c/da obtained under the applied external pressure ($dT_c/dP \approx 1.7 \text{ K GPa}^{-1}$, $dT_c/da \approx -160 \text{ K } \text{\AA}^{-1}$).⁷⁶ This difference may be attributed to the structural changes of the CuO_2 layers. In the Hg1201 phase, these layers are planar, whereas the $\text{Cu}-\text{O}-\text{Cu}$ angle in the Hg1212 phase is close to 180° .⁷⁷ High external pressure causes corrugation of the CuO_2 layers. For example, the $\text{Cu}-\text{O}-\text{Cu}$ angle in the Hg1223 structure is decreased to 175.0° at a pressure of 2 GPa, T_c being increased to 138 K. The $\text{Cu}-\text{O}-\text{Cu}$ angle in the Hg 1223 phase changes only slightly upon fluorination (178.4° and 177.3° for the oxidised⁷⁷ and fluorinated samples, respectively). The $\text{Cu}-\text{O}-\text{Cu}$ bond angle is an important parameter governing T_c . For HTSC with $T_c > 100 \text{ K}$, the deviation of this angle from 180° is no larger than 4° .

Hence, chemical modifications of the structure, which lead to a decrease in the $\text{Cu}-\text{O}$ distance without a change in the degree of corrugation of the CuO_2 layers, is a promising way of increasing T_c in complex superconducting copper oxides.

3. Fluorine incorporation into structures of non-superconducting anion-deficient perovskite-like complex cuprates

Let us discuss the effect of fluorine incorporation on the structure and properties of anion-deficient copper-containing perovskites, which do not exhibit superconducting properties but which, nevertheless, could become superconductors if the appropriate doping level is achieved and the compound attains a structure suitable for the manifestation of superconductivity.

Perovskite-like complex cuprates with structures of brownmillerite MACuGaO_5 ($M = \text{La, Pr or Nd}$; $A = \text{Ca or Sr}$), which are denoted as Ga1201,^{49, 50} belong to the orthorhombic system (Fig. 13a) with the parameters $a \approx 4a_p$, $b \approx c \approx a_p\sqrt{2}$ (a_p is the parameter of the perovskite sublattice) and consist of alternating layers



The gallium and copper cations are in the tetrahedral and octahedral coordination environments, respectively. The GaO_4 tetrahedra in the plane of the $\text{GaO}\square$ layer share vertices to form chains along the c axis of the unit cell. The ordered arrangement of

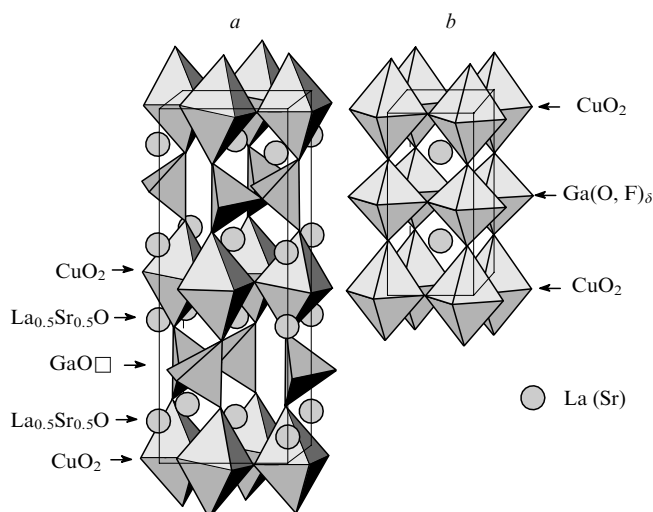
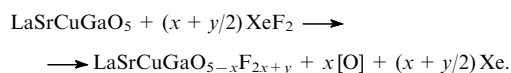


Figure 13. Crystal structures of LaSrCuGaO_5 (a) and $\text{LaSrCuGaO}_{5-x}\text{F}_{2x-y}$ (b).

the oxygen atoms and anion vacancies in these layers leads to distortion of the equatorial coordination environment about the copper atoms. In the Ga1201 compounds, two short (1.89 Å) and two long (1.96 Å) $\text{Cu}-\text{O}$ distances were found.^{78, 79} The substantial difference in the $\text{Cu}-\text{O}_{\text{eq}}$ bond lengths in the plane of the CuO_2 layers may be responsible for the fact that these compounds do not exhibit superconducting properties even if the appropriate oxidation state of copper is achieved. Actually, the $\text{La}_{1-x}\text{Sr}_{1+x}\text{CuGaO}_5$ solid solution (Ga1201 phase) ($0 \leq x \leq 1.2$, the maximum oxidation state of copper is $+2.2$) are not superconductors.⁸⁰ At the same time, homologues of the Ga1201 compounds, viz., the Ga1212 compounds, possess superconducting properties. This difference in the properties is associated with the difference in the coordination environment of the copper atoms in these compounds. In the structure of the superconductor $\text{Y}_{0.6}\text{Ca}_{0.4}\text{Sr}_2\text{Cu}_2\text{GaO}_7$ ($T_c = 44 \text{ K}$), the copper atoms occupy the centres of the square pyramids formed by the oxygen atoms, the equatorial $\text{Cu}-\text{O}$ distances being virtually equal (1.92 and 1.93 Å).⁵¹

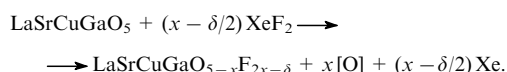
For the Ga1201 phases to exhibit superconducting properties, not only the appropriate doping level must be achieved but also strong distortion of the structure caused by the anion ordering in the $\text{GaO}\square$ layers must be diminished. This can be attained by inserting fluorine atoms into the anion vacancies. In this case, an increase in the formal oxidation state of copper will be accompanied by the formation of the five- and six-coordinate environment about the gallium atoms, which is favourable for a depression of the orthorhombic distortion and equalisation of the equatorial $\text{Cu}-\text{O}$ distances.

The treatment of LaACuGaO_5 ($A = \text{Ca, Sr}$) with xenon difluoride led to a decrease in distortion of the unit cell up to the transition of the orthorhombic phase into the tetragonal phase (for $A = \text{Sr}$) with the parameters $a \approx a_p$, $c \approx 2a_p$.⁸¹ Upon fluorination, the oxidation state of copper depends substantially on the reaction conditions. If fluorination is carried out over a long period (150 h) in the presence of a large excess of xenon difluoride at rather low temperature (573 K), the reaction proceeds according to the combined mechanism of anion exchange and fluorine incorporation:



Upon such fluorination, the oxidation state of copper reaches $+2.16$. An elevation of the temperature to 673 K is accompanied by a slight reduction in the oxidation state of copper (to $+1.95$)

due to the fact that the anion exchange becomes the predominant process:



The result of structural transformation occurring upon fluorination is shown in Fig. 13 *b*. Excessive fluorine atoms partially occupy the vacancies in the GaO_4 layers and the coordination environment about the gallium atoms becomes nearly octahedral. The oxygen and fluorine atoms and the anion vacancies are arranged in a disordered fashion in the positions $(1/2, 0, 1/2)$. In the case of the space group $P4/mmm$ and the above-mentioned unit cell parameters, the CuO_2 layers must be planar and the $\text{Cu}-\text{O}$ distances in the plane of the layer must be equal in length. In such a situation, the structure of the fluorinated phase will meet the criteria necessary for the manifestation of superconducting properties. However, all attempts to perform the transition of fluorinated samples into the superconducting state failed whatever the doping level used.

The simplest copper oxyfluorides which can exhibit superconducting properties are hypothetical solid solutions with composition $(\text{La}, \text{Sr})\text{CuO}_2\text{F}$ based on the perovskite structure. The required oxidation state of copper can be achieved through the heterovalent replacement of La with Sr in the A sublattice. These solid solutions must have a structure of tetragonally distorted perovskite containing CuO_2 planar layers and fluorine atoms in the axial positions of the octahedra about the copper atoms. These compounds can be synthesised by soft fluorination of anion-deficient perovskites in the ratio $(\text{La}, \text{Sr})/\text{Cu} = 1$.

Various perovskite-like anion-deficient copper oxides are known whose three-dimensional structures differ primarily by the character of ordering of the oxygen atoms and anion vacancies within the ab plane of the perovskite sublattice. Thus, the columns of the oxygen atoms passing along the $[001]$ direction are removed in a certain order resulting in a decrease in the coordination number of the copper atoms from 6 to 5, 4 or 2. Among these oxides are also the $(\text{La}_{1-x}\text{Sr}_x)_8\text{Cu}_8\text{O}_{20-\delta}$ solid solutions with tetragonal structures and the unit cell parameters $a \approx a_p 2\sqrt{2}$, $c \approx a_p$ (Fig. 14).^{82, 83}

For a superconducting compound to be prepared, the character of the distribution of the oxygen atoms in the starting compound must be changed upon fluorination so as to form the CuO_2 planes. Fluorination of $\text{La}_{6.5}\text{Sr}_{1.5}\text{Cu}_8\text{O}_{19.65}$ with xenon difluoride afforded a tetragonal perovskite-like phase with the presumed composition $\text{La}_{0.813}\text{Sr}_{0.187}\text{Cu}(\text{O}, \text{F})_{3-\delta}$ and the unit cell parameters $a < c \approx a_p$.⁸⁴ In a single sample, the fluorinated phase always coexists with the starting phase within one crystallite (Fig. 15). Thermal treatment at 673 K in air led to decomposition of $\text{La}_{0.813}\text{Sr}_{0.187}\text{Cu}(\text{O}, \text{F})_{3-\delta}$ to give LaOF and SrF_2 , which indicates that this phase contains a substantial amount of fluorine. The structure of $\text{La}_{0.813}\text{Sr}_{0.187}\text{Cu}(\text{O}, \text{F})_{3-\delta}$ was refined by the Rietveld method and confirmed by HRTEM (see Fig. 14). In the structure of this compound, the anion positions in the equatorial environment about the copper atoms are completely occupied, whereas the vacancies are located in the axial positions. The Jahn–Teller effect induced by an octahedral coordination about some copper atoms causes elongation of the axial distances (2.026 Å) as compared to the equatorial distances (1.896 Å) and the tetragonal distortion of the perovskite unit cell. Oxyfluoride $\text{La}_{0.813}\text{Sr}_{0.187}\text{Cu}(\text{O}, \text{F})_{3-\delta}$ does not exhibit superconducting properties.

The two examples considered above show that filling of the anion vacancies upon fluorination diminishes structural distortions caused by the ordering of the oxygen vacancies. However, the statistical distribution of the fluorine and oxygen atoms and the anion vacancies over certain crystallographic positions [for example, in the equatorial environment about the gallium atoms in the structures of fluorinated brownmillerites or in the axial positions of the $\text{Cu}(\text{O}, \text{F})_{6-\delta}$ octahedra in the $\text{La}_{0.813}\text{Sr}_{0.187}$.

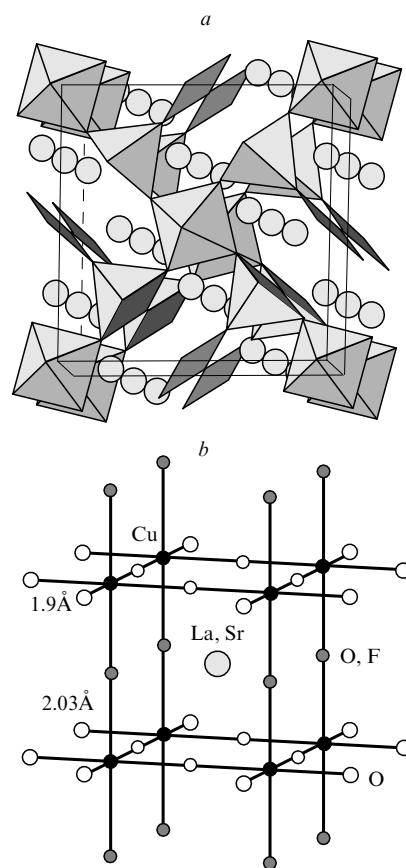


Figure 14. Scheme of the structural transformations of $\text{La}_{6.5}\text{Sr}_{1.5}\text{Cu}_8\text{O}_{19.65}$ (a) into $\text{La}_{0.813}\text{Sr}_{0.187}\text{Cu}(\text{O}, \text{F})_{3-\delta}$ (b) upon fluorination.

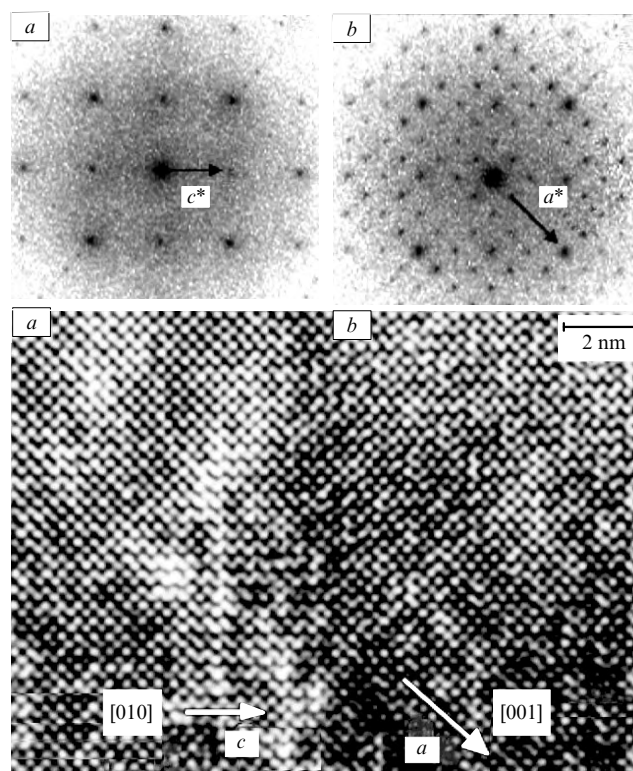


Figure 15. HRTEM images of the domains of the fluorinated $\text{La}_{0.813}\text{Sr}_{0.187}\text{Cu}(\text{O}, \text{F})_{3-\delta}$ (a) and starting $\text{La}_{6.5}\text{Sr}_{1.5}\text{Cu}_8\text{O}_{19.65}$ (b) phases. In the optical diffraction patterns, suppression of the superstructure with $a_p 2\sqrt{2}$ upon fluorination is shown.

$[\text{Cu}(\text{O},\text{F})_{3-\delta}]$ structure] may be responsible for substantial static displacements (associated with the presence of the B-type cations possessing non-completed coordination spheres) and, as a consequence, can cause local distortions of the CuO_2 layers. This fact as well as the possibility of the partial replacement of oxygen with fluorine in the CuO_2 layers may account for the fact that fluorinated anion-deficient perovskite-like cuprates do not show superconductivity.

4. Incorporation of fluorine atoms into interlayer cavities in the structures of complex cuprates

Fluorination of anion-deficient cuprates is most often accompanied by the formation of compounds with simpler high-symmetry structures, whereas fluorination of complex copper oxides with the filled anion sublattice leads most commonly to structural distortions. The $(\text{M}', \text{M}'', \text{A})_2\text{CuO}_{4-\delta}$ compounds (M' and M'' are rare-earth cations of different radii, A is an alkaline-earth cation) have structures with ordered alternation of the CuO_2 layers and the $(\text{M}, \text{A})_2\text{O}_2$ blocks. These structures contain interlayer cavities accessible to additional anions. These cuprates crystallise in three structural types, *viz.*, T , T' and T^* . In the structures of the T phases [La_2CuO_4 , $\text{La}_{2-x}\text{A}_x\text{CuO}_{4-\delta}$ (A = Sr or Ba), the K_2NiF_4 structural type], the CuO_2 layers alternate with the NaCl-type $[(\text{La}, \text{A})\text{O}][\text{O}(\text{La}, \text{A})]$ blocks (Fig. 16). Rare-earth cuprates having smaller ionic radii ($\text{M} = \text{Pr} - \text{Gd}$) crystallise in the T' type structure. The structures of the T' phases can be represented as the result of alternation of the fluorite-like $(\text{M})(\text{O}_2)(\text{M})$ fragments (see Fig. 2) and the CuO_2 layers. The T^* phases $[(\text{La}, \text{M}, \text{Sr})_2, \text{CuO}_{4-\delta}]$, $\text{M} = \text{Sm} - \text{Er}$] contain both types of blocks, *viz.*, fluorite- and NaCl-like blocks, so that the structures of these phases can be described as the following sequence of layers:



In all three structural types, the cations occupy the same positions, but these structural types differ in the distributions of the anions in the $(\text{M}, \text{A})_2\text{O}_2$ blocks. If it is considered that the cations form a close packed motif, the NaCl-type $[(\text{M}, \text{A})\text{O}][\text{O}(\text{M}, \text{A})]$ block in the T phases is formed by the arrangement of the oxygen atoms in the octahedral cavities of the close packing. In the structures of the T' phases, the fluorite-like $(\text{M})(\text{O}_2)(\text{M})$ block is formed by the arrangement of the oxygen atoms in half of the tetrahedral cavities. Hence, the anion positions in the $(\text{M}, \text{A})_2\text{O}_2$ blocks, which are occupied by the oxygen atoms in the T phase, remain vacant in the T' phase and *vice versa* (see Fig. 16). Additional anions in the structures of this

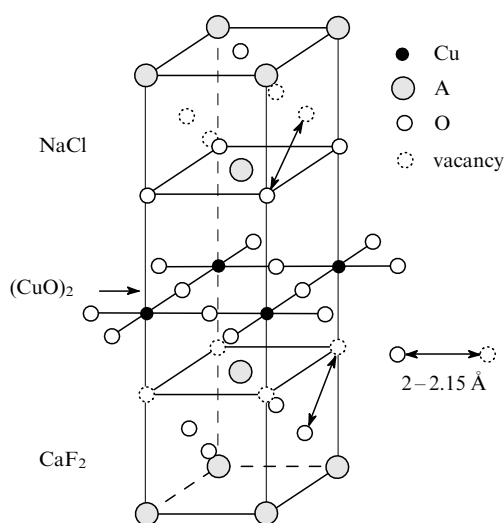
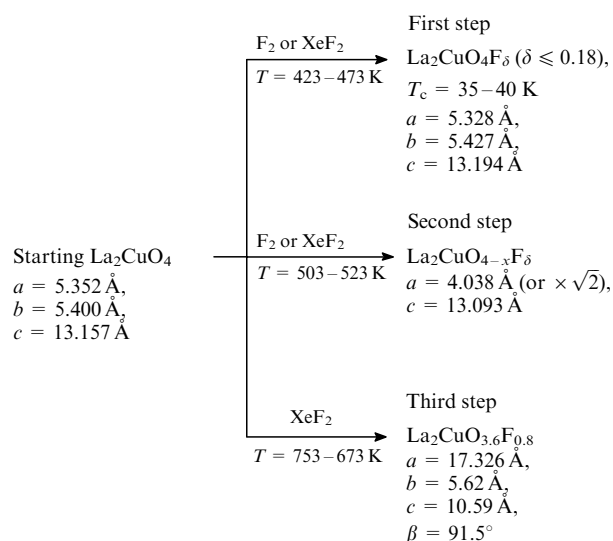


Figure 16. Scheme of formation of the intergrowth structures with alternation of CuO_2 layers and the fluorite- and/or NaCl-type $(\text{M}, \text{A})_2\text{O}_2$ blocks.

type are located in vacant interlayer tetrahedral (in the case of the NaCl-like blocks) or octahedral (in the case of the fluorite-like blocks) cavities. When both types of cavities are simultaneously occupied, the distances between the anions in the $(\text{M}, \text{A})_2\text{O}_2$ block and the anions in the interlayer cavities are no larger than 2–2.15 Å. The arrangement of like-charged ions at such short distances will destabilise the structure and it can be substantially distorted due to Coulombic repulsions between the anions.

Lanthanum cuprate La_2CuO_4 was one of the first compounds that was subjected to fluorination to obtain a superconductor.^{24, 27, 30, 85–87} Fluorination of this cuprate with various agents gave rise to oxyfluorides, which differ in the structure and properties depending on the conditions of thermal treatment. The main steps of the incorporation of fluorine into La_2CuO_4 are shown in Scheme 1.

Scheme 1



The treatment of La_2CuO_4 with fluorine or XeF_2 at a rather low temperature afforded fluorinated lanthanum cuprate with $T_c = 35 - 40$ K. The incorporation of small amounts of fluorine ($\delta \leq 0.18$) into the La_2CuO_4 structure is accompanied by an increase in the degree of orthorhombic distortion of the unit cell and an insignificant increase in the parameter c .²⁷ Neutron diffraction studies of the crystal structures of the starting and fluorinated samples demonstrated that low degrees of fluorination do not cause substantial rearrangements of the initial structure.⁸⁵ Excessive fluorine atoms are located in the interlayer cavities, which are tetrahedrally surrounded by the lanthanum atoms (NaCl-type block). The incorporation of fluorine atoms occurs analogously to that of oxygen atoms⁸⁸ and the degree of orthorhombic distortion, which depends on the amount of hyperstoichiometric anions, appeared to be similar for the oxygen-oxidised and fluorinated samples with similar anionic stoichiometry ($a = 5.332$ Å, $b = 5.423$ Å, $c = 13.222$ Å for $\text{La}_2\text{CuO}_{4.18}$).⁸⁹ Fluorination of the T phases in which lanthanum atoms are partially replaced with alkaline-earth metals gives rise to compounds exhibiting the superconducting properties at small degrees of replacement analogous to the effect of oxygen incorporation. Superconductivity was observed in the fluorinated solid solutions $\text{La}_{2-x}\text{Sr}_x\text{CuO}_4$ ($x < 0.1$, $T_c = 36 - 40$ K)^{85, 90} and $\text{La}_{2-x}\text{Ba}_x\text{CuO}_4$ ($x < 0.15$, $T_c = 32 - 42$ K).^{86, 91} In the case of higher strontium or barium contents, T_c for the initial and fluorinated samples remains identical.

The treatment of La_2CuO_4 with fluorine or XeF_2 at higher temperatures (503–523 K, the second step) gives rise to non-superconducting oxyfluoride with the body-centred tetragonal unit cell, which either corresponds to the K_2NiF_4 subcell⁸⁷ or differs from this subcell only by the parameter a equal to $\sqrt{2}a_{\text{K}_2\text{NiF}_4}$ ($a_{\text{K}_2\text{NiF}_4}$ is the unit cell parameter of K_2NiF_4).⁹² In this step, the unit cell is substantially expanded in the ab plane

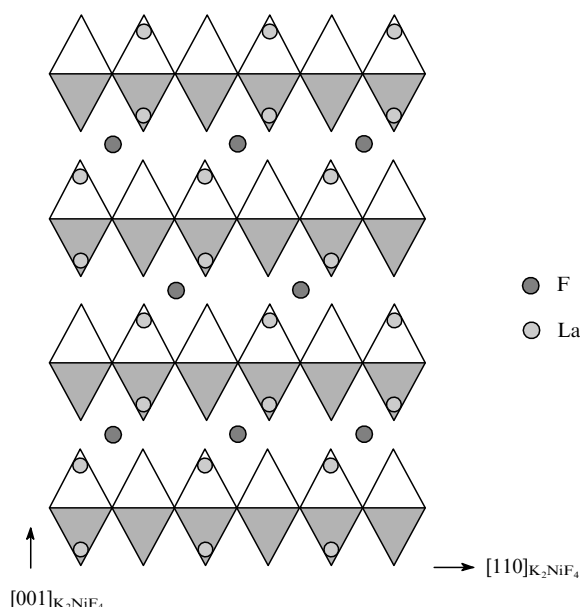


Figure 17. Model of the crystal structure of oxyfluoride formed upon fluorination of La_2CuO_4 at 523 K. The copper atoms are in an octahedral environment.

($a_{\text{K}_2\text{NiF}_4} = a/\sqrt{2} \approx 3.802 \text{ \AA}$ and $a_{\text{K}_2\text{NiF}_4} = 4.038 \text{ \AA}$ for the initial and fluorinated samples, respectively). Electron diffraction studies revealed a superstructure with $a = 2a_{\text{K}_2\text{NiF}_4}$, $c = 2c_{\text{K}_2\text{NiF}_4}$ (see Ref. 87) formed due to the alternation of the vacant and occupied tetrahedral cavities along the $[001]_{\text{K}_2\text{NiF}_4}$ and $[110]_{\text{K}_2\text{NiF}_4}$ directions (Fig. 17). This ordering may also be accompanied by cooperative rotation of the CuO_6 octahedra about the $[110]_{\text{K}_2\text{NiF}_4}$ direction to achieve the maximum distances between the oxygen atoms involved in the axial environment about the copper atoms and the anions in the interlayer cavities.

In the third step, the interaction with XeF_2 proceeds predominantly through a mechanism of anion exchange to give oxyfluoride with composition $\text{La}_2\text{CuO}_{3.6}\text{F}_{0.8}$ containing copper in the oxidation state +2. This compound belongs to the monoclinic system and its unit cell is determined by the following vectors:⁸⁷

$$\begin{aligned} \mathbf{a}_m &= 2(\mathbf{a}_{\text{K}_2\text{NiF}_4} + \mathbf{b}_{\text{K}_2\text{NiF}_4}) + \mathbf{c}_{\text{K}_2\text{NiF}_4}, \\ \mathbf{b}_m &= -\mathbf{a}_{\text{K}_2\text{NiF}_4} + \mathbf{b}_{\text{K}_2\text{NiF}_4}, \\ \mathbf{c}_m &= -\frac{1}{2}(3\mathbf{a}_{\text{K}_2\text{NiF}_4} + 3\mathbf{b}_{\text{K}_2\text{NiF}_4} - \mathbf{c}_{\text{K}_2\text{NiF}_4}), \\ \beta &\approx 91.5^\circ. \end{aligned}$$

The structural model established based on the results of a electron diffraction study and the HRTEM method is shown in Fig. 18. The fluorine atoms occupy 40% of the tetrahedral cavities in an ordered fashion. In this case, the oxygen atoms are partially removed from the LaO layers and a part of the CuO_6 octahedra are transformed into the CuO_5 square pyramids. The remaining octahedra are rotated about the b_m axis in such a way that the distances between the axial oxygen atoms and the fluorine atoms become lower. The blocks in which the tetrahedral positions are occupied and the axial oxygen atoms are removed (fluorite fragments) alternate with the NaCl -type fragments. However, the alternation of these blocks, unlike that observed in the T^* phases, occurs not only along the $[001]_{\text{K}_2\text{NiF}_4}$ direction but also along the $[110]_{\text{K}_2\text{NiF}_4}$ direction.

Lanthanum cuprate La_2CuO_4 can be considered as the first member of the homologous series of cuprates with structures of the Ruddlesden–Popper phases $(\text{M},\text{A})_{n+1}\text{Cu}_n\text{O}_{2n+2+\delta}$ ($\text{M} = \text{REE}$, $\text{A} = \text{Ca}$ or Sr) with $n = 1$. The structure of the

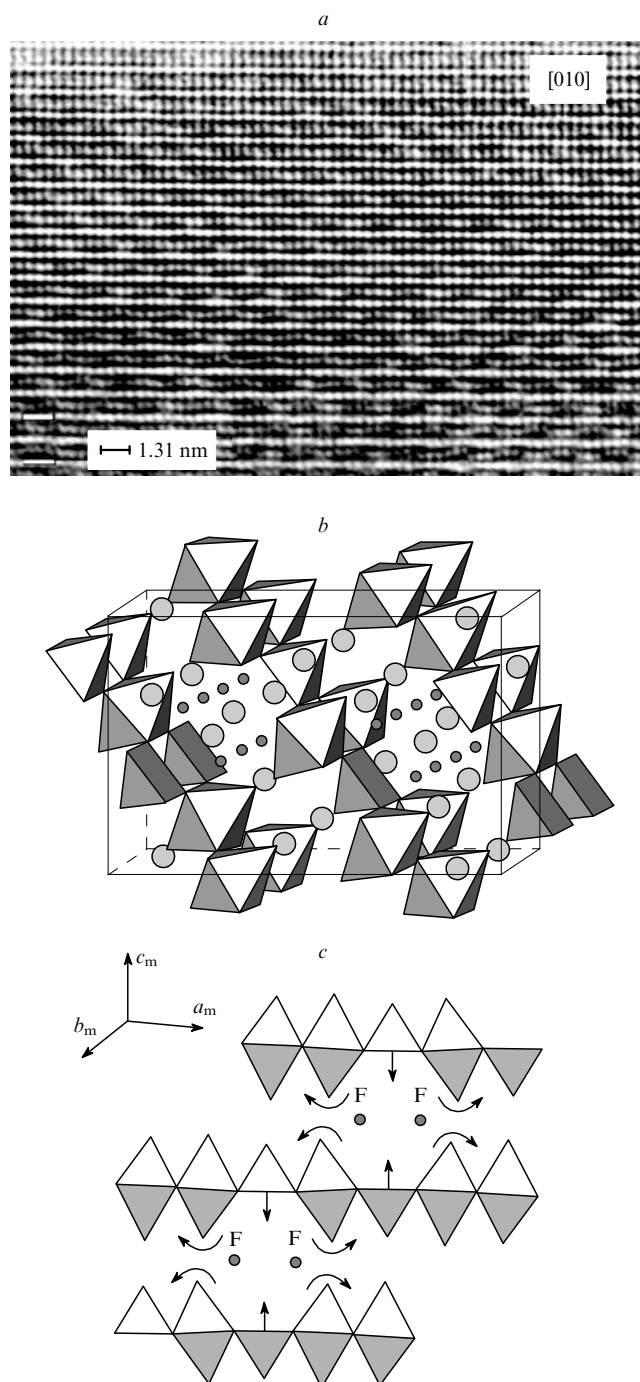
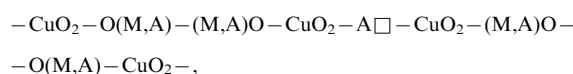


Figure 18. HRTEM images (a), the structural model (the copper atoms are in the octahedra and tetragonal pyramids) (b) and the projection displaying the directions of cooperative atomic displacements in the $\text{La}_2\text{CuO}_{3.6}\text{F}_{0.8}$ phase (c).

homologue with $n = 2$ ($\text{M}_{2-x}\text{A}_{1+x}\text{Cu}_2\text{O}_{6+\delta}$) contains doubled CuO_2 layers separated by $\text{A}\square$ layers:



the cation positions in the $\text{A}\square$ layer can be occupied simultaneously by rare-earth and alkaline-earth atoms as, for example, in the case of $\text{A} = \text{Sr}$ (Fig. 19). In this compound, the copper atoms have a square-pyramidal coordination. This structure, unlike the structure of the preceding member of the homologous series, contains two possible positions suitable for location of additional

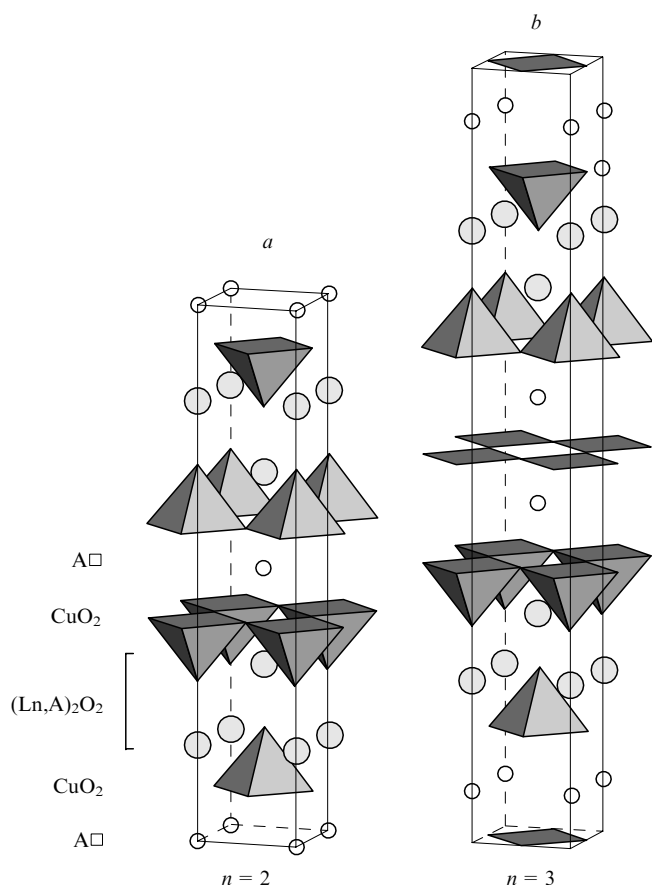


Figure 19. Crystal structures of the members of the homologous Ruddlesden–Popper series with $n = 2$ (a), 3 (b).

anions, *viz.*, in tetrahedral cavities of the $(\text{Ln},\text{A})_2\text{O}_2$ block and in the $\text{A}\square$ layer with completion of the coordination environment about copper to an octahedron.

The behaviour of these compounds upon fluorination differs from that of La_2CuO_4 . The treatment of $\text{La}_{1.9}\text{Sr}_{1.1}\text{Cu}_2\text{O}_{6.05}$ and $\text{La}_{1.9}\text{Ca}_{1.1}\text{Cu}_2\text{O}_{5.95}$ with reagents, such as F_2 , NH_4F or CuF_2 , led initially to an increase in the parameters a and c of the tetragonal unit cell. However, further increase in the degree of fluorination caused the transformation of the Sr-containing sample into the orthorhombic phase accompanied by a decrease in the unit cell parameters in the ab plane and a substantial increase in the parameter c (from 20.048 to 21.68 Å).²⁵ The authors of the cited study²⁵ related the formation of the orthorhombic phase characterised by the larger parameter c (and, correspondingly, by the larger distance between the CuO_2 layers) to the facts that the positions in the $\text{A}\square$ layer are occupied by fluorine atoms and some copper atoms have an octahedral environment. For $\text{La}_{1.9}\text{Ca}_{1.1}\text{Cu}_2\text{O}_{5.95}$, this effect was not observed due, apparently, to the smaller distance between the CuO_2 layers because the calcium atom is smaller than the strontium atom.

Superconducting oxyfluorides of this series with $n = 2, 3$ were synthesised at high pressure. Samples with compositions $\text{Sr}_2\text{CaCu}_2\text{O}_{4.6}\text{F}_2$ and $\text{Sr}_2\text{Ca}_2\text{Cu}_3\text{O}_{6.2}\text{F}_{3.2}$ showed bulk superconductivity ($T_c = 99$ and 111 K, respectively) in spite of the fact that they contained substantial amounts of impurity phases.¹¹ The $\text{Sr}_2\text{NdCu}_2\text{O}_5\text{F}$ compound turned out to be single-phase and did not exhibit superconducting properties because it contained copper in the oxidation state +2. However, the $\text{Sr}_2\text{Nd}_{0.2}\text{Ca}_{0.8}\text{Cu}_2\text{O}_5\text{F}$ solid solution generated upon the partial replacement of neodymium with calcium showed the superconducting transition at 85 K.⁹ It was suggested that the fluorine atoms in all these phases are located in the NaCl-type blocks and are involved in the $(\text{SrF})(\text{FSr})$ or $(\text{SrO}_{0.5}\text{F}_{0.5})(\text{F}_{0.5}\text{O}_{0.5}\text{Sr})$ layers. The crystal

structures of superconducting complex copper oxyhalides belonging to the Ruddlesden–Popper phases have been surveyed in the review.⁹³

Of complex copper oxyfluorides, fluorine derivatives of Nd_2CuO_4 have received the most study. Most of the investigations were devoted to the structures and properties of the $\text{Nd}_2\text{CuO}_{4-x}\text{F}_x$ solid solutions in which the n -type superconductivity with $T_c = 27$ K (at $x = 0.3$) was revealed.³ As mentioned above (see Section III), the partial replacement of oxygen atoms in the fluorite-like Nd_2O_2 blocks with an equivalent amount of fluorine has virtually no effect on the crystal structure of the resulting compound. Fluorine incorporation into the Nd_2CuO_4 structure afforded a new phase with composition $\text{Nd}_2\text{CuO}_3\text{F}_2$.⁹⁴ This compound was found by electron microscopy in samples prepared by fluorination of Nd_2CuO_4 with xenon difluoride at 573–673 K. This phase crystallises in the monoclinic system (the unit cell parameters $a \approx 12.96$, $b \approx 5.5$, $c \approx 5.8$ Å, $\beta \approx 92^\circ$). The model structure of this compound was constructed from images obtained by the HRTEM method. According to this model, a portion of the anions which are located in the positions tetrahedrally coordinated by the neodymium atoms form chains along the c axis alternating with chains of the vacancies along the b direction (Fig. 20). Another portion of anions occupy axial positions in the octahedral environment about the copper atoms. The presence of copper atoms possessing octahedral coordination is responsible for the increase in the parameter c from 12.167 in the starting phase to 12.96 Å in the fluorinated compound. The layers of the $\text{Cu}(\text{O},\text{F})_6$ octahedra are distorted due to the cooperative rotation required for the maximum distance between the anions to be attained.

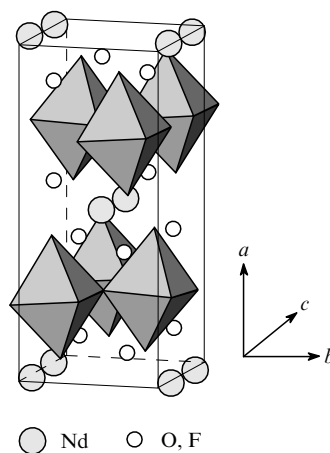


Figure 20. Crystal structure of $\text{Nd}_2\text{CuO}_3\text{F}_2$.

The $\text{Nd}_2\text{CuO}_3\text{F}_2$ compound is structurally similar to $\text{La}_2\text{CuO}_{3.6}\text{F}_{0.8}$. The structures of these compounds are analogous to the structure of the T^* phase and can be considered as intermediate between the structures of the T and T' phases. In both structures, the NaCl- and fluorite-like blocks alternate not only along the c axis of the tetragonal subcell but also in the ab plane. In both cases, the ratios between the parameters of the tetragonal subcells $c/3a \approx 1.08$ are in the T^* -phase stable region ($c/3a \approx 1.15$ for T phases, $c/3a \approx 1.06$ – 1.08 for T^* phases and $c/3a \approx 1.02$ for T' phases⁹⁵).

Apparently, the results of fluorination of the T^* phases depend substantially on their cation composition. The refinement of the crystal structures of $\text{La}_{1.25}\text{Dy}_{0.75}\text{CuO}_{3.75}\text{F}_{0.5}$ (see Ref. 34) and $\text{LaBa}_{0.2}\text{Gd}_{0.8}\text{CuO}_{3.55}\text{F}_{0.8}$,⁹⁶ which were prepared by fluorination of the corresponding cuprates with ZnF_2 and CuF_2 , demonstrated that excessive anions were located in the tetrahedral cavities of the NaCl-type blocks, while the fluorite-like blocks remained unchanged. Repulsions between the anions and/or a

reduction in the formal oxidation state of copper lead to elongation of the equatorial Cu—O distances from 1.933 to 1.942–1.962 Å as well as to a small increase in the parameter c . However, the $\text{LaBa}_{0.2}\text{Gd}_{0.8}\text{CuO}_{3.55}\text{F}_{0.8}$ structure retains tetragonal symmetry, whereas $\text{La}_{1.25}\text{Dy}_{0.75}\text{CuO}_{3.75}\text{F}_{0.5}$ crystallises in the orthorhombic system with the unit cell parameters a and b , which are increased by a factor of $\sqrt{2}$. In both cases, the atoms occupying the axial vertices in the $\text{Cu}(\text{O},\text{F})_5$ pyramids are shifted from the ideal positions in the ab plane due, probably, to their interactions with the anions located in the interlayer cavities.

Samples prepared by fluorination of the T^* phase $\text{LaHo}_{0.75}\text{Sr}_{0.25}\text{CuO}_{3.9}$ with xenon difluoride have complex microstructures, which can be described as narrow extended domains of a phase with high fluorine content (phase I) located in a matrix of the low-fluorinated orthorhombic T^* phase (phase II) (Fig. 21).⁹⁷ The results of the HRTEM study demonstrated that the structure of the fluorite-like blocks in the low-fluorinated phase II remains

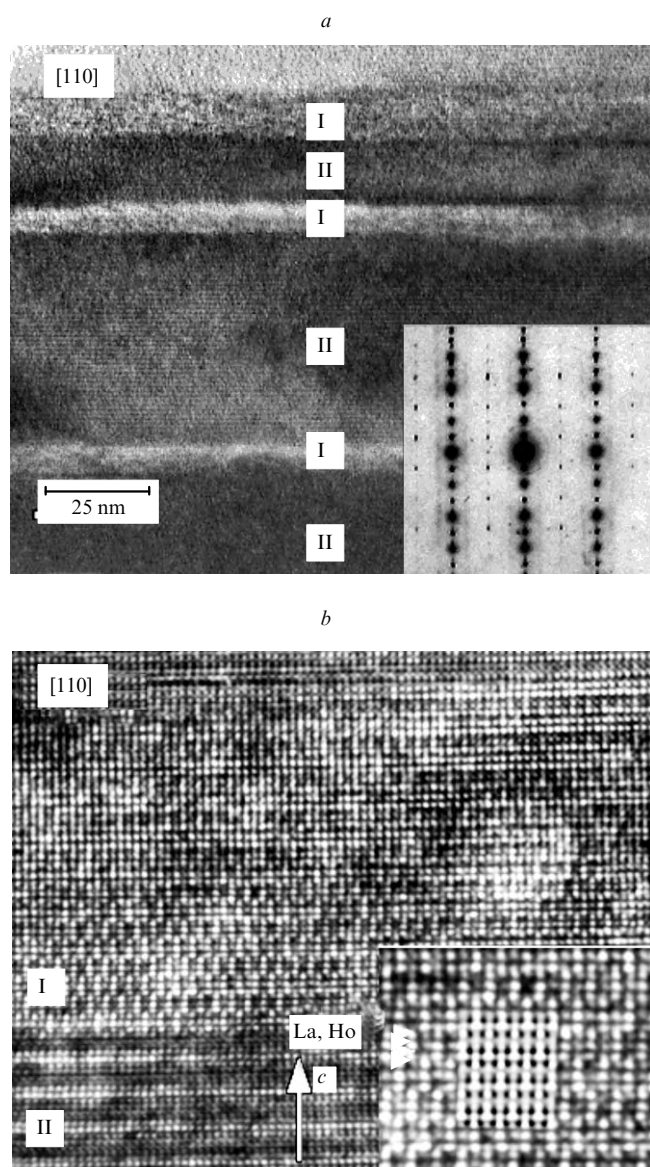


Figure 21. Electron microphotographs of the fluorinated $\text{LaHo}_{0.75}\text{Sr}_{0.25}\text{CuO}_{3.9}$ sample taken at a low magnification (a) and high resolution (b);⁹⁷ (a) the corresponding electron diffraction pattern is shown in the inset; (b) the inset presents an enlarged fragment of the image of phase I, which is superimposed on the theoretical image calculated from the proposed structural model; the $\text{La}_{0.25}\text{Ho}_{0.75}$ layers are indicated by arrows; I and II are phases with different fluorine contents.

unchanged, whereas the NaCl-type blocks acquire a structure similar to that of analogous blocks in $\text{La}_2\text{CuO}_{3.6}\text{F}_{0.8}$. Phase I belongs to the monoclinic system with the unit cell parameters $a_m \approx b_m \approx 5.5 \text{ Å} \approx a_t\sqrt{2}$, $c_m \approx 12.84 \text{ Å} \approx c_t$, $\beta \approx 91.4^\circ$ (the subscripts m and t identify the monoclinic and tetragonal unit cells, respectively). As in the case of the T' phase, an increase in the c_m parameter compared to $c_t = 12.553 \text{ Å}$ is indicative of the incorporation of additional anions into the axial positions of the coordination environment about the copper atoms. The characteristic feature of phase I is the identical distribution of the anions over the tetrahedral and octahedral positions resulting from fluorination of the initially different blocks, viz., the NaCl-type $(\text{La}_{0.75}\text{Sr}_{0.25}\text{O})(\text{OLa}_{0.75}\text{Sr}_{0.25})$ and the CaF_2 -type $(\text{La}_{0.25}\text{Ho}_{0.75})\text{O}_2(\text{La}_{0.25}\text{Ho}_{0.75})$ blocks (see Fig. 21). Consequently, not only the NaCl-type blocks but also the fluorite-like blocks undergo structural changes in the high-fluorinated samples. In the phase I, the vacant and occupied tetrahedral positions alternate in a 'staggered' fashion. The monoclinic distortion of phase I results from displacements of the A cations caused by interactions with the ordered oxygen and fluorine atoms in the tetrahedral cavities.

Hence, the fluorine incorporation upon fluorination of the T , T' and T^* phases has no direct effect on the CuO_2 planes, but these planes may be distorted due to cooperative rotation of the coordination polyhedra of the copper atoms. The $(\text{M},\text{A})_2\text{O}_2$ blocks are subjected to fluorination, the fluorine atoms first occupying the tetrahedral cavities in the NaCl-type blocks, while the fluorite-like blocks retain the initial structure under the same conditions. When two types of the anion positions are simultaneously occupied, these blocks undergo structural rearrangements, which are accompanied by the alternation of the NaCl- and fluorite-type structural fragments in directions perpendicular and parallel to the CuO_2 layers. Hence, the structures of the high-fluorinated compounds are intermediate between the structures of the T and T' phases and are structurally similar to the T^* phases. A substantial increase in the parameter c for the fluorinated T' and T^* phases occurs due to completion of the coordination polyhedron about the copper atom to a tetragonal pyramid or an octahedron.

In the fluorite- or NaCl-type $(\text{M},\text{A})_2\text{O}_2$ blocks in which the A positions are occupied by alkaline-earth and/or rare-earth cations, ionic interactions prevail. Because of this, the bonds in the $(\text{M},\text{A})\text{O}$ layers in the NaCl-type blocks are comparable in strength to the bonds between the adjacent $(\text{M},\text{A})\text{O}$ layers. The structures of Bi-containing layered cuprates $\text{Bi}_2\text{Sr}_2\text{Ca}_{n-1}\text{Cu}_n\text{O}_{2n+4+\delta}$ involve the NaCl-type Bi_2O_2 blocks. Unlike the $(\text{M},\text{A})_2\text{O}_2$ blocks containing isotropic chemical bonds, the BiO and OBi layers in the Bi_2O_2 block are linked only through van der Waals interactions, which is attributed to the crystal-chemical characteristics of the Bi^{3+} cation. Due to this structure of the Bi_2O_2 blocks, various halogen-containing agents (I_2 , Br_2 , HgBr_2 or LiI_3) can be intercalated into Bi-containing cuprates.^{98–102} The iodine atoms intercalated into the Bi2212 and Bi2223 phases form an additional layer between the BiO and OBi layers as a result of which the distance between these layers is increased and the layers are shifted with respect to each other by a vector of the perovskite-like subcell $(1/2, 1/2, 0)$ to form a primitive unit cell. After intercalation, the structural modulations of the BiO layers, which are characteristic of this family of superconductors due to the incommensurability of the Bi_2O_2 blocks and the CuO_2 layers, are retained because interactions between the intercalated atoms and the BiO and OBi layers are weak, the structures of the latter remaining virtually unchanged. In the compounds containing the intercalated F atoms, the Bi—F bond is more ionic than the bonds between the Bi atoms and other halogens and, hence, the results of incorporation of fluorine atoms into the structures of Bi-containing HTSC will be different.

Fluorination of $\text{Bi}_2\text{Sr}_{1.6}\text{La}_{0.4}\text{CuO}_{6.33}$ (Bi2201 phase, $T_c = 27 \text{ K}$) with xenon difluoride led to an increase in the unit cell parameter c and was accompanied by suppression of the

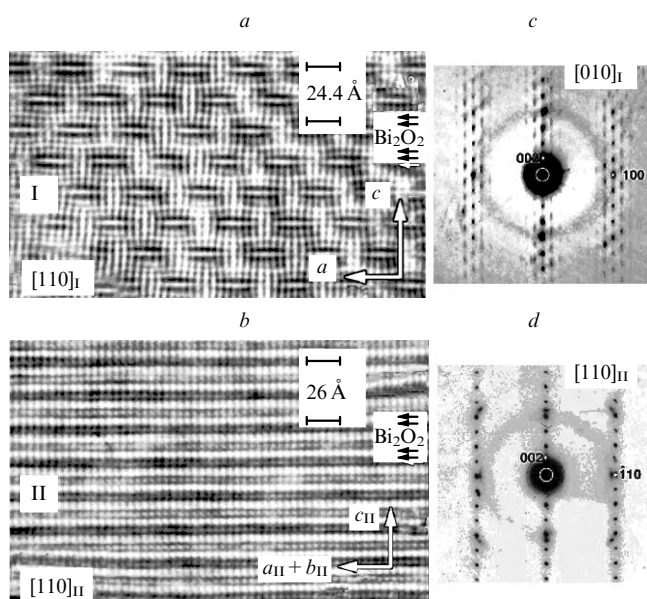


Figure 22. HRTEM images (*a*, *b*) and electron diffraction patterns (*c*, *d*) for the fluorinated Bi2201 phases of low (*a*, *c*) and high (*b*, *d*) fluorine contents.¹⁰³

It can be seen that incommensurate modulations disappear as the degree of fluorination is increased.

superstructure $\sqrt{2}a_p \times \sqrt{2}a_p$ in the *ab* plane and the disappearance of the incommensurate modulations (Fig. 22), *i.e.*, by the formation of a tetragonal primitive unit cell with $a = 3.837$, $c = 26.18$ Å.¹⁰³ Consequently, the incorporated fluorine atoms change the structure of the BiO layers. Excessive anions occupy the cavities of the Bi_2O_2 blocks tetrahedrally coordinated by the Bi atoms so that the Bi_2O_2 blocks are transformed into the $\text{Bi}_2\text{O}_{2-x}\text{F}_{2+x}$ blocks in which the Bi atoms are located in mono-capped square antiprisms to form short bonds with the F atoms and five long bonds with the O atoms (Fig. 23).

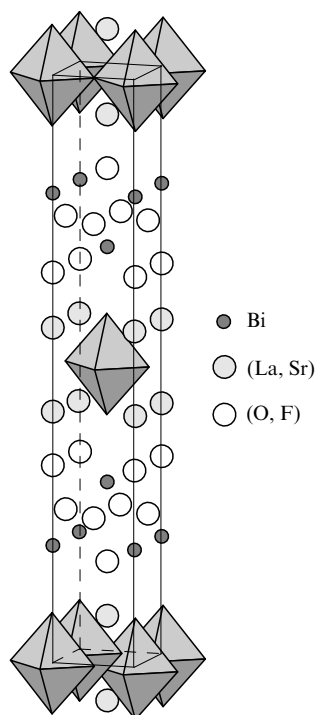


Figure 23. Crystal structure of the fluorinated Bi2201 phase.

Structurally analogous blocks were found in compounds of the homologous series of Aurivillius phases, for example, in $\text{Bi}_2\text{NbO}_5\text{F}$.¹⁰⁴ Comparison of the interlayer distances in the Bi_2O_2 blocks in the Bi2201 phase and in the $\text{Bi}_2\text{O}_2\text{F}_2$ block of the Aurivillius phase accounts for the increase in the unit cell parameter c from 24.35 to 26.18 Å upon fluorination. The distance between two bismuth-containing layers located above and below the interlayer cavities is decreased from 3.18–3.20 Å in the starting Bi2201 phase to 2.49–2.56 Å in the fluorinated Bi2201 phase. This decrease is caused by Coulombic interactions between the anions in the interlayer cavities and the Bi^{3+} cations (Fig. 24). It should be noted that the oxygen atoms in the BiO layers experience repulsions from the interlayer anions. Hence, the BiO layers in the structure of the starting Bi2201 phase are nearly planar and the distance between the bismuth- and oxygen-containing sublayers of this layer along the c axis is no higher than 0.24–0.26 Å, whereas this distance in Aurivillius phases increases to 0.92–1.07 Å. This leads to splitting of the BiO layer into two layers one of which consists of the bismuth atoms and the other is composed of the oxygen atoms. In spite of shortening of the distance between the layers containing the bismuth cations, the total increase in the size of the $\text{Bi}_2\text{O}_2\text{F}_2$ block reaches 0.7–1.0 Å, which must lead to an increase in the parameter c by 1.4–2.0 Å. An increase in the coordination number of bismuth in a fluorinated phase also leads to elongation of the Bi–O bond and an increase in the size of the block in the *ab* plane. As a result, the commensurability between the $\text{Bi}_2\text{O}_2\text{F}_2$ blocks and the CuO_2 layers is achieved thus diminishing modulations. It should be noted that the structure of the fluorinated Bi2201 phase is a hybrid combining the Bi-containing $\text{Bi}_2\text{O}_{2-x}\text{F}_{2+x}$ blocks (like in Aurivillius phases) and the perovskite-like $\text{A}_{2n}\text{Ca}_{n-1}\text{Cu}_n\text{O}_{2n+2}$ blocks ($n = 1$). Such phases belong to a new homologous series $\text{Bi}_2\text{A}_2\text{Ca}_{n-1}\text{Cu}_n(\text{O},\text{F})_{2n+6}$. The third representative of this series, *viz.*, $\text{Bi}_2\text{Sr}_2\text{Ca}_2\text{Cu}_3\text{O}_8\text{F}_4$, was prepared by treating the Bi2223 phase with $\text{NH}_4\text{F} \cdot \text{HF}$ (see Ref. 33) although the superstructure $\sqrt{2}a_p \times \sqrt{2}a_p$ is retained. The distance between the bismuth- and strontium-containing layers is increased from 2.7 Å in the starting phase to 3.6 Å in the fluorinated phase, whereas the distance between two adjacent bismuth-containing layers is decreased from 3.2 to 2.5 Å in the fluorinated phase. In the plane of the layer, the Bi–Bi distances are also elongated from 3.53 Å in the starting phase to 3.76 Å in the fluorinated phase.

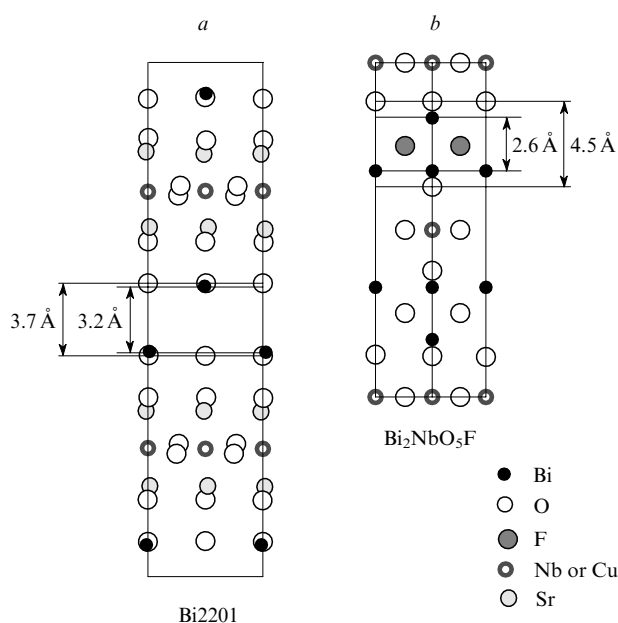


Figure 24. Crystal structures of the Bi2201 phase (*a*) and the Aurivillius phase $\text{Bi}_2\text{NbO}_5\text{F}$ (*b*).

Fluorination of the Bi2201 and Bi2223 phases led to degradation of their superconducting properties. The $\text{Bi}_2\text{Sr}_{1.6}\text{Ca}_{0.4}\text{CuO}_{6.33}$ compound ($T_c = 27$ K) lost superconductivity upon fluorination. In the Bi2223 phase (which is initially characterised by $T_c = 105$ K), the volume of the superconducting phase decreased and a second superconducting transition with $T_c = 75$ K was observed.

The advantage of the fluorinated Bi2201 phase over the starting compound in which the CuO_2 layers are substantially distorted is the absence of incommensurate modulations. Apparently, attainment of the optimum ratio between oxygen and fluorine with retention of these layers will allow one to prepare superconducting compounds based on oxyfluorides of a new homologous family.

V. Conclusion

Fluorination of complex cuprates can be used for the preparation of new compounds with structures necessary for superconducting properties to be manifested. In addition, fluorination of these compounds can be employed for attaining the required concentration of carriers (electrons or holes) in the conduction band. The character of the changes of the crystal structure upon fluorination is determined by the structural features of the starting compound and the amount of excessive anions. The following regularities can be noted:

- the replacement of oxygen atoms with an equivalent amount of fluorine atoms causes only slight changes to the unit-cell dimensions associated with a small difference in the ionic radii of O^{2-} and F^- and with elongation of the equatorial $\text{Cu}-\text{O}_{\text{eq}}$ bonds due to a decrease in the oxidation state of copper;

- the incorporation of excessive fluorine atoms and completion of the coordination polyhedron about the Cu^{2+} cations to an octahedron leads to substantial elongation of the axial $\text{Cu}-\text{O}$ bonds accompanied by an increase in the distances between the $\text{Cu}(\text{O},\text{F})_2$ and AO layers;

- the filling of anion vacancies in the structure with fluorine atoms diminishes structural distortions caused by ordering of the oxygen atoms and anion vacancies;

- location of fluorine atoms in the interlayer cavities induces rearrangement of the crystal structure to reduce Coulombic repulsions between the anions in the interlayer cavities and anions in the adjacent layers.

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Thermodynamic properties of halide compounds of tetravalent transactinides in solutions and in the gaseous and crystalline states[†]

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Abstract. Experimental and theoretical data on the structure and properties of compounds of tetravalent transactinides (TAn^{IV}) Rf ($Z = 104$), Db ($Z = 105$), Sg ($Z = 106$), Bh ($Z = 107$), Hs ($Z = 108$), Mt ($Z = 109$) and ^{110}TAn ($Z = 110$) are described systematically. The problem of disposition of the transactinide elements in the Periodic system is discussed and the properties of the $6d$ -, $5d$ -, $4d$ -, $3d$ - and $5f$ -elements are compared. Regularities of changes in the thermodynamic characteristics of TAn^{IV} compounds *versus* the atomic number, $Z(TAn)$, are elucidated. Peculiarities of changes in thermodynamic properties upon the formation of nitrate, fluoride and chloride TAn^{IV} complexes in solution are discussed. The bibliography includes 140 references.

I. Introduction

Theoretical investigations into the chemical properties of the heavy elements, *viz.*, actinides (An) and transactinides (TAn)^{1–10} involve assessment of the influence of relativistic effects (RE) on these properties. One of the major propositions of the relativity theory is that the velocity of a particle cannot exceed the velocity of light, as follows from the relativistic mass equation:

$$m = \frac{m_0}{\sqrt{1 - (v/c)^2}},$$

where m is the mass of the moving particle, m_0 is the mass of the particle at rest, v is the velocity of the particle and c is the velocity of light.

Since the mass appears in the denominator of the expression for the Bohr radius (a_0), the relativistic mean radius is smaller than the nonrelativistic radius:

$$a_0 = \frac{h^2}{\pi m Z^2 e^2},$$

where h is the Planck constant, Z is the charge of the atom and e is the charge of the electron.

There are three types of possible influence of RE on the electron shells of atoms.

1. Contraction and, hence, stabilisation of the s -, $p_{1/2}$ - and $p_{3/2}$ -shells. The s - and $p_{1/2}$ -shells are contracted to nearly the same extent while the $p_{3/2}$ -shells are much less contracted.

2. Expansion of the f - and d -shells. The s - and $p_{1/2}$ -electrons screen nuclear attraction more effectively than the f - and d -electrons which experience weaker nuclear attraction and the corresponding orbitals become more diffuse and energetically destabilised.

3. Spin–orbit splitting, which increases as Z increases.

In addition to RE, the s -, p -, d - and f -electrons are also affected by nonrelativistic shell effects. It is appropriate to consider three types of the influence of RE on the physicochemical properties of heavy elements.

1. Relativistic effects completely determine a particular property and regular trends of its changes along the period and down the group of the Periodic system.

2. Relativistic effects make a particular property more pronounced, but the regularities of its changes are controlled by nonrelativistic shell effects.

3. Relativistic and nonrelativistic shell effects act in opposite directions.

On going from the $3d$ -elements to the $4d$ -, $5d$ - and $6d$ -elements the atomic radii increase and the d - and s -orbitals become more diffuse due to nonrelativistic shell effects. Relativistic effects cause destabilisation of the d -orbitals and stabilisation of the s -orbitals. Thus, the RE and the shell effects exhibit a synergistic effect in the case of d -orbitals and an antagonistic effect in the case of s -AOs ($4s$, $5s$, $6s$, $7s$).

On going from the $3d$ -elements to the $4d$ -elements relativistic effects cause greater stabilisation of the $5s$ -electrons compared to the $4s$ -electrons. However, if we go from the $4d$ -elements to the $5d$ -elements, the effect of lanthanide contraction, which additionally stabilises the $6s$ -electrons, is superimposed on relativistic stabilisation of the $5s$ - and $6s$ -electrons. Assuming that relativistic stabilisation of the valence s -electrons dominates over the destabilising shell effects, one should expect a regular increase in the ionisation potentials (IPs) down the groups Ti–Zr–Hf,

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Cu–Ag–Au, *etc.* However, the IP values change irregularly, which reflects a complex scheme of compensation effects.

For instance, on going from the 3*d*-elements to the 4*d*-elements stronger relativistic stabilisation of the 5*s*-electrons compared to 4*s*-electrons causes a decrease rather than the expected increase in the IPs of all elements except Zr and Mo. It is impossible to differentiate the influence of the shell and relativistic effects, lanthanide contraction, *etc.*, even in the simplest case when analysing the properties of free atoms. Moreover, the contributions of these effects to the chemical properties of compounds cannot also be differentiated. This can be done only theoretically by performing calculations without and with inclusion of RE. However, calculations without inclusion of RE correspond to hypothetical systems rather than real atoms and molecules; therefore, only the experimental data can serve as a criterion for the significance of the influence of RE on the properties of heavy elements.

The actinides ($Z = 89–103$) precede the transactinide elements ($Z \geq 104$). The influence of RE on the properties of actinides, lanthanides (Ln) and transactinides has been analysed.^{1–6} Important manifestations of RE in actinides include high oxidation states of U, Np, Pu and Am and the valence of 4 or 5 in the metallic state of early actinides, which is atypical of lanthanides.

Mention was also made¹ that, despite the great importance of the contribution of RE to the properties of heavy elements, it should not be overestimated. There are numerous examples of situations where, contrary to expectations, relativistic effects do not manifest themselves in the properties of An. Of particular importance is the analysis of the influence of RE on the properties of heavy An ($Z = 98–103$) which precede the transactinides ($Z \geq 104$).

For instance, relativistic destabilisation of the 5*f*-electrons increases with $Z(\text{An})$. At first glance, this should lead to stabilisation of high oxidation states of not only the early, but also late actinides. However, the opposite effect, that is, stabilisation of the divalent state of late actinides was established experimentally. Therefore, the effect of actinide contraction appears to be much stronger than relativistic destabilisation of the 5*f*-electrons for An with $Z > 96$.

Yet another example, which has been analysed in detail⁴ using the published data, is provided by the correlations between changes in the sublimation enthalpies, $\Delta_s H^\circ$, of lanthanides and actinides and their valences V in the metallic state. Would RE affect the sublimation enthalpy, one should expect $V_{\text{An}} > V_{\text{Ln}}$ throughout the An and Ln series. However, experiments with the late An and Ln revealed another regularity, namely, $V_{\text{Ln}} > V_{\text{An}}$, which contradicts the assumption that RE have a crucial effect on the properties of the late An from Cf ($Z = 98$) to No ($Z = 102$).

Desclaux and Fricke hypothesised⁷ that strong RE will violate the logic of the Periodic system. According to calculations,⁷ the Lr atom has the $5f^{14} 7s^2 7p_{1/2} ({}^2P_{1/2}^0)$ ground-state electron configuration due to relativistic stabilisation of the $7p_{1/2}$ -electron, which means that Lr should be considered as an analogue of the Ga rather than Lu subgroup elements. Probably, calculations⁷ overestimated the influence of RE since this idea was not supported experimentally. It should be noted that the idea of relativistic stabilisation of the $7p_{1/2}$ -electron seems to be rejected. In the studies cited in review⁴ Lr was considered as an analogue of Lu and characterised by a $\Delta_s H^\circ(\text{Lr})$ value of ≈ 4 eV, which is close to the $\Delta_s H^\circ$ for Sc, Y, La, Gd, Lu, Ac and Cm, rather than ~ 2 eV for In, Ga and Tl. All estimates of the thermodynamic properties made for Lr^{III} aqua ions and for solid halides, oxides and sulfides reported in the chemical literature are close to corresponding values for Cm compounds.

According to Pyykkö's hypothesis,⁸ the most important chemical anomalies in the second half of the Periodic system are due to RE. This has been repeatedly exemplified using the difference between the chemical properties of Ag and Au, which is due

to the so-called 'relativistic maximum for gold'. However, this interpretation does not take into account specific features of the electronic structure of Ag atom (see Refs 9 and 10). Among the 3*d*-, 4*d*- and 5*d*-elements (a total of 27 elements from Sc to Au), the Ag atom has the most stable *d*-electrons: the excitation energy of the 4*d*-electron from the $\text{Ag}(4d^{10}5s)$ electron configuration is higher than for any other *d*-elements. It is the local nonrelativistic shell effect for Ag that is to a great extent responsible for distinctions between the chemical properties of Ag and Au.

Experimental data^{11–20} on the chemistry of rutherfordium (Rf), dubnium (Db), seaborgium (Sg), bohrium (Bh) and hassium (Hs) allow some generalisations and predictions. However, no measurements of the properties of TAn, which could be unambiguously interpreted as a manifestation of RE, have been reported so far.⁹ It was mentioned^{8,9,21} that interpretation of the properties of TAn required a weighed analysis of the role played by relativistic and nonrelativistic effects.

Manifestation of the spin–orbit RE can be experimentally confirmed in studies of the spectral and magnetic properties, which depend on the spin–orbit splitting energy and on the fine structure of energy levels. However, these investigations are still a long way in the future. Currently, the main avenues of research into the properties of TAn involve studies of the gas-state behaviour of TAn (first of all, volatility measurements of halides and oxides^{11,14,17}) and of the complexation of TAn in solutions.^{12,15,16,18,19}

Flerov and Zvara (Joint Institute of Nuclear Research, Dubna, Russian Federation) laid the foundation for a general strategy of studying the properties of TAn, which involves comparison of the properties of the elements in higher oxidation states in the groups Rf–Hf–Zr, Db–Ta–Nb, Sg–W–Mo, Bh–Re–Tc and Hs–Os–Ru. Currently, there are three points of view on the disposition of TAn in the Periodic table and on their relation to the 4*d*-, 5*d*- and 5*f*-elements.

1. Relativistic effects cause an inversion of the trends of changes in the properties^{14,15,19} on going from the 5*d*-elements to the 6*d*-elements, so that the properties are changed in the order 4*d*–6*d*–5*d*. Therefore the chemical properties of TAn cannot be extrapolated within particular groups. For Group IV elements, this conclusion was based on the results of quantum-chemical calculations of the effective charges q on the M atoms in gaseous molecules MCl_4 , which were found to be +1.18, +1.04 and +1.07 for Zr, Hf and Rf, respectively. Nonmonotonic change in the charges $q(\text{Zr}) > q(\text{Rf}) > q(\text{Hf})$ was used to explain the processes occurring in solutions (complexation,^{15,16} hydrolysis¹⁹) and in the crystalline state (sublimation enthalpy¹⁴).

2. Regularities typical of the *d*-elements are logically extended to the transactinides, *i.e.*, the passage 4*d*–5*d*–6*d* occurs without inversion of properties.¹⁷

3. The chemical properties of TAn are similar to those of the preceding actinide elements (Rf–Th).¹²

In this review, we analysed the thermodynamic properties of the TAn^{IV} compounds in the gas phase, aqueous solutions and in the crystalline state and compared them with the properties of compounds of the 3*d*-, 4*d*-, 5*d*- and 5*f*-elements. The subject of our study were the chlorides and bromides which are known to exist for all the TAn^{IV} , An^{IV} and *d*-transition elements M^{IV} .

When comparing the properties of TAn with those of (i) their *d*-analogues within the groups of the Periodic table and (ii) the corresponding An (Rf–Zr–Hf–Th; Db–Nb–Ta–Pa, *etc.*), researchers have to return to studying the properties of analogous compounds, since only the results obtained under the same conditions should be compared. Sometimes, the results of recent experiments with the 4*d*-, 5*d*- and 5*f*-elements are inconsistent with earlier results even at qualitative level. To appreciate the reasons for this inconsistency, in this review we considered the results of both recent (1990–2002) and earlier (1960–1975) experimental studies.

II. Structural properties: covalent and ionic radii and interatomic distances

Bokii²² pointed out that in the molecules of the A_2MX_6 ($A = K, Rb, Cs, X = Cl, Br$) compounds, e.g., K_2PtCl_6 , the measured r_{Pt-Cl} distance (2.34 Å) differs from the sum of the ionic radii of Cl^- and Pt^{4+} (1.81 Å + 0.62 Å = 2.43 Å). This allowed him to suggest that the $M-X$ bonds in these compounds are covalent rather than ionic and therefore the r_{M-X} distances cannot be calculated using the r_{ion} values. More recently,²³ the covalent radii, r_{cov} , along with the r_{ion} values were included in the set of commonly used structural parameters of the $4d$ - and $5d$ -elements.

It was found that the measured r_{M-X} distances in compounds of the $4d$ - and $5d$ -elements are linearly related to the maximum electron density radii, $r_{max}(nd)$, of the $4d$ - and $5d$ -AOs in the ground-state electron configurations of gaseous atoms

$$r_{M-X} = ar_{max}(nd) + c, \quad (1)$$

where a and c are constants and $n = 4, 5$.

Thus, if we know the $r_{max}(nd)$ values for all the $4d$ -, $5d$ - and $6d$ -elements and the r_{M-X} distances in compounds of the $4d$ - and $5d$ -elements, it is possible to estimate the corresponding distances in compounds of the $6d$ -elements. The $r_{max}(nd)$ values for the atoms of the $4d$ -, $5d$ - and $6d$ -elements were calculated using the relativistic Dirac–Fock approach.²⁴ The r_{M-Cl} values in gaseous MCl_4 ($M = Ti, V, Zr, Hf, Mo$ and W) molecules and in crystalline A_2MCl_6 ($A = K, Rb$ and $Cs; M = Ti, Zr, Mo, Tc, Pd, Hf, W, Re, Ir, Os$ and Pt) salts were measured.^{25–38} The r_{M-X} distances in compounds of the $4d$ - and $5d$ -elements were measured^{25–38} while the $r_{max}(nd)$ distances in the atoms of the $4d$ -, $5d$ -, $6d$ -elements, averaged over the degree of degeneracy of quantum numbers $j = 1 \pm 0.5$, were calculated.²⁴ Formula (1) was used to estimate the structural parameters of TAn^{IV} compounds (see Refs 4 and 21), such as r_{M-X} and $r_{cov} = r_{M-X} - r_X$ ($X = Cl, r_{Cl} = 0.99$ Å; $X = Br, r_{Br} = 1.14$ Å).

The structural data for the TAn^{IV} compounds listed in Table 1 are the r_{cov} (CN = 4) and r_{cov} (CN = 6) values, the r_{M-Cl} and r_{M-Br} values for gaseous and crystalline tetrahalides, the r_{M-Cl} values for gaseous MCl_6^{2-} anions and the lattice constants a for A_2TAnCl_6 ($A = K, Rb, Cs$) compounds.

Though the use of the r_{ion} parameters for evaluation of the $Pt-Cl$ distance in the $PtCl_6^{2-}$ anion overestimates this value by 0.09 Å (see Ref. 22), the ionic radii of the $3d$ -, $4d$ - and $5d$ -elements are listed in all crystallochemical tables, since for a particular

oxidation state and CN value they determine both the horizontal and vertical trends of changes in the structural properties. The ionic radius of Rf^{IV} was first calculated three decades ago,³⁹ more recently, this value was refined.^{40,41} For CN = 6, the estimates of $r_{ion}(Rf^{IV})$ are 0.74 (see Ref. 41), 0.75 (see Ref. 39) and 0.79 Å (see Ref. 40).

The $r_{ion}(TAn^{IV})$ values can also be estimated by extrapolating the ionic radii of the early analogues of the $4d$ -, $5d$ - and $5f$ -elements. On the one hand, the $r(M^{IV})$ values for transactinides were evaluated²¹ using the $r_{ion}(M^{IV})$ ⁴² parameters of the $4d$ - and $5d$ -elements and the calculated r_{cov} values of the $4d$ -, $5d$ - and $6d$ -elements. The estimate of $r_{ion}(Rf^{IV})$ was found to be 0.78 Å (see Table 1). On the other hand, the $r(TAn^{IV})$ parameters were evaluated using the results obtained for An . Tetravalent transactinide compounds ($Z = 104–110$) extend the series of An^{IV} compounds, which were synthesised for all actinides from Th ($Z = 90$) to Es ($Z = 99$). The ionic radii, $r_{ion}(An^{IV})$, for CN = 6 and 8 were also reported (see Ref. 43). For CN = 6, they decrease on going from Th^{IV} ($r_{ion} = 0.932$ Å) to Es^{IV} ($r_{ion} = 0.812$ Å) following a power dependence on Z . This allowed one to estimate the $r_{ion}(Rf^{IV})$ parameter, which was found to be 0.75 Å. Thus, the former value (0.78 Å) reflects the covalent character of bonding, typical of compounds of the d -elements, while the latter value (0.75 Å) reflects more ionic character of bonding, characteristic of actinides. This points to dual properties of TAn that are similar to both the $4d$ - and $5d$ -elements and the actinides. For CN = 8, the calculated $r_{ion}(Rf^{IV})$ value is 0.836 Å.²¹

Not all crystal MX_4 compounds of the $4d$ - and $5d$ -elements are isostructural,^{25–38} but for all of them the CN equals 6 rather than 4. As a rule, typical of these compounds is a distorted octahedral coordination of the M atom and the presence of both bridging and terminal X atoms. For $ZrCl_4$, the r_{Zr-Cl} distances vary between 2.307 and 2.655 Å (see Ref. 44). It is believed^{4,21} that in the crystalline tetrahalides of the $6d$ -elements the CN also equals 6. The averaged r_{M-X} distances in the crystalline (c) MX_4 ($M = Zr, Hf, Nb, Ta, Mo, W, Tc, Re$ and Os) compounds are linearly related to the $r_{max}(nd)$ values. This allowed estimation of the r_{M-X} distances in halide compounds of TAn based on the known²⁴ $r_{max}(6d)$ values (see Table 1). For both the MCl_6^{2-} anions in the gas (g) phase and $MCl_4(c)$ chlorides the CN is 6; however, unlike the crystalline chlorides, the anions contain only terminal bonds, which could be the reason for the small difference between the r_{M-Cl} distances.

Table 1. Maximum electron density radii $r_{max}(6d)$, covalent (r_{cov}) and ionic (r_{ion}) radii of TAn^{IV} for CN = 4 and CN = 6 and distances r_{M-X} in gaseous MX_4 molecules and MX_6^{2-} anions and in crystalline MCl_4 compounds (see Ref. 4). Lattice constants a of compounds A_2MCl_6 ($A = K, Rb, Cs$). All values are given in Å.

Structural parameters	Transactinides (M)						
	Rf	Db	Sg	Bh	Hs	Mt	¹¹⁰ TAn
$r_{max}(6d)$ (see ^a)	1.0417	0.976	0.924	0.881	0.846	0.814	0.786
r_{cov} (CN = 4)	1.427	1.389	1.359	1.334	1.314	1.296	1.279
r_{cov} (CN = 6)	1.551	1.514	1.486	1.462	1.442	1.424	1.409
r_{ion} (CN = 6)	0.78 (see ^b)	0.76	0.73	0.72	0.70	0.69	0.68
	0.74 (see ^c)	—	—	—	—	—	—
	0.75 (see ^d)	—	—	—	—	—	—
	0.79 (see ^e)	—	—	—	—	—	—
r_{M-Cl} , (MCl_4 , g)	2.417	2.379	2.349	2.324	2.304	2.286	2.269
r_{M-Cl} , (MCl_6^{2-} , g)	2.541	2.504	2.476	2.452	2.432	2.414	2.399
r_{M-Cl} , (MCl_4 , c)	2.556	2.532	2.507	2.465	2.439	2.414	2.372
r_{M-Br} , (MBr_4 , g)	2.567	2.529	2.499	2.474	2.454	2.436	2.419
r_{M-Br} , (MBr_6^{2-} , g)	2.691	2.654	2.626	2.602	2.582	2.564	2.549
$a(K_2MCl_6)$ ^f	10.09	9.99	9.92	9.86	9.82	9.80	9.79
$a(Rb_2MCl_6)$ ^f	10.19	10.11	10.05	10.04	9.99	9.99	9.99
$a(Cs_2MCl_6)$ ^f	10.40	10.35	10.31	10.30	10.26	10.26	10.26

^a Data taken from Ref. 24. ^b Data taken from Refs 4 and 21. ^c Data taken from Ref. 41. ^d Data taken from Ref. 39 and calculated by the author of this review. ^e Data taken from Ref. 40. ^f Calculated by the author of this review.

III. Standard formation enthalpies of gaseous and crystalline tetrahalides

Using the published thermodynamic^{45–66} and structural data^{25–38, 67–76} for tetrahalides of the 3*d*-, 4*d*-, 5*d*- and 5*f*-elements in the gas phase and in the crystalline state, we found some common parameters that were used for calculations of the standard formation enthalpies, $\Delta_f H^\circ(\text{MX}_4, \text{g})$, of the MX_4 compounds of all elements including TAn (see Ref. 67) and for prediction of the $\Delta_f H^\circ(\text{MX}_4, \text{g})$ values from the following equation

$$\Delta_f H^\circ(\text{MX}_4, \text{g}) = \Delta_s H^\circ(\text{M}) + 4\Delta_f H^\circ(\text{X}, \text{g}) - \left[a - \frac{b}{r(\text{M}-\text{X})} \right], \quad (2)$$

where $\Delta_s H^\circ(\text{M})$ is the standard sublimation enthalpy of M, $\Delta_f H^\circ(\text{X}, \text{g})$ is the standard formation enthalpy of gaseous atoms X, $a - b/r(\text{M}-\text{X})$ is the energy of all bonds, $D(\text{MX}_4, \text{g})$, in gaseous MX_4 molecule and a and b are constants. This approximation was used for calculating the thermodynamic properties of the An and Ln compounds (including aqua ions) and their redox potentials.^{45–48, 53, 59, 60, 67} Using the measured $\Delta_f H^\circ(\text{MCl}_4, \text{g})$ values (M = Ti, V, Cr, Zr, Nb, Mo, Ru, Hf, Ta, W and Os),^{30, 49–55} the a and b coefficients were determined and the $D(\text{MX}_4, \text{g})$ and $\Delta_f H^\circ(\text{MCl}_4, \text{g})$ parameters were calculated for all TAn and for Rh, Ir, Pd and Pt. The $\Delta_f H^\circ(\text{AnCl}_4, \text{g})$ values for An = Th, U and Pu were measured^{58, 61, 63, 64} while those for Am, Cm, Bk, Cf, Es were estimated.⁴⁸ The $\Delta_f H^\circ(\text{MCl}_4, \text{g})$ parameters for TAn, calculated by the author of this review, are listed in Table 2. In Fig. 1 we compare the standard formation enthalpies of gaseous tetrachlorides of the 4*d*-, 5*d*-, 6*d*- and 5*f*-elements in graphical form.

As can be seen in Fig. 1, tetrachlorides of transactinide elements lose their thermodynamic stability as the number of antibonding electrons increases from RfCl_4 to the ^{110}TAn tetrachloride. The same trend is also observed for tetrachlorides of the 4*d*- and 5*d*-elements, namely, RuCl_4 and OsCl_4 have the highest (largest positive) formation enthalpies. A decrease in the thermodynamic stability along the TAn series was also predicted for gaseous tetrabromides. Gaseous tetrahalides of Group IV–VIII elements become thermodynamically more stable on going from the light to heavy elements; the stability sequence is $4d < 5d < 6d$, $4d \approx 5d < 6d$ and $4d > 6d > 5d$.

Theoretical aspects of comparison of the 5*f*- and 6*d*-elements have been studied for long. Zachariasen⁵⁷ proposed a thoride

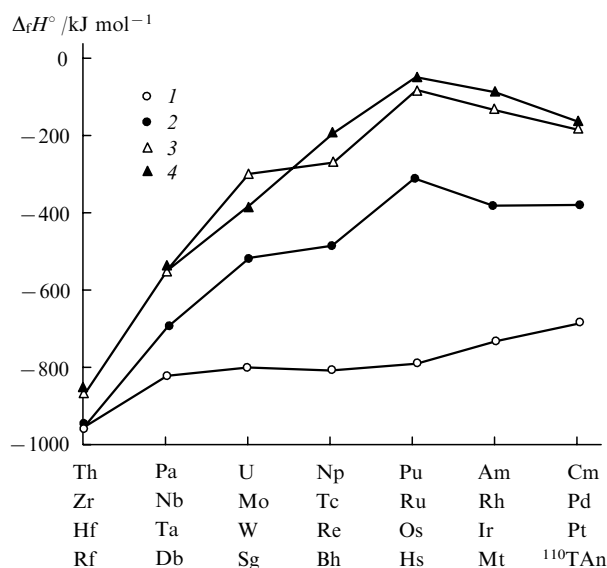


Figure 1. Comparison of $\Delta_f H^\circ(\text{MCl}_4, \text{g})$ values for actinides (1) and for the 6*d*- (2), 5*d*- (3) and 4*d*-elements (4).

theory which treated the actinides as typical 6*d*-metals. This theory was repeatedly criticised; however, it contains a grain of truth, namely, the proposition that particular chemical properties of compounds of the 5*f*-elements are similar to those of the 6*d*-elements. This also still holds.^{12, 18} In Fig. 2, we compare the bond energies, $D(\text{MCl}_4, \text{g})$, of gaseous tetrachlorides of the 4*d*-, 5*d*- and 6*d*-elements and of the actinides. Again, the $D(\text{MCl}_4, \text{g})$ values for gaseous MCl_4 (M = Zr, Nb, Mo, Ru, Hf, Ta, W, Os) molecules and the $D(\text{AnCl}_4, \text{g})$ parameters for An = Th, U and Pu were calculated using Eqn (2) in which all the values, except D , viz., $\Delta_f H^\circ(\text{MX}_4, \text{g})$, $\Delta_s H^\circ(\text{M})$ and $4\Delta_f H^\circ(\text{X}, \text{g})$ were obtained experimentally. Therefore, the D values for these compounds can be considered experimental. The bond energies of compounds for which no experimental data are available (TAn; Rh, Ir; Pd, Pt and An = Pa, Np, Am, Cm) were calculated by the author of this review. Comparison of the data presented in Figs 1 and 2 shows that the bond energies, $D(\text{AnCl}_4, \text{g})$ for the early actinides (Th–Cm) and $D(\text{MCl}_4, \text{g})$ for TAn, differ insignificantly, whereas the

Table 2. Thermodynamic parameters of transactinide compounds (in kJ mol^{-1}).

Thermodynamic parameters	Transactinides (M)						
	Rf	Db	Sg	Bh	Hs	Mt	^{110}TAn
$\Delta_s H^\circ$	634	769	836	732	791	661	527
$\Delta_f H^\circ(\text{MCl}_4, \text{g})$	–971	–707	–522	–489	–313	–381	–384
$\Delta_f H^\circ(\text{MCl}_4, \text{c})$	–1077	–848	–680	–620	–460	–493	–461
$\Delta_s H^\circ(\text{MCl}_4)$	106	141	158	131	147	112	77
$\Delta_f H^\circ(\text{MCl}_4, \text{aq})$	–1303	–1010	–808	–726	–568	–644	–662
$\Delta_f H^\circ(\text{MCl}_6^{2-}, \text{g})$	–1724	–1420	–1209	–1127	–955	–1025	–1038
$A(\text{Cl}^-, \text{g})$	–286	–246	–220	–171	–175	–177	–187
$A(\text{Cl}^-, \text{c})$	–180	–105	–62	–40	–28	–65	–110
$\Delta_h H^\circ(\text{MCl}_6^{2-}, \text{g})$ (see ^a)	–784	–795	–804	–812	–818	–824	–829
$\Delta_f H^\circ(\text{MCl}_6^{2-}, \text{aq})$	–1637	–1344	–1142	–1060	–902	–978	–996
$\Delta_f H^\circ(\text{MBr}_4, \text{g})$	–759	–548	–401	–359	–234	–289	–291
$\Delta_f H^\circ(\text{MBr}_4, \text{c})$	–879	–685	–544	–493	–358	–386	–359
$\Delta_s H^\circ(\text{MBr}_4)$	120	137	143	134	124	97	68
$A(\text{Br}^-, \text{g})$	235	126	59	27	–31	23	26
$\Delta_f H^\circ(\text{K}_2\text{MCl}_6)$	–2036	–1767	–1580	–1507	–1354	–1417	–1428
$\Delta_f H^\circ(\text{Rb}_2\text{MCl}_6)$	–2065	–1792	–1603	–1528	–1373	–1437	–1448
$\Delta_f H^\circ(\text{Cs}_2\text{MCl}_6)$	–2085	–1820	–1636	–1565	–1414	–1476	–1487

^a $\Delta_h H^\circ(\text{MCl}_6^{2-}, \text{g})$ is the hydration enthalpy of gaseous MCl_6^{2-} anions.

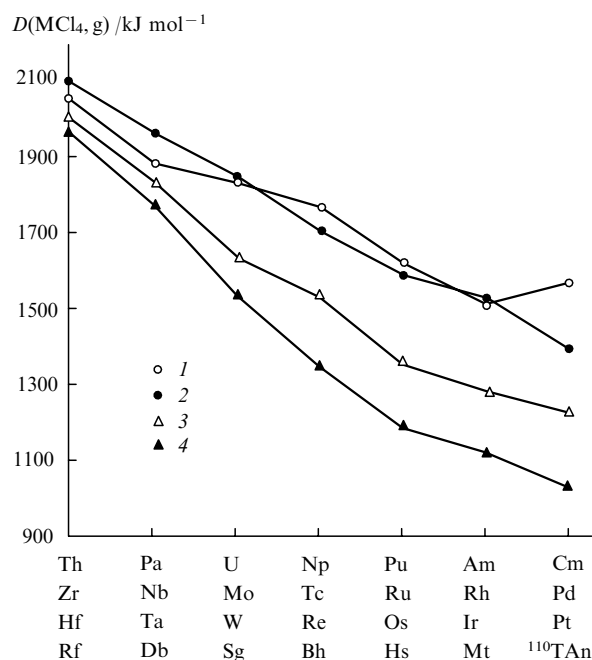


Figure 2. Bond energies $D(\text{MCl}_4, \text{g})$ of actinides (1) and of the 6d- (2), 5d- (3) and 4d-elements (4).

formation enthalpies for the following pairs of elements: Pa–Db, U–Sg, Np–Bh, Pu–Hs and Am–Mt (except for the pair Rf–Th) differ substantially, that is, smaller $\Delta_s H^\circ(\text{An})$ values [compared to $\Delta_s H^\circ(\text{M})$] lead to the higher thermodynamic stability of AnCl_4 compared to MCl_4 .

Problems concerning monotonic (passage $4d \rightarrow 5d \rightarrow 6d$) or nonmonotonic (passage $4d \rightarrow 6d \rightarrow 5d$) changes in the properties within the groups of the Periodic table and analogies between the properties of the 5f- and 6d-elements have been the subject of a considerable literature. Nonmonotonic changes in properties are associated with RE. We believe that the chemical properties (in particular, thermodynamic properties) reflect the totality of many properties of free atoms and interactions between them. An increase or a decrease in certain parameters can lead to non-monotonic changes in the thermodynamic properties within the

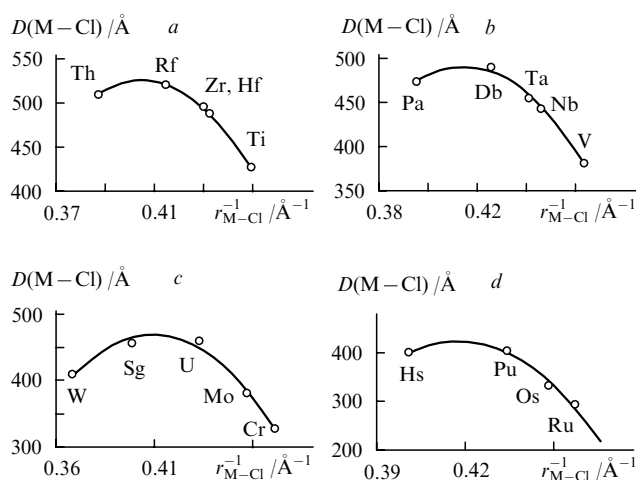


Figure 3. Bond energies $D(\text{M}-\text{Cl})$ in tetrachlorides of the d-elements as functions of $r_{\text{M}-\text{Cl}}^{-1}$. Group IV elements (a), Group V elements (b), Group VI elements (c) and Group VIII elements (d).

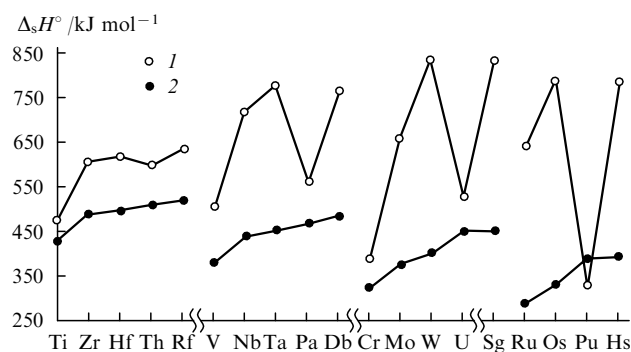


Figure 4. Changes in the $\Delta_s H^\circ(\text{M})$ (1) and $D(\text{M}-\text{Cl})$ (2) values for tetrachlorides of Group IV, V, VI and VIII elements and for the corresponding actinide pseudohomologues.

groups of the Periodic table. From this standpoint, let us compare the properties of compounds $\text{MCl}_4(\text{g})$ and $\text{AnCl}_4(\text{g})$ within particular groups. According to Eqn (2), the main properties determining the changes in the thermodynamic stability of tetrachlorides within the groups are $\Delta_s H^\circ(\text{M})$, $r_{\text{M}-\text{Cl}}$ and $D(\text{MCl}_4, \text{g})$. The bond energies $D(\text{M}-\text{Cl})$ in tetrachlorides of the d-elements of Groups IV, V, VI and VIII including the actinide pseudohomologues are plotted in Fig. 3 as functions of the $r_{\text{M}-\text{Cl}}^{-1}$ parameter. Figure 4 presents the dependence of $\Delta_s H^\circ(\text{M})$ and $D(\text{M}-\text{Cl})$ on Z in these groups.

1. TiCl_4 , ZrCl_4 , HfCl_4 , ThCl_4 and RfCl_4

For all gaseous tetrachlorides of Group IV elements (except RfCl_4), the interatomic distances were measured to an accuracy of $\pm 0.02 \text{ \AA}$ and the $\Delta_f H^\circ(\text{MCl}_4, \text{g})$ were determined. The interatomic distances are $r_{\text{Ti}-\text{Cl}} = 2.23 \text{ \AA}$; $r_{\text{Zr}-\text{Cl}} = 2.32 \text{ \AA}$, $r_{\text{Hf}-\text{Cl}} = 2.33 \text{ \AA}$ (see Ref. 25) and $r_{\text{Th}-\text{Cl}} = 2.58 \text{ \AA}$ (see Ref. 65).

Using the values $\Delta_f H^\circ(\text{ThCl}_4, \text{g}) = -964 \text{ kJ mol}^{-1}$ and $\Delta_s H^\circ(\text{Th}) = 597.1 \text{ kJ mol}^{-1}$ taken from Refs 61 and 66, one can obtain the $D(\text{ThCl}_4, \text{g})$ value equal to 2047 kJ mol^{-1} . Therefore, the bond energies, $D(\text{MCl}_4, \text{g})$, of tetrachlorides MCl_4 ($\text{M} = \text{Ti}, \text{Zr}, \text{Hf}, \text{Th}$ and Rf) are equal to 1720, 1965, 1997, 2047 and 2090 kJ mol^{-1} , respectively. A sharp, experimentally observed increase in $r_{\text{Th}-\text{Cl}}$ compared to $r_{\text{Hf}-\text{Cl}}$ can be considered as manifestation of RE which destabilise the 6d-AO of thorium. Compared to $D(\text{Hf}-\text{Cl})$, the $D(\text{Th}-\text{Cl})$ value increases rather than decreases (see Fig. 3). Based on the $\Delta_f H^\circ(\text{MCl}_4, \text{g})$ values for $\text{M} = \text{Zr}, \text{Hf}, \text{Th}$ and Rf ($-870, -889, -964$ and -971 kJ mol^{-1} , respectively), Group IV elements can be divided into pairs Zr–Hf and Th–Rf with close values of the enthalpies $\Delta_f H^\circ(\text{MCl}_4, \text{g})$. From the standpoint of thermodynamic properties, ThCl_4 belongs to the group of chlorides of the d-elements, which emphasises a specific feature of the early TAn, namely, similarity of their properties to those of An and of the d-homologues. All trends of changes in the chemical properties of compounds of Group IV elements and the similarity of Rf to Zr (see Refs 15 and 19) and to Th (see Ref. 18) are considered as manifestations of RE. Stability of the compounds under consideration, i.e., the $\Delta_f H^\circ(\text{MCl}_4, \text{g})$ value, depend on $\Delta_s H^\circ(\text{M})$, $r_{\text{M}-\text{Cl}}$ and $D(\text{M}-\text{Cl})$. Each of these quantities changes within the group in its own manner. For instance, the $\Delta_s H^\circ(\text{M})$ values increase from Th to Zr, Hf and Rf ($597, 608, 622$ and 634 kJ mol^{-1} , respectively).

$$\Delta_s H^\circ(\text{Th}) < \Delta_s H^\circ(\text{Zr}) < \Delta_s H^\circ(\text{Hf}) < \Delta_s H^\circ(\text{Rf}) \quad (3)$$

Thus, according to Eqn (2), the order of change in the sublimation enthalpies, $5f < 4d < 5d < 6d$, must correspond to the highest thermodynamic stability of ThCl_4 .

However, the $r_{\text{M}-\text{Cl}}$ values change in another manner, $4d \leq 5d < 6d < 5f$

$$r_{\text{Zr}-\text{Cl}} \leq r_{\text{Hf}-\text{Cl}} < r_{\text{Rf}-\text{Cl}} < r_{\text{Th}-\text{Cl}}, \quad (4)$$

which corresponds to the lowest thermodynamic stability of ThCl_4 . This order is due to the geometry of the molecules in question. In the gas phase, ZrCl_4 and HfCl_4 are characterised by tetrahedral coordination. This type of coordination is also assumed for RfCl_4 ; however, an electron diffraction study⁶⁵ of ThCl_4 and UCl_4 revealed a distorted C_{2v} symmetry. As a result of superimposition of the effects denoted by sequences (3) and (4), we get

$$\begin{aligned} D(\text{Zr}-\text{Cl}) &< D(\text{Hf}-\text{Cl}) < D(\text{Th}-\text{Cl}) < D(\text{Rf}-\text{Cl}) \\ \Delta_f H^\circ(\text{ZrCl}_4, \text{g}) &\geq \Delta_f H^\circ(\text{HfCl}_4, \text{g}) > \Delta_f H^\circ(\text{ThCl}_4, \text{g}) \geq \\ &\geq \Delta_f H^\circ(\text{RfCl}_4, \text{g}). \end{aligned}$$

Thus, two pairs of elements, viz., Zr–Hf and Th–Rf have similar thermodynamic properties.

Thorium is the second element of the An series. The atomic properties of Th are still not affected by the actinide contraction. Rutherfordium is the first element in the TAn series, whose properties are affected by both the actinide contraction and RE. Relativistic effects become stronger as Z increases:^{8,24} in Rf ($Z = 104$), the $6d$ -AO should experience greater relativistic destabilisation than in Th ($Z = 90$). This means that the $r_{\text{Rf}-\text{Cl}}$ distance in the RfCl_4 molecule must be at least comparable or longer than the $r_{\text{Th}-\text{Cl}}$ distance in the ThCl_4 molecule. The measured $r_{\text{Th}-\text{Cl}}$ distance (2.58 Å, see Ref. 65) and the calculated $r_{\text{Rf}-\text{Cl}}$ distance (2.417 Å, see Ref. 4) undoubtedly indicate that the effect of actinide contraction appears to be stronger than both relativistic and nonrelativistic structural-shell destabilisation of the $6d$ -AO for Rf.

2. V, Nb, Ta, Pa and Db

For compounds of Group V elements, the $\Delta_f H^\circ(\text{MCl}_4, \text{g})$ values (determined with an accuracy of ± 15) decrease on going from the light to heavy elements.^{4,68–69}

MCl_4	VCl_4	NbCl_4	TaCl_4	DbCl_4	PaCl_4
$\Delta_f H^\circ(\text{MCl}_4, \text{g}) / \text{kJ mol}^{-1}$	–535	–567	–561	–707	–809

However, if the thermodynamic stability of RfCl_4 is close to that of ThCl_4 , DbCl_4 appears to be less stable than PaCl_4 despite the fact that $r_{\text{Pa}-\text{Cl}} > r_{\text{Db}-\text{Cl}}$ (2.543 vs. 2.379 Å, respectively). On the other hand, the bond energy, $D(\text{M}-\text{Cl})$, in gaseous MCl_4 increases from V to Db as Z increases. This trend of changes in the main parameters is due to the large difference ($\sim 200 \text{ kJ mol}^{-1}$) between the sublimation enthalpies, $\Delta_s H^\circ(\text{M})$, of Pa and Db.

Element	V	Pa	Nb	Db	Ta
$\Delta_s H^\circ(\text{M}) / \text{kJ mol}^{-1}$	513	570	722	769	782

It should be noted that for Th and Rf this difference is $\sim 40 \text{ kJ mol}^{-1}$.

Figure 4 clearly displays a nonmonotonic trend in the changes in the parameters $\Delta_s H^\circ(\text{M})$ and $\Delta_s H^\circ(\text{An})$ with an increase in Z and a nearly monotonic trend of changes in $D(\text{M}-\text{Cl})$.

We also analysed the changes in the properties determining the thermodynamics of gaseous tetrachlorides of Group V–VIII elements in order to show the disposition of the TAn and An elements relative to the $3d$ -, $4d$ - and $5d$ -elements (Table 3).

Trends in the changes of the chemical properties of d -elements down the groups of the Periodic table and their comparison with the properties of An have been the subject of a considerable amount of literature.^{9,12–19} Particular emphasis is placed on how these properties change with Z , monotonically ($4d \rightarrow 5d \rightarrow 6d$) or nonmonotonically ($4d \rightarrow 6d \rightarrow 5d$). Nonmonotonic changes in particular properties are explained by nonmonotonic changes in the effective charges of gaseous molecules, which, in turn, are interpreted as the influence of RE.^{14,15,19}

However, it was recently shown⁹ that the effective charges cannot serve as quantitative criteria for the manifestation of RE. The data presented in Figs 3 and 4 and the above-mentioned $\Delta_f H^\circ(\text{MCl}_4, \text{g})$ and $\Delta_s H^\circ(\text{M})$ values taken from Refs 9, 10, 21, 48, 59, and 67 or calculated by the author of this review suggest that the thermodynamic properties represent a complex combination of different properties. For instance, compensation effects in the parameters $\Delta_s H^\circ(\text{M})$ and $D(\text{M}-\text{Cl})$ can cause both monotonic and nonmonotonic dependences of the $\Delta_f H^\circ(\text{MCl}_4, \text{g})$ values within the groups. The absolute values of the parameters $\Delta_f H^\circ(\text{MCl}_4, \text{g})$ are closest for Zr, Hf, Th and Rf. For heavier analogues, that is, Nb, Ta, Db, Pa; Mo, W, Sg, U; Tc, Re, Bh and Np the difference between TAn and An increases as the number of localised f -electrons in An increases; therefore, it is beyond reason to compare the TAn and An elements. The main regularities revealed for tetrachlorides also manifest themselves to a certain extent for tetrabromides.

A method for calculating the formation enthalpies of crystalline compounds (LnX_3 , AnX_3 and AnX_4 ; $\text{X} = \text{F}, \text{Cl}, \text{Br}, \text{I}$) was proposed.^{48,59} It is based on consideration of the formation of crystalline compounds from ions. This approach was used to calculate the formation enthalpies of crystalline compounds from gaseous atoms.^{4,21,67} The formation enthalpies of crystalline compounds were calculated by the following equation

$$\Delta_f H^\circ(\text{MX}_4, \text{c}) = \Delta_s H^\circ(\text{M}) + 4\Delta_f H^\circ(\text{X}, \text{g}) - U(\text{MX}_4, \text{c}), \quad (5)$$

where $U(\text{MX}_4, \text{c})$ is the crystal lattice energy.

The lattice energies can be estimated using the lattice parameters^{30,45–48} or the $r_{\text{M}-\text{X}}$ distances. For instance, calculations with known $r_{\text{M}-\text{X}}$ and $U(\text{MX}_4, \text{c})$ values or with $r_{\text{An}-\text{X}}$ and $U(\text{AnX}_4, \text{c})$ values determined from the experimental $\Delta_f H^\circ(\text{MX}_4, \text{c})$ ($\text{M} = \text{Zr}, \text{Hf}, \text{Ta}, \text{Nb}, \text{Mo}, \text{W}, \text{Tc}, \text{Re}, \text{Ru}, \text{Os}, \text{Pt}, \text{Th}, \text{Pa}, \text{U}, \text{Np}, \text{Pu}$) parameters^{45–76} revealed correlations between $r_{\text{M}-\text{X}}$ and $U(\text{MX}_4, \text{c})$ or between $r_{\text{An}-\text{X}}$ and $U(\text{AnX}_4, \text{c})$, which allowed one to calculate the $\Delta_f H^\circ(\text{MX}_4, \text{c})$ values for all the crystalline tetrahalides of the d -elements of Rows 4–6 and for the actinides. The lattice energies of Pd, Rh, Ir and TAn were calculated^{4,21} and those of Am, Cm, Bk, Cf and Es determined.⁴⁸ The $\Delta_f H^\circ(\text{MX}_4, \text{c})$ values for TAn are listed in Table 2.

Table 3. Sequence of changes in the properties of Group V–VIII elements and their compounds.

Parameters	Sequence of changes in properties			
	Group V elements and Pa: V(3d), Nb(4d), Ta(5d), Db(6d), Pa(5f)	Group VI elements and U: Cr(3d), Mo(4d), W(5d), Sg(6d), U(5f)	Group VII elements and Np: Mn(3d), Tc(4d), Re(5d), Bh(6d), Np(5f)	Group VIII elements and Pu: Fe(3d), Ru(4d), Os(5d), Hs(6d), Pu(5f)
$\Delta_s H^\circ(\text{M})$	$3d < 5f < 4d < 6d < 5d$	$3d < 5f < 4d < 6d \leq 5d$	$3d < 5f < 4d < 6d < 5d$	$5f < 3d < 4d < 5d \approx 6d$
$r(\text{M}-\text{Cl})$	$3d < 4d < 5d < 6d < 5f$	$3d < 4d < 5d < 6d < 5f$	$3d < 4d < 5d < 6d < 5f$	$4d < 5d < 6d < 5f$
$D(\text{M}-\text{Cl})$	$3d < 4d < 5d < 5f < 6d$	$3d < 4d < 5d < 5f \leq 6d$	$4d < 5d < 6d < 5f$	$4d < 5d < 6d < 5f$
$\Delta_f H^\circ(\text{MCl}_4, \text{g})$	$3d > 5d \approx 4d > 6d > 5f$	$5d > 4d > 3d > 6d > 5f$	$4d > 5d > 6d > 5f$	$4d > 5d > 6d > 5f$

IV. Volatility of transactinide compounds as a function of their structure in the crystalline and gaseous states

1. Comparison of earlier and recently obtained results

One of the main experimental methods used for determining the sublimation enthalpies of TAn is the volatility measurements of their halides and oxyhalides.^{11, 13, 14, 17, 77–85} Volatile compounds of metals are compounds that can undergo sublimation and condensation at moderate (< 700–800 K) temperatures. However, both the experimental data and their theoretical interpretation are contradictory. It was not an occasion that the authors of monograph⁷⁷ wrote that ‘volatility belongs to such properties of chemical compounds that are hard to predict even qualitatively’. They also mentioned that, despite the existence of two experimental methods for studying the volatility properties (measurements of sublimation enthalpies and determination of the temperature dependence of the vapour pressure, $P = f(T)$), only the second approach allows one to obtain complete and reliable information on the volatility properties. For instance, the sublimation enthalpies of ZrCl_4 and HfCl_4 were reported to be equal, *viz.*, $\Delta_s H^\circ(\text{ZrCl}_4) = \Delta_s H^\circ(\text{HfCl}_4) = 100 \text{ kJ mol}^{-1}$,^{26, 86} however, measurements of the $P = f(T)$ dependence over a wide temperature range pointed to the higher volatility of HfCl_4 compared to ZrCl_4 . Theoretical predictions of volatility properties are also complicated by the need to take into account the molecular structure in the crystalline and gaseous states.

Chemical experiments with TAn are carried out using single atoms (the so-called ‘one atom-at-a-time’ technique). Since in these experiments we deal with single molecules, neither $P = f(T)$ nor $\Delta_s H^\circ$ can be measured. Therefore, TAn are studied by isothermal gas chromatography and thermochromatography. The parameter measured in gas chromatography studies²⁰ is the enthalpy of adsorption, $\Delta_a H_T^\circ$, on a chromatographic surface (usually, quartz). The sublimation enthalpies of chlorides and oxychlorides, $\Delta_s H_{298}^\circ$, are calculated from a linear correlation between these values, $\Delta_s H_{298}^\circ$ and $\Delta_a H_T^\circ$. However, the results obtained using this procedure are less reliable than those of the direct measurements of $\Delta_s H_{298}^\circ$. From the viewpoint of the reliability of the results obtained and based on conclusions drawn in monograph,⁷⁷ the experimental methods used in volatility studies can be listed in the following order

$$P = f(T) > \text{direct measurements of } \Delta_s H^\circ > \text{correlation of } \Delta_s H^\circ \text{ and } \Delta_a H_T^\circ.$$

In addition, a drawback of the experiments with TAn ‘is that the chemical composition of compounds under study cannot be identified and that possible chemical formulae are postulated based on the results of experiments with early homologues’.¹⁴ These experiments are carried out assuming a complete analogy between the chemical properties of the 4d-, 5d- and 6d-elements within the groups of the Periodic table and the same type of compounds of the same chemical composition, though it is not universally true. For instance, in Groups VI and VII almost all halide compounds of rhenium are volatile at room or higher temperatures.⁷⁰ ReO_3Cl and ReOCl_4 that are hard to separate are formed under the same conditions.⁷⁰ Even more complicated is the situation observed in the case of the identification of volatile compounds of Group VI elements.⁷⁰ For instance, pairs of compounds MoO_2Cl_2 and MoOCl_4 or WO_2Cl_2 and WOCl_4 are formed under the same conditions; MoO_2Cl_2 and MoOCl_4 can be chemically separated only by *in vacuo* sublimation at 70–80 °C; WO_2Cl_2 undergoes disproportionation resulting in WOCl_4 , which in dioxygen atmosphere adds a O_2 molecule and releases Cl_2 , thus again forming WO_2Cl_2 . Recently,⁸⁷ thermodynamic analysis was performed on all possible Mo and W compounds that can be formed in the gas phase.

Further, assuming a complete analogy between the chemical properties of the 4d-, 5d- and 6d-elements within the corresponding groups, the same adsorption mechanism is postulated for all

homologues. Clearly, adsorption depends on the character of bonding between individual molecules or their ensembles and the surface. Surface reactions are neither microscopic nor macroscopic; they belong to a broad class of ‘intermediate’ reactions which comprises both microscopic and macroscopic reactions.⁸⁸

The surface of quartz is an arena in which different chemical processes occur. Quartz possesses no strong basic or acid properties. Depending on temperature, its surface can adsorb protons, hydroxy groups, polarised siloxane groups, chlorine and dioxygen molecules, *etc.*⁸⁸ The minimum energy of the van der Waals interaction necessary for physisorption to occur is $\approx 20 \text{ kJ mol}^{-1}$. The $-\Delta_a H_T^\circ$ values measured in the experiments with TAn and their homologues lie between 50 and 250 kJ mol^{-1} . These magnitudes of the heats of adsorption suggest different adsorption mechanisms including the formation of chemical bonds $\text{M}-\text{Cl}$, $\text{M}-\text{Si}$, $\text{M}-\text{OH}$, *etc.*, between the adsorbed molecules and quartz surface irrespective of one molecule or ensemble of gaseous molecules is adsorbed on the surface. Yet another problem is the heterogeneity of the real quartz surface and possible modification of this surface by some components of the carrier gas. Therefore, taking into account the conclusions drawn in monograph⁷⁷ and the postulates proposed by the authors of other studies,^{14, 17} the results obtained from the correlation of $\Delta_s H^\circ$ with $\Delta_a H_T^\circ$ seem to be even less reliable.

Theoretical chemistry uses four approaches to volatility studies.

The first approach is based on calculations of (i) bond covalencies and effective charges in gaseous molecules or (ii) dipole moments of these molecules using the same charges. Changes in the effective charges are interpreted as a manifestation of RE. This approach ignores the mechanism of adsorption and, hence, the structure of solids. The high covalency of the $\text{M}-\text{Cl}$ bonds in gaseous molecules is assumed to correspond to high volatility of respective crystalline compounds. This model was used to rationalise the trend in the changes in the volatility of chlorides MCl_4 ($\text{M} = \text{Rf}, \text{Hf}, \text{Zr}$).¹⁴ However, experimental data showed that the covalency of the $\text{M}-\text{X}$ bonds in gaseous MX_4 molecules cannot serve as criterion for volatility. Undoubtedly, TiF_4 is a more ionic compound than TiI_4 ; nevertheless, both of them are characterised by the same volatility.⁷⁰ The volatility of the covalent compound UCl_6 is much lower than that of ionic compound UF_6 ; the ionic compounds UF_6 , NpF_6 and PuF_6 exhibit the highest volatilities among all the simple and complex An compounds.⁶¹ The results of calculations of gaseous Group VI dioxyhalides MO_2Cl_2 ($\text{M} = \text{Mo}, \text{W}, \text{Sg}$), carried out in the framework of a relativistic discrete variation approach have been reported.¹⁵ According to calculations,¹⁵ SgO_2Cl_2 is characterised by the largest contribution of covalent bonding and should be the most volatile compound within the group. However, experiments showed the opposite: SgO_2Cl_2 possesses the lowest volatility within the group of the Periodic table.¹⁴ It was then assumed¹⁵ that volatility is determined by the dipole moments of gaseous molecules, $\mu(\text{MO}_2\text{Cl}_2)$; however, experimental data revealed that neither bond covalency nor dipole moments of gaseous molecules can serve as criterion for volatility. For instance, gaseous molecules AnF_6 ($\text{An} = \text{U}, \text{Np}, \text{Pu}$) have equal dipole moments, $\mu(\text{AnF}_6)$; however, NpF_6 in the crystalline state has abnormally high vapour pressure.⁶¹ Experimental data showed that the approach based on calculations of bond covalencies and effective charges¹⁴ and dipole moments¹⁵ of gaseous molecules is incorrect and inapplicable in the case of the prediction of volatility.

The second approach was proposed by Zhuikov *et al.*⁷⁸ who assessed the volatility of the tetrachlorides RfCl_4 , HfCl_4 and ZrCl_4 from the parameters of thermodynamic cycle including the cohesive energy of the metal. In contrast to the preceding case, this model, though indirectly, takes into account two states of matter.

Eichler⁷⁹ hypothesised that the formation enthalpy of gaseous metal atoms can serve as a measure of sublimation enthalpies of

chemical compounds and suggested a correlation between these parameters (third approach).

An experimental indication of the volatility of metal compounds is the possibility of sublimation of the substance under study.⁷⁷ Therefore, in early studies^{21, 67} researchers used the difference between the standard formation enthalpies of a compound in the crystalline and gaseous states as a possible characteristic of volatility (fourth approach).

The need to take into account the distinctions between the structure of two phase states (probably, in terms of adsorption mechanism) when calculating the sublimation enthalpies of chemical compounds has been proposed^{11, 13, 67, 77, 78, 79} and can be exemplified as follows.

Group IV. Titanium tetrachloride in the gaseous and crystalline states has a monomeric structure (CN = 4), which is responsible for the small $\Delta_s H^\circ(\text{TiCl}_4)$ value (52 kJ mol⁻¹).²⁶

Similarly to TiCl₄, tetrachlorides of zirconium and hafnium in the gas phase have a tetrahedral structure (CN = 4). However, in the crystalline state these compounds are polymers with octahedral coordination (CN = 6). For the sublimation enthalpies of these compounds, we get $\Delta_s H^\circ(\text{ZrCl}_4) \approx \Delta_s H^\circ(\text{HfCl}_4) \approx 100$ kJ mol⁻¹.²⁶ An increase of 2 in the CN for the crystalline state compared to the gaseous state causes a nearly twofold increase in the parameters $\Delta_s H^\circ(\text{ZrCl}_4)$ and $\Delta_s H^\circ(\text{HfCl}_4)$ compared to $\Delta_s H^\circ(\text{TiCl}_4)$.

For thorium tetrachloride, the CN is 4 in the gaseous state and 8 in the crystalline state.^{61, 65} An increase of 4 in the CN for the crystalline state compared to the gaseous state caused a nearly fourfold increase in the parameter $\Delta_s H^\circ(\text{ThCl}_4)$ (249 ± 20 kJ mol⁻¹) compared to $\Delta_s H^\circ(\text{TiCl}_4)$. Therefore, the CN in gaseous molecules remains unchanged (CN = 4) on going from TiCl₄ to ThCl₄; however, the structure of crystalline compounds becomes more complex, which results in an increase in $\Delta_s H^\circ(\text{MCl}_4)$. If all crystal compounds were built of monomeric molecules similar to TiCl₄, they would be characterised by a small sublimation enthalpy (~50 kJ mol⁻¹). Probably, the properties of adsorbed molecules are similar to those of the molecules in the crystalline rather than the gaseous state.

The sublimation enthalpies, $\Delta_s H^\circ(\text{MCl}_4)$, correlate with the $r(\text{M}^{\text{IV}})$ of Ti, Zr, Hf and Th in the crystalline state.

M^{IV}	CN	Ionic radius $r(\text{M}^{\text{IV}})/\text{\AA}$	$\Delta_s H^\circ(\text{MCl}_4)$ /kJ mol ⁻¹
Ti	4	0.60	52
Zr	6	0.72	100
Hf	6	0.73	100
Th	8	1.048	249

The formula is as follows

$$\Delta_s H^\circ(\text{MCl}_4) \approx 442 r(\text{M}^{\text{IV}}) - 215 \text{ kJ mol}^{-1}.$$

Substituting the value $r(\text{Rf}^{\text{IV}})(\text{CN} = 6) = 0.75 - 0.78 \text{ \AA}$, we get $\Delta_s H^\circ(\text{RfCl}_4) = 117 - 130 \text{ kJ mol}^{-1}$, which is close to the experimental value $\Delta_s H^\circ(\text{RfCl}_4) = 109 \pm 10 \text{ kJ mol}^{-1}$.¹⁴ It seems logical to assume that adsorption of RfCl₄ causes expansion of its coordination sphere and an increase in CN to 6 (similarly to ZrCl₄ and HfCl₄) rather than 8 as in the case of ThCl₄.

Other values of the parameter $\Delta_s H^\circ(\text{RfCl}_4)$ reported in the literature are 90 ± 15 (see Ref. 80) and 122–138 kJ mol⁻¹ (see Ref. 83). They lie within the interval 110 ± 30 kJ mol⁻¹, which is consistent with the value reported by Türlér.¹⁴

Thus, the results of volatility studies can provide the possibility of modelling the structure of crystalline TAn compounds. The volatility of compounds of Group VI–VII elements can be analysed analogously.

Group VI. Nearly two decades ago Academician V I Spitsyn brought the attention of the author of this review to the problem¹ of analysing the chemical properties of Mo and W compounds in order to find optimum conditions for their separation. The main conclusion drawn after solving this problem was that separation

of Mo and W requires the use of their compounds in their lower oxidation states. It was found that the higher the oxidation state the less significant the distinctions between the chemical behaviour of Mo and W and that maximum similarity of the Mo and W compounds is observed for the oxidation state VI. Currently, some effort has been made to reveal distinctions between the chemical behaviour of compounds of Mo^{VI}, W^{VI} and Sg^{VI} in the gaseous state and in solution. The main problem of volatility studies of Group VI compounds is to identify the substances formed in the gas phase.^{70, 87}

The thermodynamic stability of the W and Mo compounds was also used as a criterion for identification.⁸⁷ It was concluded⁸⁷ that MoO₂Cl₂, WO₂Cl₂ and SgO₂Cl₂ have similar thermodynamic properties (their boiling points are close). The stability of MO₂Cl₂ and MOCl₄ towards thermal decomposition was determined using the energy of the charge-transfer transition, ΔE_{ct} , in the electronic spectra.¹⁵ This method was also used for estimating the redox potentials of Pu(VII)/Pu(VI), Np(VII)/Np(VI), *etc.*^{1–3, 45–47} in solutions from the measured ΔE_{ct} values for their complexes. However, these spectral transitions are by no means related to the gas-phase stability of compounds which is determined by the standard formation enthalpy. Based on the results of determination of ΔE_{ct} values, MO₂Cl₂ was suggested to be more stable towards thermal dissociation than MOCl₄ (see Ref. 15). However, the standard formation enthalpies ($\Delta_f H^\circ$) of gaseous MO₂Cl₂ and MOCl₄ (M = Mo, W) molecules changes in the order WO₂Cl₂ < MoO₂Cl₂ = WOCl₄ < MoOCl₄ (see Ref. 87). This trend is quite remarkable since it contradicts the conclusions drawn by Kratz.¹⁵ Taking into account the results of studies,^{70, 87} the theoretically predicted¹⁵ trend in changes in the volatility of oxychlorides of Mo, W and Sg seems to be doubtful; in addition, there is no proof so far that the experimental¹⁴ sublimation enthalpies [$\Delta_s H^\circ = 114 \pm 11$, 124 ± 10 and $127 \pm 10(21)$ kJ mol⁻¹] can be unambiguously attributed to the compounds MoO₂Cl₂, WO₂Cl₂ and SgO₂Cl₂, respectively. In the gas phase, MoO₂Cl₂, WO₂Cl₂, WOCl₄ and MoOCl₄ mainly have the monomeric structure; however, in the crystalline state the CN increases and these compounds have a polymeric structure. Compounds MO₂Cl₂ (M = Mo, W) readily add neutral oxygen-containing molecules to give complexes MO₂Cl₂ · 2L (L = HCONMe₂, Me₂SO, *etc.*). In the crystalline state, MoO₂Cl₂ · 2L has a monomeric structure while WO₂Cl₂ · 2L has a polymeric structure.⁷⁰ In this connection, a new problem arises since different adsorption mechanisms of Mo and W(Sg) compounds become possible. Probably, a more conservative interpretation of the chemical properties of Sg in the gas phase is required, which takes into account the accuracy of the experimental data. It cannot be ruled out that conclusions drawn by Kratz¹⁵ about the chemical behaviour of Sg should be revised since there is no proof that only one type of compounds, *viz.*, MO₂Cl₂ (M = Mo, W, Sg) is formed in the gas phase.

Group VII. In the gaseous state, the CN of oxychlorides MnO₃Cl, TcO₃Cl and ReO₃Cl equals 4. Transition to the crystalline state leads to the formation of bridging bonds and the CN value increases. This should cause an increase in volatility in the order MnO₃Cl < TcO₃Cl < ReO₃Cl < BhO₃Cl. For TcO₃Cl, ReO₃Cl and BhO₃Cl this sequence was obtained experimentally,¹⁷ which is consistent with recently reported results. For instance, MnO₃Cl undergoes sublimation at –68 °C (see Ref. 70) while the sublimation temperatures of TcO₃Cl, ReO₃Cl and BhO₃Cl are respectively –20–40, 20–80 and 80–180 °C (see Ref. 17).

Group VIII. It does not always happen that the structure of compounds changes upon transition from the gaseous to the crystalline state. Compounds HsO₄ and OsO₄ were predicted⁶⁷ to have a monomeric structure in the crystalline state.

In conclusion, let us compare the results concerning the trend in changes of the volatility of tetrahalides and its interpretations given by different authors.

Earlier results²⁶ obtained from measurements of the temperature dependence of the vapour pressure, $P = f(T)$, show that the

volatility changes in the order $\text{HfCl}_4 > \text{HfBr}_4 > \text{ZrCl}_4 > \text{ZrBr}_4$. According to Türlér,¹⁴ it changes in another manner, namely, $\text{ZrBr}_4 \geq \text{ZrCl}_4 > \text{HfCl}_4 > \text{HfBr}_4$. Some other examples of inconsistency between the results of earlier and recent studies can be given. For instance, it was established that NbBr_5 has higher volatility than TaBr_5 .⁸⁴ These results were shown⁸⁵ to contradict those obtained earlier from the $P = f(T)$ measurements [according to monograph,²⁶ all tantalum halides (TaF_5 , TaCl_5 , TaBr_5) have higher volatilities than the corresponding niobium halides (NbF_5 , NbCl_5 , NbBr_5)].

Seemingly, one can conclude that the results of volatility measurements performed by classical methods [$P = f(T)$] using macroamounts of substances always differ from those obtained in experiments with microamounts. However, sometimes the results of both types of experiments coincide. For instance, TcO_3F was reported⁸⁹ to be more volatile than ReO_3F and a similar trend was revealed for TcO_3Cl and ReO_3Cl .¹⁷ Lower volatility of NbOCl_3 compared to NbCl_5 was reported in both earlier^{26,86} and recent studies.¹⁴

Inconsistency of the results obtained seems to be due not only to the fact that the volatility is measured using macroamounts or microamounts of chemical compounds. The main reason is that the chemical composition of compounds studied in modern experiments can hardly be established, whereas in earlier studies the chemical composition of the gas phase was thoroughly investigated. Earlier, all the compounds formed as well as decomposition products were analysed when performing $P = f(T)$ measurements. For instance, studies of NbOCl_3 were carried out taking into account the presence of accompanying chloride NbCl_5 in the vapour (see Ref. 26).

It is hard to agree with the conclusion¹⁴ that 'relativistic effects are most experimentally pronounced' in the volatilities of TAn halides and oxyhalides determined using correlation with adsorption enthalpies. This conclusion is based on the results of bond covalency calculations in gaseous molecules; however, this parameter is by no means related to volatility. Türlér also stated¹⁴ that 'recent experiments demonstrated that the chemical properties of heavy elements can no longer be predicted based on simple down-the-group extrapolations because of the influence of RE'. At the same time, he postulated the same chemical composition and adsorption mechanism for all compounds of the $4d$ -, $5d$ -, $6d$ -elements within corresponding groups. Thus, these conclusions contradict the initial postulates.

The authors of studies^{14,15} pose illusive problems that are insoluble due to large experimental errors and the above-mentioned postulates. They draw definite conclusions about the influence of RE on the adsorption enthalpy without knowledge of the molecules that are formed on the surface.

Gas-state chemistry of TAn compounds has been successfully progressing in spite of great experimental problems. Probably, one can assume that the $6d$ -elements and the early $4d$ - and $5d$ -homologues can form compounds of analogous chemical composition; however, unambiguous identification of these compounds is impossible.

2. Sublimation enthalpies of TAn tetrahalides

The sublimation enthalpies, $\Delta_s H^\circ(\text{MX}_4)$, of MX_4 ($\text{X} = \text{Cl}, \text{Br}$) compounds were calculated by the author of this review for tetrahalides of the $4d$ -, $5d$ - and $6d$ -elements and actinides as the differences between the standard formation enthalpies of the corresponding compounds in the gaseous and crystalline states. The sublimation enthalpies of TAn compounds are listed in Table 2. Calculations were carried out assuming that the CN for compounds of the $4d$ -, $5d$ - and $6d$ -elements equals 4 in the gaseous state and 6 in the crystalline state. The experimental CN values for AnCl_4 compounds were reported by Brown.⁶¹ Comparison of the calculated and experimental $\Delta_s H^\circ(\text{MX}_4)$ values for compounds of

the $4d$ - and $5d$ -elements allowed us to estimate the error (uncertainty) of calculations at $\pm 15 \text{ kJ mol}^{-1}$. The $\Delta_s H^\circ(\text{MCl}_4)$ values (in kJ mol^{-1}) obtained for tetrachlorides of Group V–VIII elements are listed below:

M (Group IV)	Zr	Hf	Rf
$\Delta_s H^\circ(\text{MCl}_4) / \text{kJ mol}^{-1}$	112	102	106
M (Group V)	Nb	Ta	Db
$\Delta_s H^\circ(\text{MCl}_4) / \text{kJ mol}^{-1}$	128	144	141
M (Group VI)	Mo	W	Sg
$\Delta_s H^\circ(\text{MCl}_4) / \text{kJ mol}^{-1}$	113	160	158
M (Group VII)	Tc	Re	Bh
$\Delta_s H^\circ(\text{MCl}_4) / \text{kJ mol}^{-1}$	112	141	131
M (Group VIII)	Ru	Os	Hs
$\Delta_s H^\circ(\text{MCl}_4) / \text{kJ mol}^{-1}$	109	147	147
M (Group VIII)	Rh	Ir	Mt
$\Delta_s H^\circ(\text{MCl}_4) / \text{kJ mol}^{-1}$	83	115	112

Vertical trends in the changes of the $\Delta_s H^\circ(\text{MCl}_4)$ values are different, namely, $5d \leq 6d < 4d$ for Group IV, $4d < 6d \leq 5d$ for Group V and $4d < 6d \leq 5d$ for Group VI.

As mentioned above, many of the thermodynamic properties of Group IV elements are similar. The sublimation enthalpies of the tetrachlorides of Group IV elements are also close. The calculated sublimation enthalpies of An tetrachlorides (in kJ mol^{-1}) are listed below:

Actinide	Th	Pa	U	Np	Pu	Am	Cm	Bk	Cf
$\Delta_s H^\circ(\text{AnCl}_4)$	249	220	213	168	172	110	128	131	62

The error (uncertainty) of calculations of the $\Delta_s H^\circ(\text{AnCl}_4)$ parameters was estimated at $\pm 20 \text{ kJ mol}^{-1}$ based on their comparison with the corresponding experimental values for An = Th, U and Pu (see Refs 61 and 70).

Two different trends should be recognised when comparing the sublimation enthalpies of tetrachlorides of the d - and $5f$ -elements, namely, the volatility of early An compounds decreases while that of the d -element compounds increase as Z increases. Among the early An compounds, the volatility of tetrachlorides is much higher than that of tetrachlorides of the d -elements (the difference is $\approx 100 \text{ kJ mol}^{-1}$). This difference decreases near the middle of the actinide series and then the volatilities of the tetrachlorides differ insignificantly. The volatility of tetrachlorides of the heavy d - and f -elements decreases with an increase in Z .

The trend in the changes in the volatility of AnCl_4 compounds and tetrachlorides of d -elements (MCl_4) deserves attention. Eichler⁷⁹ suggested a correlation between the $\Delta_s H^\circ(\text{M})$ and $\Delta_s H^\circ(\text{MCl}_4)$ values. We tested this idea using An and AnCl_4 compounds as an example. Comparison of the experimental and calculated $\Delta_s H^\circ(\text{An})$ and $\Delta_s H^\circ(\text{AnCl}_4)$ values along the actinide series confirmed that changes in these parameters follow the same trend. Based on correlation between these values, one can even estimate the $\Delta_s H^\circ(\text{AnCl}_4)$ parameters to an accuracy of $\pm 40 \text{ kJ mol}^{-1}$. This is quite good accuracy for prediction of a trend that reflects a decrease in $\Delta_s H^\circ(\text{AnCl}_4)$ with a decrease in $\Delta_s H^\circ(\text{An})$. In turn, a dramatic decrease in $\Delta_s H^\circ(\text{An})$ on going from early to late An is due to the change in the valence V_{An} in the metallic state.

For the $4d$ -, $5d$ - and $6d$ -transition metals the dependence of $\Delta_s H^\circ(\text{M})$ on $Z(\text{M})$ is nearly parabolic: the $\Delta_s H^\circ(\text{M})$ values increase on going from the early to the middle of the series and then decrease towards the end of the series. It cannot be ruled out that this type of correlation⁷⁹ can be used for the first (Rf–Bh) and second (Bh–¹¹²TAn) half of the TAn series separately.

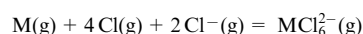
V. Standard formation enthalpies of gaseous MCl_6^{2-} anions and affinity of tetrachlorides towards chloride ions

Using the formation enthalpies of gaseous MCl_6^{2-} anions, $\Delta_f H^\circ(\text{MCl}_6^{2-}, \text{g})$, one can estimate the affinity of gaseous and crystalline tetrachlorides towards chloride ions and thus compare the trends of changes in these important parameters within the groups of the 4*d*-, 5*d*- and 6*d*-elements. In addition, this allows comparison of the thermodynamic properties of hexachlorides in aqueous solutions:

$$\Delta_f H^\circ(\text{MCl}_6^{2-}, \text{g}) = \Delta_f H^\circ(\text{MCl}_6^{2-}, \text{aq}) - \Delta_h H^\circ(\text{MCl}_6^{2-}, \text{g}) + C, \quad (6)$$

where $\Delta_h H^\circ(\text{MCl}_6^{2-}, \text{g})$ is the hydration enthalpy of the gaseous MCl_6^{2-} anion and C is a constant [$C = -2\Delta_f H^\circ(\text{H}^+, \text{g}) - 2\Delta_h H^\circ(\text{H}^+, \text{g})$].

The formation enthalpy of gaseous anions, $\Delta_f H^\circ(\text{MCl}_6^{2-}, \text{g})$, is the main parameter used for calculating the formation enthalpy of crystalline salts A_2MCl_6 . For the reaction listed below



the $\Delta_f H^\circ(\text{MCl}_6^{2-}, \text{g})$ values can be predicted using the equation

$$\Delta_f H^\circ(\text{MCl}_6^{2-}, \text{g}) = \Delta_s H^\circ(\text{M}) + 4\Delta_f H^\circ(\text{Cl}, \text{g}) + 2\Delta_f H^\circ(\text{Cl}^-, \text{g}) - \left[c - \frac{d}{r(\text{M}-\text{Cl})} \right], \quad (7)$$

where the last term,

$$c - \frac{d}{r(\text{M}-\text{Cl})} = D(\text{MCl}_6^{2-}),$$

is the bond energy in the anion, the coefficients c and d are found from experimental $\Delta_f H^\circ(\text{MCl}_6^{2-}, \text{g})$ values for the 4*d*- and 5*d*-elements; the $r(\text{M}-\text{Cl})$ values for CN = 6 are listed in Table 1.

Using Eqn (7), one can calculate the $D(\text{M}-\text{Cl})$ values for all the 4*d*-, 5*d*- and 6*d*-elements and the $\Delta_f H^\circ(\text{MCl}_6^{2-}, \text{g})$ values for TAn. These calculations were performed by the author of this review for anions of the 4*d*- and 5*d*-elements with an accuracy (uncertainty) of $\pm 15 \text{ kJ mol}^{-1}$. The formation enthalpies $\Delta_f H^\circ(\text{MCl}_6^{2-}, \text{g})$, $\Delta_f H^\circ(\text{MCl}_6^{2-}, \text{aq})$ and $\Delta_h H^\circ(\text{MCl}_6^{2-}, \text{g})$ are listed in Table 2.

It was found that the thermodynamic stability of gaseous MCl_6^{2-} anions and aqua ions ($\text{MCl}_6^{2-}, \text{aq}$) decreases with an increase in $Z(\text{TAn})$, whereas the order of changes in these values within particular groups is as follows: 4*d* < 5*d* < 6*d*. The same trends for the TAn series are also observed for MBr_6^{2-} anions.

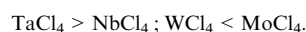
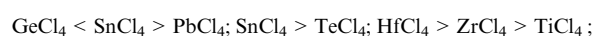
The affinity $A(\text{Cl}^-, \text{g})$ of MCl_4 compounds in the crystalline and gaseous states towards two Cl^- ions can be calculated using the following equations

$$A(\text{Cl}^-, \text{g}) = \Delta_f H^\circ(\text{MCl}_6^{2-}, \text{g}) - \Delta_f H^\circ(\text{MCl}_4, \text{g}) - 2\Delta_f H^\circ(\text{Cl}^-, \text{g})$$

and

$$A(\text{Cl}^-, \text{c}) = \Delta_f H^\circ(\text{MCl}_6^{2-}, \text{g}) - \Delta_f H^\circ(\text{MCl}_4, \text{c}) - 2\Delta_f H^\circ(\text{Cl}^-, \text{g}).$$

Both monotonic and nonmonotonic trends in changes in the affinity towards chloride ions within groups were found experimentally for tetrachlorides of *p*- and *d*-elements⁹⁰



In the text below we compare the $A(\text{Cl}^-, \text{g})$ values for tetrachlorides of the 4*d*-, 5*d*- and 6*d*-elements²¹ and actinides.⁹¹ (The values for TiCl_4 and ThCl_4 were taken from Ref. 30).

1. Tetrachlorides of Group IV elements

MCl_4	RfCl_4	ThCl_4	HfCl_4	ZrCl_4	TiCl_4
$A(\text{Cl}^-, \text{g}) / \text{kJ mol}^{-1}$	-286	-287	-284	-190	-76

Thus, the heavy Group IV elements are characterised by nearly equal affinity towards chloride ions, which decreases on going to the early elements of this Group.

2. Tetrachlorides of Group V elements

MCl_4	TaCl_4	DbCl_4	NbCl_4
$A(\text{Cl}^-, \text{g}) / \text{kJ mol}^{-1}$	-266	-246	-169

3. Tetrachlorides of Group VI elements

Inversion of $A(\text{Cl}^-, \text{g})$ values^{30,90} for MoCl_4 and WCl_4 is observed, so that the $A(\text{Cl}^-, \text{g})$ value for UCl_4 (-270 kJ mol^{-1})³⁰ 'completes' the picture:

MCl_4	UCl_4	SgCl_4	MoCl_4	WCl_4
$A(\text{Cl}^-, \text{g}) / \text{kJ mol}^{-1}$	-270	-220	-219	-214

4. Tetrachlorides of Group VII elements

MCl_4	ReCl_4	BhCl_4	TcCl_4
$A(\text{Cl}^-, \text{g}) / \text{kJ mol}^{-1}$	-181	-171	-168

5. Tetrachlorides of Group VIII elements

MCl_4	RuCl_4	OsCl_4	HsCl_4
$A(\text{Cl}^-, \text{g}) / \text{kJ mol}^{-1}$	-223	-209	-175

For actinides NpCl_4 and PuCl_4 , the $A(\text{Cl}^-, \text{g})$ values ($\approx -270 \pm 20 \text{ kJ mol}^{-1}$) are larger than those obtained for the *d*-elements of Groups VII and VIII.

Thus, RfCl_4 , ThCl_4 and HfCl_4 are better acceptors of chloride ions than ZrCl_4 while DbCl_4 and TaCl_4 are better acceptors of chloride ions compared to NbCl_4 . From this point of view, chlorides of Group IV elements (RfCl_4 , ThCl_4 , HfCl_4 , ZrCl_4) are 'better' than the corresponding chlorides of Group V elements (DbCl_4 , PaCl_4 , TaCl_4 , NbCl_4). However, UCl_4 is a better acceptor of chloride ions than SgCl_4 , MoCl_4 and WCl_4 , while NpCl_4 and PuCl_4 are better acceptors of chloride ions compared to BhCl_4 and HsCl_4 .

Some experimental studies on the chemistry of Rf, Db and Sg revealed nonmonotonic changes in the properties in the order 4*d* > 6*d* > 5*d*. 'Prediction of an inverse trend for the properties on going from the 5*d*-elements to the 6*d*-elements' was stated¹⁵ to be a new effect in chemistry. Theoretically, inversion was rationalised by the influence of Re on TAn; however, trends observed experimentally in the chemistry of the 3*d*-, 4*d*-, 5*d*- and 5*f*-elements are not reduced only to inversion. For instance, studying the above-mentioned property, viz. the affinity of tetrahalides towards chloride ions, reveals different trends.

The affinities of crystalline TAn tetrachlorides toward chloride ions, $A(\text{Cl}^-, \text{c})$, are listed in Table 2. They are less negative than the corresponding $A(\text{Cl}^-, \text{g})$ values.

VI. Solution behaviour of transactinides

A series of earlier and more recent studies concerned with the investigation of the nitrate, fluoride and chloride complexes of the *d*-elements including An was reported.^{12, 15, 16, 18, 92-140} Recently, TAn complexes have been studied along with complexes of the 4*d*-, 5*d*- and 5*f*-elements. The behaviour of the compounds of the 4*d*- and 5*d*-elements in aqueous solutions was previously investigated by extraction in a two-phase system; this method has been used so far in studies of the 4*d*-, 5*d*- and 6*d*-elements. For as long as four or five decades, Zr and Hf have been extracted from solutions of mineral acids (HCl , HNO_3 , HClO_4) by tri-*n*-butyl phosphate (TBP), which is also used for extraction of Zr and Hf with Rf additives in order to compare the stability of neutral complexes (RfCl_4)_{aq}, (HfCl_4)_{aq} and (ZrCl_4)_{aq}. Previously, the influence of hydrolysis on the complexation and extraction of Zr^{IV} and Hf^{IV} was studied; recently, Rf^{IV} has been the subject of intensive research.

However, the conclusions drawn from the results of complexation investigations in the earlier and recent studies do not always coincide. In modern literature, the results are rationalised by the influence of RE and by specific features of single-atom experiments. We believe that there are also some other reasons for inconsistency between the recent and previously obtained results. They are discussed below.

1. Anionic chloride complexes

Quaternary ammonium salts are known to be extractants of Zr^{IV} and Hf^{IV} in the form of anions. Early studies revealed inhibition of both hydrolysis and polymerisation in the aqueous phase in the acid medium at a low concentration of cations.¹⁴⁰ These conditions are similar to those of the experiments with TAn (studies of the behaviour of single atoms) and their homologues within groups of the Periodic system. Extraction studies in the two-phase system using quaternary ammonium salts as extractants demonstrated^{92,93} that Rf, Hf and Zr form anionic MCl_6^{2-} complexes which are more stable than AnCl_6^{2-} complexes. It was also revealed⁹⁴ that the RfCl_6^{2-} anion is more stable than the HfCl_6^{2-} and ZrCl_6^{2-} anions. The stability of $\text{MCl}_6^{2-}(\text{aq})$ anions for Group IV elements was shown to increase on going from the light to heavy elements.²¹ For instance, the $\Delta_f H^\circ(\text{MCl}_6^{2-}, \text{aq})$ for Zr, Hf and Rf are -1473 , -1577 and -1637 kJ mol⁻¹, respectively. Thus, the stability of the anions increases in the order $\text{ZrCl}_6^{2-} < \text{HfCl}_6^{2-} < \text{RfCl}_6^{2-}$, which is consistent with the results of earlier studies.^{92–94} It was also found that, despite greater stability of the $\text{MCl}_6^{2-}(\text{aq})$ anions ($\text{M} = \text{TAn}$) compared to the corresponding anions containing the 4d- and 5d-elements, no monotonic increase in stability on going from the 4d-elements to the 6d-elements is observed for all groups of the Periodic table. In particular, a nonmonotonic change in the thermodynamic stability of $\text{MCl}_6^{2-}(\text{g})$ and $\text{MCl}_6^{2-}(\text{aq})$ anions in the order $\text{Sg} > \text{Mo} > \text{W}$ is predicted for the Group VI elements.

2. Neutral chloride complexes

It was pointed out^{15,19} that the results of experimental extraction studies of neutral chloride complexes of Rf from concentrated (8–12 M) HCl solutions in TBP, obtained by different authors^{12, 15, 16, 19, 116, 129–132} contradict one another. It was suggested¹² that the extraction behaviour of Rf is similar to that of Th and Pu rather than Zr and Hf. Recently reported^{19, 130} extractive power sequences corresponding to the changes in stability of neutral complexes are different, that is $\text{Zr} > \text{Rf} > \text{Hf}$ (see Ref. 19) and $\text{Zr} > \text{Hf} > \text{Rf}$ (see Ref. 130). From the standpoint of the ability of the Zr, Hf and Rf complexes to undergo hydrolysis, these elements can be ordered as follows: $\text{Hf} > \text{Rf} > \text{Zr}$ (see Ref. 19). Competition between hydrolysis and formation of inner-sphere complexes during extraction was suggested^{15,19}



It is believed¹⁵ that no extraction of the hydrolysed complexes occurs in the organic phase because of the formation of strong hydrogen bonds between OH^- and H_2O in the aqueous phase.

Generally, earlier experimental studies^{117–120, 133–136} revealed that under specific conditions hydrolysed complexes of both Zr^{IV} and Hf^{IV} are extracted along with non-hydrolysed complexes. It was also shown that hydrolysed compounds of Zr and Hf exist in weak acid solutions only at high concentrations of Zr^{IV} and Hf^{IV}.

It was postulated^{15,19} that the trend in the changes of the effective charges $q(\text{Zr}) > q(\text{Rf}) > q(\text{Hf})$ in gaseous MCl_4 molecules [$q(\text{ZrCl}_4) = 1.18$, $q(\text{RfCl}_4) = 1.07$ and $q(\text{HfCl}_4) = 1.04$] holds for all processes occurring in solution: the ability to undergo hydrolysis ($\text{Hf} > \text{Rf} > \text{Zr}$), the formation of complexes $\text{MCl}_4(\text{aq})$ ($\text{Zr} > \text{Rf} > \text{Hf}$) and extractive power ($\text{Zr} > \text{Rf} > \text{Hf}$). However, the accuracy of quantum-chemical calculations of the effective charges was shown⁹ to be by a factor of 25 to 30 lower than the difference between the charges q on Rf and Hf (± 1 vs. 0.03, respectively) which was used for the interpretation^{15,19} of proc-

esses occurring in solution. Therefore, the use of similar quantum-chemical approaches in this case is incorrect.

Previously,⁷⁰ it was found that HCl solutions contain mainly hydrolysed polymeric outer-sphere complexes $[\text{M}_4(\text{OH})_8(\text{H}_2\text{O})_{16}]\text{Cl}_8$ ($\text{M} = \text{Zr}, \text{Hf}$) stabilised due to the formation of M–M bonds and bridging M–OH–M bonds. These data contradict the hypothesis proposed by Kratz.¹⁵ Structural studies showed that in solution the metal atoms form trimeric and tetrameric clusters that also stabilise the hydrolysed complexes. Hydrolysed monomeric inner-sphere complexes are thermodynamically unstable in the absence of these stabilising factors in concentrated HCl solutions.

Specific conditions of experiments with single TAn atoms exclude the possibility of formation of hydrolysed cluster-like structures $[\text{TAn}_4(\text{OH})_8(\text{H}_2\text{O})_{16}]\text{Cl}_8$. Hydrolysed monomeric outer-sphere complexes $[\text{TAn}(\text{OH})_2(\text{H}_2\text{O})_4]\text{Cl}_2$ are unstable in this case. It should be noted that hydrolysis does not determine the extraction sequence in studies with single TAn atoms in concentrated HCl solutions.

Earlier studies^{133–136, 140} on extraction of Zr^{IV} and Hf^{IV} from concentrated acid solutions modelled modern experimental conditions. Therefore, the results obtained in these works can be used to support the idea proposed in this review that in the TAn chemistry hydrolysis does not determine the extraction sequence. In the above-mentioned studies, microamounts of Zr^{IV} and Hf^{IV} were used to inhibit both hydrolysis and formation of polymeric structures. The formation of simple adducts (MCl_4, aq) · 2 TBP in the organic phase under favourable conditions (concentrated acid solutions at low concentration of Zr^{IV} and Hf^{IV}) was revealed.^{134,135} This suggests that inner-sphere complexes $\text{RfCl}_4(\text{H}_2\text{O})_m$ are mainly formed in solution and that two H_2O molecules are replaced by two TBP molecules in extraction. Kacher *et al.*¹³⁰ studied extraction from 8 M HCl in TBP and experimentally established the extraction sequence $\text{Zr} > \text{Hf} > \text{Rf}$, which is due to the formation of more stable complexes $\text{RfCl}_4(\text{aq})$. Formation of hydrated complexes $\text{Rf}^{\text{IV}}(\text{H}_2\text{O})_x$ was postulated by Bilewicz *et al.*¹²²

One would suggest the existence of hydrated $\text{TAn}^{\text{IV}}(\text{aq})$ complexes [in particular, $\text{Rf}^{\text{IV}}(\text{aq})$] in specific conditions of single-atom experiments and estimate the $\Delta_f H^\circ(\text{TAn}^{\text{IV}}, \text{aq})$ and $\Delta_f H^\circ(\text{MCl}_4, \text{aq})$ values for TAn (see Table 2). For Group IV elements, the stability of $\text{M}^{\text{IV}}(\text{aq})$ and $\text{MCl}_4(\text{aq})$ increases nearly monotonically from Zr to Th: $\Delta_f H^\circ(\text{ZrCl}_4, \text{aq}) = -1139$, $\Delta_f H^\circ(\text{HfCl}_4, \text{aq}) = -1243$, $\Delta_f H^\circ(\text{RfCl}_4, \text{aq}) = -1303$ and $-\Delta_f H^\circ(\text{ThCl}_4, \text{aq}) = -1486$ kJ mol⁻¹.

Estimation of the hydrolysis constant for weak acid solutions seems to be of considerable interest. Gregorich¹² showed that the ability of Rf^{IV} to undergo hydrolysis is similar to that of An^{IV} rather than Hf^{IV} and Zr^{IV}. Using experimental data, it was found that the first hydrolysis constant, $\log K_H$, for the Rf^{IV} ion lies between the $\log K_H$ values of thorium and plutonium ions: $\log K_H(\text{Pu}^{\text{IV}}) > \log K_H(\text{Rf}^{\text{IV}}) > \log K_H(\text{Th}^{\text{IV}})$. A rough qualitative correlation between the ionic radii $r(\text{M}^{\text{IV}}, \text{CN} = 6)$ and $\log K_H(\text{M}^{\text{IV}})$ values, namely, a decrease in $\log K_H(\text{M}^{\text{IV}})$ with an increase in $r(\text{M}^{\text{IV}})$ can be observed:

Ion					Pu ^{IV}	Ce ^{IV}	U ^{IV}	Th ^{IV}
log <i>K</i> _H (M ^{IV})					−0.5	−0.7	−1.5	−3.2
Ion	Zr ^{IV}	Hf ^{IV}	Rf ^{IV}	Pu ^{IV}	Ce ^{IV}	U ^{IV}	Th ^{IV}	
<i>r</i> (M ^{IV})/Å	0.72	0.73	0.78	0.86	0.87	0.89	0.93	

The ionic radius of Rf lies between those of Zr–Hf and An. This reflects a qualitative similarity of Rf to An established in hydrolysis studies.¹²

3. Nitrate complexes

Recently,^{95,96} the stability of nitrate complexes of trivalent lanthanides was studied in the framework of the structural-thermodynamic model. Application of this model to stability studies of nitrate complexes of Zr^{IV}, Hf^{IV}, Rf^{IV}, Ce^{IV} and Th^{IV}

in weak acid solutions revealed that the formation of nitrate aqua complexes $[M(NO_3)_x]^{(4-x)+}$ ($M = \text{Zr, Hf, Rf, Pu, Ce, Th}$; $x = 1-3$) causes a decrease in ΔG° on going from Zr to Th.

Complexes	$\Delta G^\circ[M(NO_3)_x]^{(4-x)+}$					
	Zr	Hf	Rf	Pu	Ce	Th
$[MNO_3]^3+(\text{aq})$	1.4	+0.9	-1.4	-3.8	-4.5	-6.9
$[M(NO_3)_2]^{2+}(\text{aq})$	+6.0	+5.5	+0.4	-5.6	-6.7	-8.7

These results are consistent with those of earlier experimental studies,⁹⁷⁻¹⁰⁵ according to which Rf forms cationic outer-sphere complexes with NO_3^- anions in weak nitrate solutions more readily than Zr and Hf but with somewhat more difficulty than f-elements.

4. Fluoride complexes

In the framework of the same model the author of this review showed that the change in the free energy, ΔG° , in the formation of inner-sphere complexes $[MF]^{3+}(\text{aq})$ corresponds to an insignificant change in the ΔG° energy on going from Zr to Th. The $\Delta G^\circ\{[MF]^{3+}(\text{aq})\}$ values for $M = \text{Zr, Hf, Rf}$ and Th are -42.0 , -40.0 , -38.0 and $-36.0 \text{ kJ mol}^{-1}$, respectively. Therefore, based on the results of calculations of the stability of cationic complexes $[RfF]^{3+}(\text{aq})$, Rf is similar to its analogues and should be placed between Zr-Hf and Th, though the ΔG° values differ insignificantly. These theoretical results correlate with the $\Delta G_{\text{HF}}^\circ$ and $\Delta G_{\text{F}^-}^\circ$ values obtained in earlier experimental studies^{106-112, 139} of the formation of (i) cationic fluoride complexes of Zr, Hf and Th, *e.g.*, $\{[MF]^{3+}[\text{H}^+](\text{aq})\}$, by addition of HF molecule followed by elimination of a proton and (ii) complexes $[MF]^{3+}(\text{aq})$. In the case of formation of inner-sphere complexes $[MF]^{3+}(\text{aq})$, the fluoride ligand can be considered as an undissociated acid or an anion, which leads to different $\Delta G_{\text{HF}}^\circ$ and $\Delta G_{\text{F}^-}^\circ$ values for the same M (the difference is 5 to 10 kJ mol^{-1}). According to Tananaev,¹⁰⁶ the free energy changes by -34 kJ mol^{-1} upon the formation of the $[\text{ThF}]^{3+}(\text{aq})$ complex, whereas Ahrlund¹³⁹ reported a value of -44 kJ mol^{-1} . Based on these results, one can conclude that stabilities of the cationic complexes $[\text{ThF}]^{3+}(\text{aq})$, $[\text{HfF}]^{3+}(\text{aq})$ and $[\text{ZrF}]^{3+}(\text{aq})$ differ insignificantly. The experimental¹¹³⁻¹¹⁵ and calculated^{4, 21} stabilities (β) of the actinide complexes $[\text{AnF}]^{3+}(\text{aq})$ or $[\text{AnF}_2]^{2+}(\text{aq})$ suggest greater similarity of Rf to its analogues within the group (Hf and Zr) rather than to actinides:

$$\log \beta_2\{[\text{RfF}_2]^{2+}(\text{aq})\} = 7.7; \log \beta_2\{[\text{HfF}_2]^{2+}(\text{aq})\} = 7.8;$$

$$\log \beta_2\{[\text{PaF}_2]^{2+}(\text{aq})\} = 8.3; \log \beta_2\{[\text{UF}_2]^{2+}(\text{aq})\} = 12.4,$$

where β_2 is the stability constant of the complex containing two ligands.

Another conclusion was drawn from the sorption studies of Rf, Hf, Zr and Th in mixed HNO_3 -HF solutions on both cation and anion exchange columns.^{16, 18, 116} In the formation of fluoride complexes, Rf behaves in a different manner compared to Hf and Zr and is more similar to Th in accord with the decreasing stability of the complexes, $\text{Zr}^{\text{IV}} \approx \text{Hf}^{\text{IV}} > \text{Rf}^{\text{IV}} > \text{Th}^{\text{IV}}$. The trend was theoretically explained by the fact that F^- is a hard anion and better (stronger) interacts with small cations (Zr^{IV} and Hf^{IV}), whereas the behaviour of Rf is a direct consequence of RE.¹⁸

We believe that discussion of manifestations of RE in complexes of unknown chemical composition and type (fluoride, nitrate or mixed fluoride nitrate, inner-sphere or outer-sphere, *etc.*) is inadmissible. These statements discredit the basic idea of manifestation of relativism in chemical properties.

Based on the results of earlier studies,^{107, 117-120, 133-138} one can conclude that mixed rather than simple fluoride complexes are formed under experimental conditions reported by Shädel *et al.*^{16, 18, 116} A salient feature of the chemistry of Hf^{IV} and Zr^{IV} is a synergistic effect in the extraction of these elements from

solutions of two inorganic acids (HNO_3 -HF, HNO_3 -HCl, HNO_3 - HClO_4), that is, obtaining high separation coefficients of Zr^{IV} and Hf^{IV} as a result of the formation of mixed complexes upon addition of the second acid and variation of its concentration.^{99, 117-120, 133-139} The synergistic effect is due to the formation of the Zr^{IV} and Hf^{IV} complexes of different composition, on which lies the basis of the process of their separation by extraction from a mixture of two inorganic acids. Earlier studies of mixed complexes, *e.g.*, $\text{MF}_x(\text{NO}_3)_{4-x}$, revealed changes in the number x (*i.e.*, the F^-/NO_3^- ratio) depending on the metal (Zr^{IV} , Hf^{IV} , Th^{IV}). The existence of the complexes $\text{ZrF}(\text{NO}_3)_3$ (see Ref. 117), $\text{HfF}_2(\text{ClO}_4)_2$ (see Ref. 107), $\text{ZrCl}_{4-x}(\text{NO}_3)_x$ (see Ref. 118), $\text{M}(\text{NO}_3)_x(\text{ClO}_4)_{4-x}$ ($M = \text{Zr, Hf}$) (see Refs 119, 136-138), $\text{HfCl}_x(\text{ClO}_4)_{4-x}$ (see Refs 136-138), $\text{ZrCl}_5\text{NO}_3^{2-}$ (see Ref. 136), *etc.*, was established. Thus, comparison of earlier results on the complexation and extraction of Zr^{IV} , Hf^{IV} and Th^{IV} with recently obtained data for Rf^{IV} , Zr^{IV} , Hf^{IV} and Th^{IV} provides strong evidence that the authors of study¹⁸ did not take into account the results of earlier studies and were based on the assumptions that (i) NO_3^- anions are not involved in complexation and (ii) Zr^{IV} , Hf^{IV} , Th^{IV} and Rf^{IV} form the same type of fluoride complexes for all cations, which seems to be doubtful.¹³³⁻¹³⁹

The results of study¹⁸ were recently revised¹¹⁶ and the authors agreed that the NO_3^- anion may be involved in complex formation. However, their major conclusion that Rh is similar to Th and different from Zr and Hf in the formation of fluoride complexes remained unchanged.

The structure of neutral crystalline complexes $\text{MF}_4(\text{H}_2\text{O})_3$ ($M = \text{Hf, Zr}$) was studied by X-ray diffraction analysis.^{120, 121} Complex $\text{ZrF}_4(\text{H}_2\text{O})_3$ has a dimeric structure while complex $\text{HfF}_4(\text{H}_2\text{O})_3$ has a polymeric structure. For both complexes, the CN value equals 8 due to the formation of bridging bonds. The $\text{ZrF}_4(\text{H}_2\text{O})_3$ molecule has three $\text{Zr}-\text{OH}_2$ bonds and five $\text{Zr}-\text{F}$ bonds while the $\text{HfF}_4(\text{H}_2\text{O})_3$ molecule containing one molecule of bound water has six $\text{Hf}-\text{F}$ bonds and two $\text{Hf}-\text{OH}_2$ bonds. As can be seen, Hf exhibits higher affinity towards F^- than Zr. One can assume that this trend will be more pronounced on going to Rf. This is confirmed by the formation enthalpies, $\Delta_f H^\circ(\text{MF}_4, \text{c})$, of crystalline compounds, which decrease on going to heavier elements.

$\text{MF}_4(\text{c})$	ZrF_4	HfF_4	RfF_4
$\Delta_f H^\circ / \text{kJ mol}^{-1}$	-1912	-1930	-1997

The reliably proven¹²³⁻¹²⁷ existence of anionic form $[\text{RfF}_6]^{2-}$ is in good agreement with the chemical properties of the 4d- and 5d-elements. At the same time, it is known that, despite the predominance of the complexes $[\text{HfF}_6]^{2-}$ in acidic aqueous solutions with the HF : Hf ratio greater than 1, changes in this ratio can also result in other anionic forms. In this connection, it is pertinent to remember the study by Tananaev and Guzeva¹²⁸ who showed that the thermal stability of alkali metal salts of Zr and Hf changes in the order $[\text{MF}_7]^{3-} > [\text{MF}_6]^{2-} > [\text{MF}_5]^-$. In addition, Varga and Hume¹⁰⁷ revealed instability of $[\text{HfF}_5]^{2-}$ in solution. Taken together, these facts do not exclude the possibility of formation of not only $[\text{RfF}_6]^{2-}$, but also $[\text{RfF}_7]^{3-}$ in solution; however, this is only a hypothesis proposed by the author of this review.

VII. Standard formation enthalpies, $\Delta_f H^\circ(\text{A}_2\text{MCl}_6)$, of crystalline compounds

Standard formation enthalpies of crystalline compounds A_2MCl_6 with K^+ , Rb^+ and Cs^+ cations were obtained for many 4d- and 5d-elements.^{22, 26, 29, 30, 31, 49-55} For instance, the $\Delta_f H^\circ(\text{K}_2\text{MCl}_6, \text{c})$ values for K_2MCl_6 salts are known for all 5d-metals from Hf to Pt and for almost all 4d-metals. For the 3d-, 4d- and 5d-elements, the standard formation enthalpies of gaseous MCl_6^{2-} ions and crystalline salts K_2MCl_6 are linearly related. Knowing the standard formation enthalpies of gaseous MCl_6^{2-} ions for the 4d-, 5d- and 6d-elements and the experimental $\Delta_f H^\circ(\text{K}_2\text{MCl}_6, \text{c})$ values for the

4d- and 5d-elements, one can calculate the $\Delta_f H^\circ(\text{K}_2\text{MCl}_6, \text{c})$ parameters for TAn with an accuracy of $\pm 15 \text{ kJ mol}^{-1}$. The experimental $\Delta_f H^\circ(\text{K}_2\text{MCl}_6, \text{c})$, $\Delta_f H^\circ(\text{Rb}_2\text{MCl}_6, \text{c})$ and $\Delta_f H^\circ(\text{Cs}_2\text{MCl}_6, \text{c})$ values for compounds of the 3d-, 4d- and 5d-elements are related by simple relationships that can be used for calculating the $\Delta_f H^\circ$ values for compounds of the 6d-elements ($\Delta_f H^\circ$ are given in kJ mol^{-1})

$$\Delta_f H^\circ(\text{Rb}_2\text{MCl}_6, \text{c}) = 1.014 \Delta_f H^\circ(\text{K}_2\text{MCl}_6, \text{c}),$$

$$\Delta_f H^\circ(\text{Cs}_2\text{MCl}_6, \text{c}) = 0.983 \Delta_f H^\circ(\text{K}_2\text{MCl}_6, \text{c}) - 83.$$

The calculated formation enthalpies, $\Delta_f H^\circ(\text{K}_2\text{MCl}_6, \text{c})$, $\Delta_f H^\circ(\text{Rb}_2\text{MCl}_6, \text{c})$ and $\Delta_f H^\circ(\text{Cs}_2\text{MCl}_6, \text{c})$ of transactinide salts are listed in Table 2. The crystal lattice energies, $U(\text{A}_2\text{MCl}_6, \text{c})$, and the lattice constants, $a(\text{A}_2\text{MCl}_6, \text{c})$, are known to be linearly related.³⁰ Therefore, knowledge of the $\Delta_f H^\circ(\text{A}_2\text{MCl}_6, \text{c})$ values allows calculations of $U(\text{A}_2\text{MCl}_6, \text{c})$ and lattice constants $a(\text{A}_2\text{MCl}_6, \text{c})$ for transactinide salts with K^+ , Rb^+ and Cs^+ cations (see Table 1).

VIII. Conclusion

In this review we have shown that TAn possess dual properties, which can be similar to those of both the 4d- and 5d-elements and (in some instances) the early actinides. However, this similarity becomes less pronounced with an increase in $Z(\text{An})$ or $Z(\text{TAn})$. The volatility of the tetrahalides of early actinides becomes lower as the atomic number of An increases; however, it increases for compounds of the 4d- and 5d-elements. The greatest similarity is observed for the thermodynamic properties of Group IV elements (Zr–Hf–Rf–Th). The thermodynamic stability of halide compounds of tetravalent transactinides in the gaseous and crystalline states and in aqueous solution decreases with an increase in $Z(\text{TAn})$; however, it increases within particular groups of the Periodic table on going from the light to heavy elements.

A possible reason for the inconsistency between the results of earlier (1960–1970) and more recent (1990–2000) studies of the volatility of halides and oxyhalides of the d-elements and of extraction, hydrolysis and complexation in solution is that in transactinide chemistry the experimental data are interpreted in the framework of the hypothesis that RE cause changes in the chemical properties down the groups of the Periodic system. However, the influence of RE on the chemical properties of transactinides is to a great extent compensated by actinide contraction. It should be emphasised that no experimental data on the properties of TAn, which could be unambiguously interpreted as a manifestation of relativistic effects, have been reported so far.

Yet another reason for the above-mentioned inconsistency is the lack of methods that allow identification of the chemical composition of transactinide compounds formed. Single-atom experiments are carried out assuming complete analogy between the chemical properties of the 4d-, 5d- and 6d-elements within the groups of the Periodic system, i.e., the same type of compounds of the same composition (this is not always true). In the early studies the chemical composition of newly formed compounds of the 4d- and 5d-elements was thoroughly analysed and, as a rule, established.

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Generation of radicals by bimolecular reactions

E T Denisov, T G Denisova

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Abstract. The published data on bimolecular processes of radical generation in chain degradation, polymerisation, oxidation and halogenation reactions of organic compounds are systematised and analysed within the framework of the parabolic model of homolytic bimolecular reactions. The specific features of these highly endothermic reactions are discussed with a special emphasis on their striking similarity to radical abstraction processes with identical reaction centres in the transition state. The feasibility of theoretical evaluation of the activation energies and the rate constants of bimolecular reactions in radical generation is demonstrated. The bibliography includes 86 references.

I. Introduction

Initiators, light and penetrating radiation are widely used to induce chain reactions. However, it is known that chain reactions can also be generated in the absence of initiating factors. Very often, the role of free radical sources in chain degradation, oxidation, halogenation and polymerisation reactions is played by various bimolecular processes. This idea was first suggested by N N Semenov.¹ Studies of autoinitiation mechanisms of liquid-phase oxidation of hydrocarbons have shown that various bimolecular reactions of hydroperoxides with the original hydrocarbon and its oxidation products, such as alcohols, ketones and acids occur in the reaction medium. The rates of such reactions are several orders of magnitude higher than the rate of the homolytic cleavage of the weak O–O bond in ROOH.^{2–8} In the absence of the hydroperoxide, free radicals are formed in bi- and trimolecular reactions of oxygen with hydrocarbons involving the C–H and C=C bonds.^{2, 3, 5–10}

Generation of radicals by bimolecular reactions is largely endothermic and proceeds at a very slow rate. The methods for the study of their kinetics involve the use of free radical acceptors, inhibitors (in the case of oxidation reactions) or the rate of determination of the chain reactions triggered by bimolecular processes.^{2, 7, 9} If a chain reaction does not take place in the system under study, the rate of radical generation is judged upon by the decrement of one of reaction components. Studies of such reactions present difficulties which are not always overcome. The rates of such reactions are usually low because of high activation energies. In many cases, generation of radicals occurs in parallel by several bimolecular reactions and the rate of only one of them (as a rule, the fastest reaction) can be measured. Therefore, theoretical evaluation of rate constants for such reactions is an urgent task.

As bimolecular processes of radical formation are endothermic, the determination of their activation energies E is seemingly easy. The corresponding equation may appear as:

$$E \approx \Delta H,$$

where ΔH is the enthalpy of the reaction.¹ However, this condition is not always fulfilled. Strictly speaking, for endothermic reactions:

$$E = \Delta H + \Delta E,$$

the increment ΔE can be large enough ($\sim 10 \text{ kJ mol}^{-1}$) even for highly endothermic reactions ($\Delta H \geq 150 \text{ kJ mol}^{-1}$). The determination of the coefficient A (the pre-exponential factor) in the Arrhenius equation:

$$E = RT \ln \frac{A}{k},$$

which was found to be enthalpy-dependent, also presents a problem.¹¹ These difficulties were successfully overcome in the framework of the parabolic model of a bimolecular homolytic reaction. Earlier, we used this model for determining the activation energies of radical abstraction and addition reactions.^{12, 13} In more recent experiments, we used the parabolic model for the description of a vast variety of bimolecular homolytic reactions.^{14–28} The present review is devoted to the analysis and comparison of experimental and calculated data (e.g., activation

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energies and rate constants) for generation of radicals by homolytic bimolecular reactions.

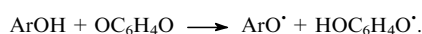
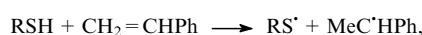
II. Classification of bimolecular reactions in radical generation

A bimolecular initiation reaction can dominate over the monomolecular decomposition of the reagent molecule involving the weakest bond, if $\Delta H < D_{\min}$ (where $D_{\min}$ is the bond stability).

In many bimolecular reactions, the energy of cleavage of a weak bond is compensated for by the energy of formation of a rather stable bond.

All known bimolecular homolytic reactions may be divided into three types:

1. Abstraction reactions of hydrogen or halogen (X) from the RH or the YX molecule by an acceptor molecule possessing a multiple bond (C=C, C $\equiv$ N, C=O, O=O, etc.), e.g.:

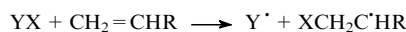


In the first reaction, the cleavage of the C–H bond is partly compensated for by the formation of the O–H bond in the hydroperoxide radical formed. For example, for the reaction where RH is cumene for which $D(\text{C–H}) = 335 \text{ kJ mol}^{-1}$ (D is the bond strength), the enthalpy is equal to 135 kJ mol^{-1} .

$$\Delta H = D(\text{C–H}) - D(\text{H–O}_2) = 355 - 220 = 135 \text{ kJ mol}^{-1}.$$

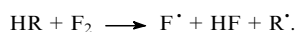
At the same time, the energy of the weakest bond C–CH₃ in cumene is equal to 300 kJ mol^{-1} . Hence, $\Delta H \ll D_{\min}$.

The X–X (or Y–X) bonds in halogen molecules are weak, while the C–X bonds in halide molecules are strong. Thus the bond energies of F₂, ICl and Cl₂ molecules are equal to 159, 211 and 243 kJ mol^{-1} , respectively. The enthalpy of the reaction:



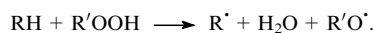
is low and is sometimes negative. Therefore, these reactions proceed rather rapidly. The role of halogen atom acceptors in such reactions is played by alkenes, alkynes, imines, nitriles and nitro compounds.

2. Dissociative abstraction reactions in which the cleavage of two bonds is accompanied by the formation of a molecule with a strong bond, e.g.:



Since the F–F bond is weak (159 kJ mol^{-1}) and the H–F bond is very strong (570 kJ mol^{-1}), for many hydrocarbons with $D(\text{C–H}) < 411 \text{ kJ mol}^{-1}$ this reaction is exothermic.

A similar situation is typical of bimolecular reactions involving hydrogen peroxide and hydroperoxides:

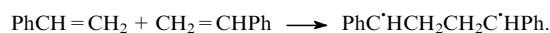


In these reactions, the energies of cleavage of two bonds (R–H and R'O–OH) are largely compensated for by the energy of formation of a stable O–H bond in the H₂O molecule (498 kJ mol^{-1}); in many cases, the change in the reaction enthalpy:

$$\Delta H = D(\text{O–H}) + D(\text{O–O}) - 498$$

is less pronounced than the change in the dissociation energy of the least stable O–O bond in the hydroperoxide molecule.

3. Reactions of biradical generation. The $\sigma\text{–C–C}$ bond of hydrocarbons is always stronger than the $\pi\text{–C–C}$ bond. For example, for the ethane molecule $D(\sigma\text{–C–C}) = 378 \text{ kJ mol}^{-1}$, whereas for the ethylene molecule $D(\pi\text{–C–C}) = 270 \text{ kJ mol}^{-1}$. In the presence of substituents at the double bond of a hydrocarbon molecule, a biradical is formed with relatively low energy consumption, e.g.:

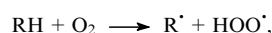


Chain reactions are initiated in the presence of active reagents, such as oxygen or a monomer (e.g., in polymerisation reactions).

Thus, the bimolecular reactions in radical generation are rather diverse: they involve C–H, N–H, O–H and S–H bonds of saturated molecules, on the one hand, and O₂, O₃, F₂, Cl₂ and other halogen-containing molecules, peroxides, disulfides and molecules containing multiple bonds, on the other hand.

III. The parabolic model of a bimolecular reaction

Generation of radicals by a bimolecular homolytic reaction, such as:



is interpreted within the framework of the parabolic model^{12, 13} as a result of intersection of two parabolic potential curves plotted on the coordinates of the amplitude of the stretching vibration of atoms involved in bond formation *versus* potential energy. The main parameters of this reaction are as follows:

1. Reaction enthalpy ΔH_e which includes the difference between the zero-point vibrational energies of the reacting bonds:

$$\Delta H_e = D_i - D_f + 0.5hN_A(v_i - v_f), \quad (1)$$

where D_i and D_f are dissociation energies and v_i and v_f are the stretching vibration frequencies of the bond that is cleaved (i) and of the bond that is formed (f), respectively, h is Planck's constant and N_A is Avogadro's number.

2. Activation energy E_e which includes the zero-point vibrational energy of the bond being attacked:

$$E_e = E + 0.5(hN_A v_i - RT), \quad (2)$$

where E is the experimental activation energy.

3. Distance r_e which is equal to the sum of the amplitudes of stretching vibrations of the reacting bonds in the transition state.

4. Dynamic characteristics of the bond that is cleaved (b_i) and that is formed (b_f):

$$b_i = \pi v_i (2\mu_i)^{1/2},$$

$$b_f = \pi v_f (2\mu_f)^{1/2},$$

where μ_i and μ_f are the reduced masses of the atoms forming these bonds and $2b^2$ is the force constant of the bond.

The above parameters are related to one another by the following expression:

$$br_e = \alpha \sqrt{E_e - \Delta H_e} + \sqrt{E_e}, \quad (3)$$

where $\alpha = b_i/b_f$, $b = b_i$.

By using the parameter br_e , it is possible to calculate the activation energy of the thermally neutral reaction E_{e0} :

$$\sqrt{E_{e0}} = \frac{br_e}{1 + \alpha}, \quad (4)$$

which is characteristic of the whole class of reactions with $br_e = \text{const}$.

As a rule, the coefficient A in the Arrhenius equation (calculated in relation to one reacting bond) for the same class of reactions is the same, which makes it possible to calculate E from the rate constant k :

$$E = RT \ln \left(n \frac{A}{k} \right), \quad (5)$$

where n is the number of reacting bonds.

Since in all elementary reactions $E > 0$, relation (3) is fulfilled for $\Delta H_e > \Delta H_{e \min}$. If $\Delta H_e < \Delta H_{e \min}$, the activation energy E is very small and is equal to $0.5 RT$.¹¹

In the case of highly endothermic reactions, the activation energy and the enthalpy are very close.¹¹ According to the parabolic model, for $\Delta H_e > \Delta H_{e \max}$:

$$E = \Delta H + 0.5 RT. \quad (6)$$

The threshold value of $\Delta H_{e \max}$ is related to parameters which characterise a certain class of reactions by the following expression:¹²

$$\Delta H_{e \max} = (br_e)^2 - 2\alpha br_e \sqrt{0.5hN_A v_f} + 0.5hN_A v_f (\alpha^2 - 1). \quad (7)$$

If reactions with high enthalpy ($\Delta H_e > \Delta H_{e \max}$) belong to the same class, the pre-exponential factor A is not constant, but rather is a function of reaction enthalpy. Within the framework of the parabolic model, this dependence appears as:¹¹

$$A = A_0 \left[1 + \beta \left(\sqrt{\Delta H_e} - \sqrt{\Delta H_{e \max}} \right) \right]^2, \quad (8)$$

where $\beta = 1.3$.

If a reaction belongs to a class described by kinetic parameters (A , r_e , b , b_i , b_f , α , $1/2hN_A v_i$, $1/2hN_A v_f$), its rate constant and activation energy can be calculated from the formula:

$$k = n A_0 \exp \left(-\frac{E}{RT} \right), \quad (9)$$

as well as from the ratio given below.¹²

For reactions with $\Delta H_e < \Delta H_{e \max}$:

for $\alpha = 1$:

$$\sqrt{E_e} = \frac{br_e}{2} + \frac{\Delta H_e}{2br_e}, \quad (10)$$

for $\alpha \neq 1$:

$$\sqrt{E_e} = \frac{br_e}{1 - \alpha^2} \left[1 - \alpha \sqrt{1 - \frac{1 - \alpha^2}{(br_e)^2} \Delta H_e} \right], \quad (11)$$

for low values of α , where $\Delta H_e(1 - \alpha^2) \ll (br_e)^2$:

$$\sqrt{E_e} = \frac{br_e}{1 + \alpha} + \frac{\alpha \Delta H_e}{2br_e}. \quad (12)$$

For reactions with $\Delta H_e > \Delta H_{e \max}$, the activation energy is calculated by the formula (6) and the rate constant is calculated by the formula (13) taking into account the dependence of the pre-exponential factor on ΔH_e :

$$k = A_0 e^{-1/2} \left[1 + \beta \left(\sqrt{\Delta H_e} - \sqrt{\Delta H_{e \max}} \right) \right]^2 \exp \left(-\frac{\Delta H}{RT} \right). \quad (13)$$

The calculations of activation energies and rate constants of bimolecular homolytic reactions should take into consideration the following factors.

1. If the enthalpy of the reaction is such that $\Delta H_e < \Delta H_{e \max}$, then $E > \Delta H$ and the activation energy should be calculated by one of the formulae (10)–(12). In its turn, the threshold value of $\Delta H_{e \max}$ depends on parameters α , r_e , b and the zero-point vibrational energy of the bond that is cleaved. It should be borne in mind that the threshold value of $\Delta H_{e \max}$ varies widely for different classes of reactions. The dependencies of the difference $E - \Delta H$ on ΔH for four classes of reactions are shown in Fig. 1. As can be seen, in the range where $E > \Delta H$ on going from $\text{XCl} + \text{RH}$ to $\text{ROOH} + \text{RH}$ reactions, the enthalpies of the reactions vary from ~ 20 to 250 kJ mol^{-1} , i.e., by more than one order of magnitude. Consequently, before one uses a simple formula (6) for the calculation of activation energies, it is necessary to be sure that $\Delta H_e > \Delta H_{e \max}$. However, in this case the pre-exponential factor in the Arrhenius plot depends on ΔH (i.e., $A \neq \text{const}$) due to the intersection of potential curves of the reacting bonds at a

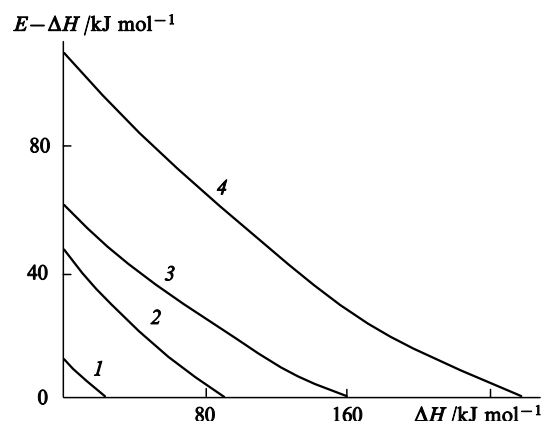


Figure 1. The dependence of the difference $E - \Delta H$ on the enthalpy ΔH for the reactions $\text{XCl} + \text{RH}$ (1), $\text{XF} + \text{RH}$ (2), $\text{RCH}=\text{CH}_2 + \text{RH}$ (3), $\text{ROOH} + \text{RH}$ (4).

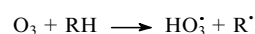
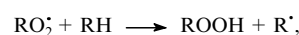
distance exceeding r_e , and the dependence is described by the formula (8), while the rate constant is described by the formula (13).

2. Bimolecular reactions with cleavage of two bonds differ from those in which only one bond is cleaved. In the latter case, the probability of concentration of the activation energy on one bond is expressed by the exponential function $\exp(-E/RT)$. If two bonds are cleaved, the probability of simultaneous concentration of energy on the both cleavable bonds manifests a more complex dependence on E . The rate constant for such a reaction is expressed by the formula:²⁹

$$k = A_0 \left(\frac{2RT}{\pi E} \right)^{1/2} \exp \left(-\frac{E}{RT} \right). \quad (14)$$

Within the framework of the parabolic model, the activation energy for the above-described case can be presented in an alternative way. For example, the activation energy of the reaction of RH with F_2 can be characterised by the coordinate of the point of intersection of the potential curves for $\text{R}-\text{H}$ and $\text{H}-\text{F}$ or $\text{F}-\text{F}$ and $\text{H}-\text{F}$ bonds. Naturally, the kinetic characteristics of the same reaction will be different. Preference in such cases will be given to the variant where both bonds (i.e., that is cleaved and that is formed) involve a light atom.

3. The kinetic parameters, e.g., br_e , can be determined from the experimental data only for reactions where $\Delta H_e < \Delta H_{e \max}$. Unfortunately, such reactions are very few in number. It is noteworthy that bimolecular radical and molecular reactions are similar.^{25–27} If such reactions have identical reaction centres, their main characteristics (α , br_e , E_{e0} and $0.5hN_A v$) are also identical or similar. For example, the reactions:

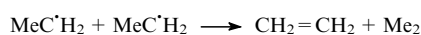


are characterised by the same set of parameters:^{12,14} $br_e = 13.61 \text{ (kJ mol}^{-1}\text{)}^{1/2}$, $\alpha = 0.814$, $0.5hN_A v = 17.4 \text{ kJ mol}^{-1}$, $0.5hN_A(v_i - v_f) = -3.8 \text{ kJ mol}^{-1}$ and $E_{e0} = 56.3 \text{ kJ mol}^{-1}$. This makes it possible to estimate the activation energies and rate constants for homolytic reactions of the 'molecule + molecule' type by using the known parameters of reactions (with an analogous reaction centre) of the 'radical + molecule' type. Examples of generation of radicals by such bimolecular reactions and their analogues, viz., radical reactions characterised by the same set of parameters, are given below.

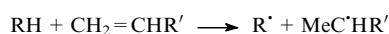
Bimolecular homolytic reaction	Radical reaction, an analogue of the bimolecular reaction
$\text{RCH}=\text{CH}_2 + \text{R}'\text{H} \longrightarrow \text{RC}'\text{HMe} + \text{R}''$	$\text{R}' + \text{R}'\text{H} \longrightarrow \text{RH} + \text{R}''$
$\text{R}'\text{R}''\text{C}=\text{O} + \text{RH} \longrightarrow \text{R}'\text{R}''\text{C}'\text{OH} + \text{R}'$	$\text{RO}' + \text{R}'\text{H} \longrightarrow \text{ROH} + \text{R}''$
$\text{OC}_6\text{H}_4\text{O} + \text{RH} \longrightarrow \text{HOC}_6\text{H}_4\text{O}' + \text{R}'$	$\text{ArO}' + \text{RH} \longrightarrow \text{ArOH} + \text{R}'$
$\text{F}_2 + \text{RH} \longrightarrow \text{F}' + \text{HF} + \text{R}'$	$\text{F}' + \text{RH} \longrightarrow \text{HF} + \text{R}'$
$\text{F}_2 + \text{CH}_2=\text{CHR} \longrightarrow \text{F}' + \text{CH}_2\text{FC}'\text{HR}$	$\text{F}' + \text{CH}_2=\text{CHR} \longrightarrow \text{CH}_2\text{FC}'\text{HR}$
$\text{Cl}_2 + \text{RH} \longrightarrow \text{Cl}' + \text{HCl} + \text{R}'$	$\text{Cl}' + \text{RH} \longrightarrow \text{HCl} + \text{R}'$
$\text{Cl}_2 + \text{CH}_2=\text{CHR} \longrightarrow \text{Cl}' + \text{CH}_2\text{ClC}'\text{HR}$	$\text{Cl}' + \text{CH}_2=\text{CHR} \longrightarrow \text{CH}_2\text{ClC}'\text{HR}$
$\text{O}_2 + \text{RH} \longrightarrow \text{HO}_2' + \text{R}'$	$\text{RO}_2' + \text{RH} \longrightarrow \text{ROOH} + \text{R}'$
$\text{O}_3 + \text{RH} \longrightarrow \text{HO}_3' + \text{R}'$	$\text{RO}_2' + \text{RH} \longrightarrow \text{ROOH} + \text{R}'$
$\text{O}_2 + \text{CH}_2=\text{CHR} \longrightarrow \text{'OOCH}_2\text{C}'\text{HR}$	$\text{RO}_2' + \text{CH}_2=\text{CHR} \longrightarrow \text{'OOCH}_2\text{C}'\text{HR}$
$\text{ROOH} + \text{ROOH} \longrightarrow \text{RO}' + \text{H}_2\text{O} + \text{RO}_2'$	$\text{R}'\text{R}''\text{C}'\text{OH} + \text{ROOH} \longrightarrow \text{R}'\text{R}''\text{C}=\text{O} + \text{H}_2\text{O} + \text{RO}'$
$\text{RH} + \text{ROOH} \longrightarrow \text{R}' + \text{H}_2\text{O} + \text{RO}'$	$\text{RC}'\text{HMe} + \text{ROOH} \longrightarrow \text{RCH}=\text{CH}_2 + \text{H}_2\text{O} + \text{RO}'$
$\text{RCH}=\text{CH}_2 + \text{R}'\text{OOH} \longrightarrow \text{RC}'\text{HCH}_2\text{OH} + \text{R}'\text{O}'$	$\text{R}' + \text{ROOH} \longrightarrow \text{ROH} + \text{RO}'$

IV. Retrodisproportionation reactions

Disproportionation of alkyl radicals proceeds at a very fast rate which is close to the rate of molecular collisions in the gas phase and the diffusion-controlled rate in the liquid phase.³⁰ Disproportionation is a highly exothermic reaction, *e.g.*, ΔH for the disproportionation of ethyl radicals:



is equal to -270 kJ mol^{-1} . The reverse reaction, *i.e.*, retrodisproportionation:



represents an endothermic process which proceeds at a very slow rate. The retrodisproportionation reactions investigated in great detail by Ruchardt *et al.*^{10, 31–37} play a prominent role in chain processes of hydrocarbon cracking, polymerisation and oxidation. The activation energies and enthalpies of such reactions were found to be very similar. The attack of an alkene on the weak C–H bond of the hydrocarbon playing the role of a hydrogen donor is consistent with the kinetic isotope effect.³¹ The solvent polarity weakly affects the rate constant for this reaction. However, the rates of reactions in which the role of a hydrogen acceptor is played by benzoquinone strongly depend on the solvent polarity. The values of experimentally determined rate constants and activation energies for reactions of alkenes and benzoquinone with 9,10-dihydroanthracene are given in Table 1.

The structures of reaction centres of retrodisproportionation and radical abstraction reactions are similar: $\text{C}=\text{C}\cdots\text{H}\cdots\text{R}$ and $-\text{C}\cdots\text{H}\cdots\text{R}$. This circumstance was taken into consideration in the calculations based on the use of the parabolic model.¹⁵ The kinetic and thermodynamic parameters of the corresponding disproportionation reactions are given in Tables 2 and 3.[†]

[†] The alkyl, allyl and benzyl radicals in the Tables are designated as R^1 , R^2 and R^3 , respectively.

Table 1. The activation energies and rate constants for the retrodisproportionation reaction of 9,10-dihydroanthracene with alkenes (PhOPh is used as solvent).^{31–37}

Alkene	T/K	E	$\log A$	$k(550 \text{ K})$
Styrene	553–583	111.5	6.60	1.02×10^{-4}
2-Phenylbut-1-ene	553–583	149.1	9.48	2.09×10^{-5}
3-Methyl-2-phenylbut-1-ene	553–583	131.1	7.67	1.66×10^{-5}
3,3-Dimethyl-2-phenylbut-1-ene	553–583	148.3	8.32	1.72×10^{-6}
2,6-Dimethylstyrene	553–583	139.5	8.08	6.78×10^{-6}
1,1-Diphenylethylene	553–583	139.9	9.39	1.27×10^{-4}
1,2-Diphenylethylene	553–583	162.1	9.72	2.11×10^{-6}
Acenaphthene	553–583	114.8	7.36	2.87×10^{-4}
Indene	553–583	155.8	9.70	8.01×10^{-6}
1,2-Dihydronaphthalene	553–583	154.5	9.56	7.71×10^{-6}
2,2-Dimethyl-1-methylideneindane	553–583	132.8	8.50	7.72×10^{-5}
2,2-Diethyl-1-methylideneindane	553–583	139.1	9.13	8.31×10^{-5}
Dibenzofulvene	553–583	96.8	7.10	8.07×10^{-3}
9-Ethylidenefluorene	553–583	130.3	9.22	7.00×10^{-4}
9-Isopropylidenefluorene	553–583	141.2	9.11	5.01×10^{-5}
9-(1,1-Dicyanoethyl)-fluorene	553–583	139.9	9.17	7.65×10^{-5}
Triphenylethylene	553–583	155.0	9.02	1.99×10^{-6}
Cyclohexa-1,3-diene	553–583	129.0	8.30	1.12×10^{-4}
Cycloheptatriene	553–583	137.8	8.71	4.20×10^{-5}
2,4,4-Triacetoxylbut-1-ene	553–583	137.8	8.13	1.10×10^{-5}
Azobenzene	463–523	112.0	8.43	6.21×10^{-3}
4,4'-Dimethylazobenzene	463–523	111.2	8.16	3.97×10^{-3}
4,4'-Di- <i>tert</i> -butylazobenzene	463–523	115.0	8.67	5.60×10^{-3}
4,4'-Dimethoxyazobenzene	463–523	116.6	8.51	3.11×10^{-3}
4,4'-Dichloroazobenzene	463–523	115.0	9.08	1.44×10^{-2}
4,4'-Dibromoazobenzene	463–523	119.6	9.73	2.35×10^{-2}
4,4'-Diaminoazobenzene	463–523	121.3	8.82	1.99×10^{-3}
2,3-Dichloro-5,6-dicyano-1,4-benzoquinone ^a	298–338	51.56	7.11	1.62×10^2
2,3-Dichloro-5,6-dicyano-1,4-benzoquinone ^b	298–338	37.4	5.11	36.2
2,3-Dichloro-5,6-dicyano-1,4-benzoquinone ^c	298–338	43.6	6.28	1.37×10^2

Note. Hereinafter, the dimensionalities of the activation energies, the pre-exponential factor A and the rate constants are kJ mol^{-1} , $\text{litre mol}^{-1} \text{ s}^{-1}$ and $\text{litre mol}^{-1} \text{ s}^{-1}$. ^a In dioxane; ^b in acetonitrile; ^c in acetic acid, respectively.

The enthalpies for the retrodisproportionation reactions involving hydrogen acceptors, such as ethylene, but-1-ene, cyclohexa-1,3-diene, *etc.*, are listed in Table 4; the calculated rate constants and activation energies of retrodisproportionation reactions involving styrene and benzoquinone as hydrogen acceptors are given in Tables 5 and 6. The results of these calculations are in good agreement with the experimental data. For example, the calculated and experimental values of $k(550 \text{ K})$ for the retrodisproportionation of styrene with 9,10-dihydroanthracene are equal to 9.2×10^{-5} and $1.0 \times 10^{-4} \text{ litre mol}^{-1} \text{ s}^{-1}$, respectively.³¹

Table 2. The kinetic parameters of retrodisproportionation reactions.¹⁵

HY	α	$10^{-11} b$	$0.5 h N_A v_i$	$0.5 h N_A (v_i - v_f)$	$(r^\#/r_e)_0$	HY	α	$10^{-11} b$	$0.5 h N_A v_i$	$0.5 h N_A (v_i - v_f)$	$(r^\#/r_e)_0$
$RCH=CH_2 + HY \longrightarrow RC^{\cdot}HCH_3 + Y^{\cdot}$						$R'R''C=O + HY \longrightarrow R'R''C^{\cdot}OH + Y^{\cdot}$					
HR	1.000	3.743	17.4	0.0	0.500	HR	0.796	3.743	17.4	-4.3	0.557
HNR ₂	1.150	4.306	20.0	2.6	0.465	HNR ₂	0.916	4.306	20.0	-1.7	0.522
HOR	1.256	4.701	21.7	4.3	0.443	HOR	1.00	4.701	21.7	0.0	0.500
HOOR ¹	1.229	4.600	21.2	3.8	0.449	HOOR	0.978	4.600	21.2	-0.5	0.505
HSiR ₃	0.767	2.871	13.1	-4.3	0.566	HSiR ₃	0.611	2.871	13.1	-8.6	0.621
HSR	0.808	3.026	13.8	-3.6	0.553	HSR	0.644	3.026	13.8	-7.9	0.608
HGeR ₃	0.747	2.796	12.6	-4.8	0.572	HGeR ₃	0.595	2.796	12.6	-9.1	0.627
HSnR ₃	0.720	2.695	12.1	-5.3	0.581	HSnR ₃	0.573	2.695	12.1	-9.6	0.636
$RC\equiv CH + HY \longrightarrow RC^{\cdot}=CH_2 + Y^{\cdot}$						$RCH=NR' (RN=NR, RC\equiv N) + HY \longrightarrow$ $\longrightarrow RC^{\cdot}HNHR' (RNHN'R, RC^{\cdot}=NH) + Y^{\cdot}$					
HR	0.945	3.743	17.4	-1.0	0.514	HR	0.869	3.743	17.4	-2.6	0.535
HNR ₂	1.087	4.306	20.0	1.6	0.479	HNR ₂	1.000	4.306	20.0	0.0	0.500
HOR	1.187	4.701	21.7	3.3	0.457	HOR	1.092	4.701	21.7	1.7	0.478
HOOR	1.161	4.600	21.2	2.8	0.463	HOOR	1.068	4.600	21.2	1.2	0.484
HSiR ₃	0.725	2.871	13.1	-5.3	0.580	HSiR ₃	0.667	2.871	13.1	-6.9	0.600
HSR	0.764	3.026	13.8	-4.6	0.567	HSR	0.703	3.026	13.8	-6.2	0.587
HGeR ₃	0.706	2.796	12.6	-5.8	0.586	HGeR ₃	0.649	0.279	12.6	-7.4	0.606
HSnR ₃	0.680	2.695	12.1	-6.3	0.595	HSnR ₃	0.626	2.700	12.1	-7.9	0.615

Note. Hereinafter, the dimensions of parameters b , $0.5hN_A v_i$ and $0.5hN_A (v_i - v_f)$ are $(\text{kJ mol}^{-1})^{1/2} \text{ m}^{-1}$ and kJ mol^{-1} , respectively; $r^\#$ is the amplitude of the oscillation of the bond that is cleaved in the transition state; the ratio $(r^\#/r_e)_0$ is given for the condition $\Delta H = 0$.

Table 3. The kinetic and thermodynamic parameters of retrodisproportionation reactions.

HY	br_e	E_{c0}	$10^{-8} A_0$	$\Delta H_{c \text{ max}}$	HY	br_e	E_{c0}	$10^{-8} A_0$	$\Delta H_{c \text{ max}}$
$RCH=CH_2 + HY \longrightarrow RC^{\cdot}HCH_3 + Y^{\cdot}$ (see Refs 26 and 27)					$PhCH=CH_2 + HY \longrightarrow PhC^{\cdot}HCH_3 + Y^{\cdot}$ (see Refs 26 and 27)				
R ¹ H	17.30	74.8	10	155.0	HNR ₂	18.64	75.2	1.2	174.2
R ² H	18.60	86.5	1.0	190.8	HOR	16.96	56.5	1.0	120.0
R ³ H	17.80	79.2	1.0	168.3	HOOR	17.60	62.3	1.0	138.1
H ₂ NR	17.14	63.5	1.2	135.0	HSiR ₃	13.54	58.7	10	102.8
HNR ₂	18.07	70.6	1.2	158.8	HSR	12.00	44.0	2.0	57.1
HOR	16.46	53.2	1.0	108.5	HGeR ₃	14.18	65.9	10	120.3
HOOR	16.73	56.3	1.0	117.2	HSnR ₃	14.03	66.5	10	120.7
HSiR ₃	13.18	55.6	10	95.1	$RC\equiv CH + HY \longrightarrow RC^{\cdot}=CH_2 + Y^{\cdot}$ (see Refs 26 and 27)				
HSR	11.80	42.6	2.0	53.7	R ¹ H	16.88	75.3	10	146.1
HGeR ₃	13.82	62.6	10	112.1	R ² H	18.18	87.4	1.0	181.1
HSnR ₃	13.67	63.2	10	112.6	R ³ H	17.18	78.0	1.0	153.9
$RCH=CHCH=CH_2 + HY \longrightarrow RCH=CHC^{\cdot}HCH_3 + Y^{\cdot}$ (see Refs 26 and 27)					H ₂ NR	16.72	64.2	1.2	127.0
R ¹ H	18.60	86.5	10	190.8	HNR ₂	17.65	71.5	1.2	150.2
R ² H	19.25	92.6	1.0	210.0	HOR	15.95	53.2	1.0	99.5
R ³ H	18.85	88.8	1.0	198.1	HOOR	16.22	56.3	0.1	107.9
H ₂ NR	18.64	75.2	1.2	174.2	HSiR ₃	12.00	48.4	10	74.8
HNR ₂	19.57	82.8	1.2	200.8	HSR	11.38	41.6	0.2	47.2
HOR	17.76	62.0	1.0	139.4	HGeR ₃	12.56	54.2	10	88.5
HOOR	18.68	70.2	1.0	166.4	HSnR ₃	12.62	56.4	10	93.1
HSiR ₃	14.12	64.6	10	115.6	$R'R''C=O + HY \longrightarrow R'R''C^{\cdot}OH + Y^{\cdot}$ (see Refs 26 and 27)				
HSR	12.32	46.4	2.0	62.7	R ¹ H	13.10	53.2	10	66.6
HGeR ₃	14.76	71.4	10	134.0	R ² H	14.14	62.0	1.0	87.1
HSnR ₃	14.65	72.5	10	135.4	R ³ H	13.50	56.5	1.0	74.2
$PhCH=CH_2 + HY \longrightarrow PhC^{\cdot}HCH_3 + Y^{\cdot}$ (see Refs 26 and 27)					H ₂ NR	11.95	38.9	1.0	37.3
R ¹ H	17.80	79.2	10	168.3	HNR ₂	12.88	45.2	10	52.4
R ² H	18.45	85.1	1.0	186.5	HOR	13.62	46.4	10	61.3
R ³ H	18.05	81.4	1.0	175.2	HOOR	14.13	51.0	10	70.1
H ₂ NR	17.71	67.8	1.2	149.3	HSiR ₃	10.13	39.5	10	49.6
					HSR	10.39	39.9	10	32.9

Table 3 (continued).

HY	br_e	E_{e0}	$10^{-8}A_0$	$\Delta H_{e\max}$	HY	br_e	E_{e0}	$10^{-8}A_0$	$\Delta H_{e\max}$
$R'R''C=O + HY \longrightarrow R'R''C'OH + Y^*$ (see Refs 26 and 27)					$RCH=NPh + HY \longrightarrow RC'HNNHPh + Y^*$ (see Ref. 28)				
HGeR ₃	10.56	43.8	10	58.8	H ₂ NR	19.10	91.2	4.0	194.0
HSnR ₃	11.00	48.9	10	69.0	HNR ₂	20.00	100.0	2.0	221.1
$RCH=NH + HY \longrightarrow RC'HNH_2 + Y^*$ (see Ref. 28)					HOR	13.45	41.3	0.2	87.5
R ¹ H	14.90	63.6	1.5	101.3	HOOR	11.94	33.3	0.2	31.3
R ² H	16.21	75.2	0.15	131.9	HSiR ₃	9.54	32.8	1.5	23.0
R ³ H	15.40	67.9	0.15	112.5	HSR	7.85	21.2	0.2	2.1
H ₂ NR	21.00	110.2	4.0	253.2	HGeR ₃	10.36	39.5	1.5	35.6
HNR ₂	21.90	119.9	2.0	283.7	HSnR ₃	9.15	31.7	1.5	20.3
HOR	13.05	38.9	0.2	46.7	$RC\equiv N + HY \longrightarrow RC'=NH + Y^*$ (see Ref. 28)				
HOOR	11.54	31.1	0.2	25.7	R ¹ H	15.33	67.3	3.0	111.0
$RCH=NH + HY \longrightarrow RC'HNH_2 + Y^*$ (see Ref. 28)					R ² H	16.64	79.3	0.3	142.7
HSiR ₃	11.44	47.1	1.5	68.4	R ³ H	15.83	71.7	0.3	122.6
HSR	9.75	32.8	0.2	23.6	H ₂ NR	21.43	114.8	8.0	267.6
HGeR ₃	12.26	55.3	1.5	67.7	HNR ₂	22.33	124.7	4.0	298.9
HSnR ₃	11.05	46.2	1.5	57.8	HOR	14.00	44.8	0.4	127.7
$R'CH=NR'' + HY \longrightarrow R'C'HNHR'' + Y^*$ (see Ref. 28)					HOOR	12.50	36.5	0.4	39.6
R ¹ H	15.80	71.5	1.5	121.9	HSiR ₃	11.90	51.0	3.0	59.6
R ² H	17.10	83.7	0.15	154.6	HSR	10.18	35.7	0.4	29.5
R ³ H	16.30	76.1	0.15	134.1	HGeR ₃	12.70	59.3	3.0	76.0
H ₂ NR	21.90	119.9	4.0	283.7	HSnR ₃	11.50	50.0	3.0	55.7
HNR ₂	22.80	130.0	2.0	315.9	$RN=NR + HY \longrightarrow RN'NHR + Y^*$ (see Ref. 28)				
HOR	13.94	44.4	0.2	122.8	R ¹ H	13.80	54.5	3.0	78.3
HOOR	12.44	36.2	0.2	38.7	R ² H	15.10	65.3	3.0	105.7
HSiR ₃	12.34	54.8	1.5	67.6	R ³ H	14.30	58.5	3.0	88.4
HSR	10.65	39.1	0.2	36.3	H ₂ NR	19.90	99.0	4.0	218.0
HGeR ₃	13.16	63.7	1.5	85.2	HNR ₂	20.80	108.2	4.0	246.6
HSnR ₃	11.95	54.0	1.5	63.7	HOR	12.44	35.4	4.0	32.9
$RCH=NPh + HY \longrightarrow RC'HNNHPh + Y^*$ (see Ref. 28)					HOOR	10.94	28.0	0.4	18.0
R ¹ H	13.00	48.4	1.5	63.1	HSiR ₃	10.37	38.7	3.0	241.5
R ² H	14.30	58.5	0.15	88.4	HSR	8.65	25.7	4.0	10.3
R ³ H	13.50	52.2	0.15	72.4	HGeR ₃	11.17	45.9	3.0	48.3
					HSnR ₃	10.03	38.0	3.0	32.3

Note. Hereinafter, the dimensions of parameter br_e and the enthalpies of the reaction are $(\text{kJ mol}^{-1})^{1/2}$ and kJ mol^{-1} , respectively.

Table 4. The enthalpies of the retrodisproportionation reactions $RH + X = Y$.¹⁵

RH	$CH_2=CH_2$	$CH_2=CH_2$	1,3-cyclo-C ₆ H ₈	PhN=CH ₂	PhC(O)H	OC=CH ₂	MeN=CH ₂	PhN=O	MeN=NMe
EtMeHC—H	262.6	273.0	207.6	239.2	263.0	246.6	262.9	190.0	248.7
Me ₃ C—H	249.6	260.0	194.6	226.2	250.0	233.6	249.9	177.0	235.7
	268.1	278.5	213.1	244.7	268.5	252.1	268.4	195.5	254.2
	258.0	268.4	203.0	234.6	258.4	242.0	258.3	185.4	244.1
	253.5	263.9	198.5	230.1	253.9	237.5	253.8	180.9	239.6
	245.1	255.5	190.1	221.7	245.5	229.1	245.4	172.5	231.2
cis-Decalin	237.2	247.6	182.2	213.8	237.6	221.2	237.5	164.6	223.3
H ₂ (CH ₂ =CH)C—H	217.6	228.0	162.6	194.2	218.0	201.6	217.9	145.0	203.7
H(CH ₂ =CH)C(Me)—H	199.4	209.8	144.4	176.0	199.8	183.4	199.7	126.8	185.5
Me ₂ (CH ₂ =CH)C—H	189.2	199.6	134.2	165.8	189.6	173.2	189.5	116.6	175.3
cis-MeCH=CHC(H)(Me)—H	193.6	204.0	138.6	170.2	194.0	177.6	193.9	121.0	179.7
H(Me ₂ C=CH)C(Me)—H	181.6	192.0	126.6	158.2	182.0	165.6	181.9	109.0	167.7

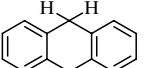
Table 4 (continued).

RH	CH ₂ =CH ₂	CH ₂ =CH ₂ Et	1,3-cyclo-C ₆ H ₈	PhN=CH ₂	PhC(O)H	OC=CH ₂	MeN=CH ₂	PhN=O	MeN=NMe
Me ₂ (Me ₂ C=CMe)C-H	172.4	182.8	117.4	149.0	172.8	156.4	172.7	998.0	158.5
Me(CH ₂ =CH) ₂ C-H	156.8	167.2	101.8	133.4	157.2	140.8	157.1	842.0	142.9
	191.1	201.5	136.1	167.7	191.5	175.1	191.4	118.5	177.2
	180.5	190.9	125.5	157.1	180.9	164.5	180.8	107.9	166.6
	162.2	172.6	107.2	138.8	162.6	146.2	162.5	896.0	148.3
	150.6	161.0	956.0	127.2	151.0	134.6	150.9	780.0	136.7
Me ₂ (MeC≡C)C-H	179.0	189.4	124.0	155.6	179.4	163.0	179.3	106.4	165.1
MePhHC-H	213.7	224.1	158.7	190.3	214.1	197.7	214.0	141.1	199.8
Me ₂ PhC-H	204.3	214.7	149.3	180.9	204.7	188.3	204.6	131.7	190.4
	195.2	205.6	140.2	171.8	195.6	179.2	195.5	122.6	181.3
	171.6	182.0	116.6	148.2	172.0	155.6	171.9	990.0	157.7
Me ₂ (NH ₂)C-H	229.1	239.5	174.1	205.7	229.5	213.1	229.4	156.5	215.2
(CH ₂ =CHC(H)-H) ₃ N	195.2	205.6	140.2	171.8	195.6	179.2	195.5	122.6	181.3
Me ₂ C(OH)-H	240.1	250.5	185.1	216.7	240.5	224.1	240.4	167.5	226.2
	179.3	189.7	124.3	155.9	179.7	163.3	179.6	106.7	165.4
HO(MeCH=CMe)C(Me)-H	174.8	185.2	119.8	151.4	175.2	158.8	175.1	102.2	160.9
	187.1	197.5	132.1	163.7	187.5	171.1	187.4	114.5	173.2
PhC(O)-H	197.6	208.0	142.6	174.2	198.0	181.6	197.9	125.0	183.7
	243.7	254.1	188.7	220.3	244.1	227.7	244.0	171.1	229.8
Me ₂ (Pr ⁱ O)C-H	240.4	250.8	185.4	217.0	240.8	224.4	240.7	167.8	226.5
(CH ₂ =CHC(H)-H) ₂ O	209.6	220.0	154.6	186.2	210.0	193.6	209.9	137.0	195.7
Ph ₂ C(OMe)-H	203.8	214.2	148.8	180.4	204.2	187.8	204.1	131.2	189.9
Ph(COOH)C(H)-H	216.6	227.0	161.6	193.2	217.0	200.6	216.9	144.0	202.7
Bu ⁱ OO-H	208.2	218.6	153.2	184.8	208.6	192.2	208.5	135.6	194.3
Bu ₃ Si-H	200.6	211.0	145.6	177.2	201.0	184.6	200.9	128.0	186.7
Ph ₃ Ge-H	172.1	182.5	117.1	148.7	172.5	156.1	172.4	99.5	158.2
Ph ₃ Sn-H	146.5	156.9	915.0	123.1	146.9	130.5	146.8	73.9	132.6

Table 5. The rate constants and activation energies for the reactions PhCH=CH₂ + RH → PhC[•]HCH₃ + R[•] calculated within the framework of the parabolic model.¹⁵

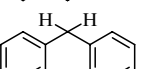
RH	D ^a	n	E	logA	k (550 K)	RH	D ^a	n	E	logA	k (550 K)
EtMeHC-H	413.0	4	225.0	10.70	2.15 × 10 ⁻¹¹	Me ₂ (CH ₂ =CH)C-H	339.6	1	161.0	8.00	5.12 × 10 ⁻⁸
Me ₃ C-H	400.0	1	212.0	9.94	6.40 × 10 ⁻¹¹	cis-MeCH=CHC(H)(Me)-H	344.0	2	164.2	8.30	5.08 × 10 ⁻⁸
	418.5	8	230.5	11.06	1.48 × 10 ⁻¹¹	H(Me ₂ C=CH)C(Me)-H	332.0	2	155.6	8.30	3.34 × 10 ⁻⁷
	408.4	10	220.4	11.05	1.31 × 10 ⁻¹⁰	Me ₂ (Me ₂ C=CMe)C-H	322.8	1	149.1	8.00	6.91 × 10 ⁻⁷
	395.5	1	207.5	9.88	1.49 × 10 ⁻¹⁰	Me(CH ₂ =CH) ₂ C-H	307.2	1	138.5	8.00	7.02 × 10 ⁻⁶
cis-Decalin	387.6	2	199.6	10.06	1.27 × 10 ⁻⁹		341.5	4	162.4	9.60	1.50 × 10 ⁻⁶
H ₂ (CH ₂ =CH)C-H	368.0	3	182.0	8.48	1.57 × 10 ⁻⁹		330.9	4	154.9	9.60	7.74 × 10 ⁻⁶
H(CH ₂ =CH)C(Me)-H	349.8	2	168.4	8.30	2.03 × 10 ⁻⁸		312.6	4	142.1	9.60	1.27 × 10 ⁻⁴

Table 5 (continued).

RH	<i>D</i> ^a	<i>n</i>	<i>E</i>	log <i>A</i>	<i>k</i> (550 K)	RH	<i>D</i> ^a	<i>n</i>	<i>E</i>	log <i>A</i>	<i>k</i> (550 K)
	301.0	2	134.1	9.30	3.67×10^{-4}	(CH ₂ =CHC(H)–H) ₃ N	345.6	6	169.5	8.78	4.81×10^{-8}
Me ₂ (MeC≡C)C–H	329.4	1	153.8	8.00	2.47×10^{-7}	Me ₂ C(OH)–H	390.5	1	202.5	9.81	3.79×10^{-10}
MePhHC–H	364.1	2	176.1	8.30	3.76×10^{-9}		329.7	1	158.9	9.00	8.11×10^{-7}
Me ₂ PhC–H	354.7	1	169.7	8.00	7.65×10^{-9}	HO(MeCH=CMe)C(Me)–H	325.2	1	155.8	8.00	1.60×10^{-7}
	345.6	4	162.5	9.60	1.47×10^{-6}	PhC(O)–H	348.0	1	164.3	8.00	2.49×10^{-8}
	322.0	4	131.7	9.60	9.20×10^{-5}		394.1	4	206.1	10.46	7.70×10^{-10}
Me ₂ (NH ₂)C–H	379.5	1	191.5	9.61	2.65×10^{-9}	Ph ₂ C(OMe)–H	354.2	1	168.9	8.00	9.11×10^{-9}
						Ph(COOH)C(H)–H	367.0	2	179.0	8.30	2.00×10^{-9}
						Bu ^t OO–H	358.6	1	170.0	9.83	4.84×10^{-7}
						Bu ₃ Si–H	351.0	1	163.0	10.27	6.16×10^{-6}

^a Hereinafter, the strength of the bond (*D*) has dimensions kJ mol^{–1}.

Table 6. The rate constants and activation energies for the reactions $p\text{-OC}_6\text{H}_4\text{O} + \text{RH} \longrightarrow p\text{-HOC}_6\text{H}_4\text{O}^\bullet + \text{R}^\bullet$ calculated within the framework of the parabolic model.¹⁵

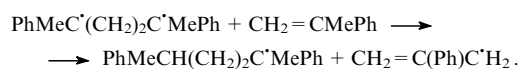
RH	<i>D</i>	<i>n</i>	ΔH	log <i>A</i>	<i>k</i> (550 K)	RH	<i>D</i>	<i>n</i>	ΔH	log <i>A</i>	<i>k</i> (550 K)
EtMeHC–H	413.0	4	186.7	11.70	5.64×10^{-7}	Me ₂ (MeC≡C)C–H	329.4	1	103.1	9.81	0.62
Me ₃ C–H	400.0	1	173.7	11.03	2.05×10^{-6}	MePhHC–H	364.1	2	137.8	10.97	4.57×10^{-3}
	418.5	8	192.2	12.03	3.61×10^{-7}	Me ₂ PhC–H	354.7	1	128.4	10.56	1.41×10^{-2}
	408.4	10	182.1	12.08	3.64×10^{-6}		345.6	4	119.3	11.05	0.31
	395.5	1	169.2	11.00	5.14×10^{-6}		322.0	4	95.70	10.60	19.5
<i>cis</i> -Decalin	387.6	2	161.3	11.25	5.14×10^{-5}	Me ₂ (NH ₂)C–H	379.5	1	153.2	10.89	1.33×10^{-4}
H ₂ (CH ₂ =CH)C–H	368.0	3	141.7	11.00	2.12×10^{-3}	(CH ₂ =CHC(H)–H) ₃ N	345.6	6	119.3	10.98	0.27
H(CH ₂ =CH)C(Me)–H	349.8	2	123.5	10.57	4.20×10^{-2}	Me ₂ C(OH)–H	390.5	1	164.2	10.97	1.43×10^{-5}
Me ₂ (CH ₂ =CH)C–H	339.6	1	113.3	10.08	0.12		329.7	1	103.4	9.82	0.59
<i>cis</i> -MeCH=CHC(H)(Me)–H	344.0	2	117.7	10.47	0.12	HO(MeCH=CMe)C(Me)–H	325.2	1	98.90	9.66	1.11
H(Me ₂ C=CH)C(Me)–H	332.0	2	105.7	10.19	0.84	PhC(O)–H	348.0	1	121.7	10.48	5.02×10^{-2}
Me ₂ (Me ₂ C=CMe)C–H	322.8	1	96.50	8.43	0.18		394.1	4	167.8	11.59	2.74×10^{-5}
Me(CH ₂ =CH) ₂ C–H	307.2	1	80.90	8.00	0.53	Me ₂ (Pr ^t O)C–H	390.8	2	164.5	11.27	2.68×10^{-5}
	341.5	4	115.2	10.72	0.36	Ph ₂ C(OMe)–H	354.2	1	127.9	10.56	1.55×10^{-2}
	330.9	4	104.6	10.45	1.99	Ph(COOH)C(H)–H	367.0	2	140.7	11.00	2.59×10^{-3}
	312.6	4	86.30	9.52	12.5	Bu ^t OO–H	358.6	1	132.3	10.71	8.31×10^{-3}
	301.0	2	74.70	8.30	2.42	Bu ₃ Si–H	351.0	1	124.7	10.84	5.90×10^{-2}

V. Thermal generation of radicals in monomers

Radical polymerisation reactions are triggered by various processes. However, in some cases spontaneous polymerisation of monomers occurs without initiation.^{38,39} Using spontaneous polymerisation of styrene as an example, Mayo⁴⁰ has shown that the rate of thermal generation of radicals is directly proportional to the third power of the styrene concentration. More recent findings suggest that thermal polymerisation is initiated by mono- rather than by biradicals. Two mechanisms of thermal initiation of radical polymerisation are described below.³⁹

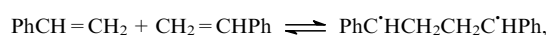
1. The interaction of two monomeric molecules yields a biradical, *e.g.*:

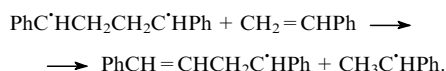
$\text{PhMeC}=\text{CH}_2 + \text{CH}_2=\text{CMePh} \rightleftharpoons \text{PhMeC}^\bullet\text{CH}_2\text{CH}_2\text{C}^\bullet\text{MePh}$, which further enters into a radical abstraction reaction with the monomeric molecule:



Each of the radicals formed initiates the growth of the macromolecule.

2. The biradical formed in the course of a reversible bimolecular reaction enters into a reaction of hydrogen transfer from the radical to the monomer:





The rate of radical generation for both reaction mechanisms is determined from the following ratio:

$$v_i = kK[\text{CH}_2=\text{CHR}]^3, \quad (15)$$

where k is the rate constant for the reaction of the biradical with the monomer and K is the equilibrium constant of the reversible reaction of biradical formation.

The values of the constant K (ΔH and ΔS values are taken from the database⁴¹) and the dissociation energies of the C–H bonds (see Ref. 42) calculated by the equation:

$$-RT \ln K = \Delta H - T\Delta S \quad (16)$$

are given in Table 7; the values of E and k for bimolecular radical reactions established with the use of the parabolic model and the parameters listed in Table 2 are given in Tables 8 and 9.

Table 7. The enthalpy, entropy, Gibbs potential (ΔG /kJ mol^{−1}) and equilibrium constant of the reaction $2\text{RCH}=\text{CH}_2 \longrightarrow \text{RC}^{\bullet}\text{HCH}_2\text{CH}_2\text{C}^{\bullet}\text{HR}$.^{41, 42}

Monomer	ΔH	ΔS	ΔG (298 K)	K (450 K)
$\text{CH}_2=\text{CH}_2$	177.0	−111.0	210.1	4.54×10^{-24}
$\text{CH}_2=\text{CHMe}$	182.9	−128.1	221.1	1.20×10^{-28}
$\text{CH}_2=\text{CHEt}$	185.4	−126.6	223.1	7.36×10^{-29}
$\text{CH}_2=\text{CHCH}=\text{CH}_2$	86.5	−103.4	117.3	4.60×10^{-16}
$\text{CH}_2=\text{CHPh}$	98.7	−127.8	136.8	7.38×10^{-19}
$\text{CH}_2=\text{CMePh}$	99.0	−148.8	143.3	5.45×10^{-20}
$\text{CH}_2=\text{CHCOOMe}$	170.4	−125.2	207.7	4.80×10^{-27}
$\text{CH}_2=\text{CMeCOOMe}$	166.2	−140.8	208.2	2.26×10^{-27}
$\text{CH}_2=\text{CHCOOEt}$	169.4	−125.2	206.7	6.27×10^{-27}
$\text{CH}_2=\text{CHCl}$	167.0	−117.0	201.9	3.19×10^{-26}

Table 8. The activation energies and rate constants for the reaction $\text{RCH}=\text{CH}_2 + \text{RC}^{\bullet}\text{HCH}_2\text{CH}_2\text{C}^{\bullet}\text{HR} \longrightarrow \text{RC}^{\bullet}\text{HCH}_3 + \text{RCH}=\text{CHCH}_2\text{C}^{\bullet}\text{HR}$ calculated within the framework of the parabolic model.¹⁵

$\text{RCH}=\text{CH}_2$	$\text{RC}^{\bullet}\text{HCH}_2\text{CH}_2\text{C}^{\bullet}\text{HR}$	E	$\log A$	k (450 K)	Kk (450 K) (see ^a)
$\text{CH}_2=\text{CH}_2$	$\text{C}^{\bullet}\text{H}_2\text{CH}_2\text{CH}_2\text{C}^{\bullet}\text{H}_2$	53.6	9.60	2.41×10^3	1.09×10^{-20}
$\text{CH}_2=\text{CHCH}=\text{CH}_2$	$\text{C}^{\bullet}\text{H}_2\text{CH}_2\text{CH}_2\text{C}^{\bullet}\text{H}_2$	44.0	9.60	3.12×10^4	1.42×10^{-19}
$\text{CH}_2=\text{CHPh}$	$\text{C}^{\bullet}\text{H}_2\text{CH}_2\text{CH}_2\text{C}^{\bullet}\text{H}_2$	40.0	9.30	4.55×10^4	2.07×10^{-19}
$\text{CH}_2=\text{CH}_2$	$(\text{CH}_2=\text{CHC}^{\bullet}\text{HCH}_2)_2$	77.4	9.60	4.15	1.91×10^{-15}
$\text{CH}_2=\text{CHCH}=\text{CH}_2$	$(\text{CH}_2=\text{CHC}^{\bullet}\text{HCH}_2)_2$	70.3	9.60	2.77×10	1.27×10^{-14}
$\text{CH}_2=\text{CHPh}$	$(\text{CH}_2=\text{CHC}^{\bullet}\text{HCH}_2)_2$	66.8	9.30	3.52×10	1.62×10^{-14}
$\text{CH}_2=\text{CH}_2$	$\text{PhC}^{\bullet}\text{HCH}_2\text{CH}_2\text{C}^{\bullet}\text{HPh}$	78.4	9.60	3.17	2.34×10^{-18}
$\text{CH}_2=\text{CHCH}=\text{CH}_2$	$\text{PhC}^{\bullet}\text{HCH}_2\text{CH}_2\text{C}^{\bullet}\text{HPh}$	60.2	9.60	4.11×10^2	3.03×10^{-16}
$\text{CH}_2=\text{CHPh}$	$\text{PhC}^{\bullet}\text{HCH}_2\text{CH}_2\text{C}^{\bullet}\text{HPh}$	60.1	9.30	2.11×10^2	1.56×10^{-16}
$\text{CH}_2=\text{CH}_2$	$(\text{CH}_2\text{C}^{\bullet}\text{MeCOOMe})_2$	56.5	9.60	1.11×10^3	2.51×10^{-24}
$\text{CH}_2=\text{CHCH}=\text{CH}_2$	$(\text{CH}_2\text{C}^{\bullet}\text{MeCOOMe})_2$	46.6	9.60	1.56×10^4	3.52×10^{-23}
$\text{CH}_2=\text{CHPh}$	$(\text{CH}_2\text{C}^{\bullet}\text{MeCOOMe})_2$	42.6	9.30	2.27×10^4	5.13×10^{-23}
$\text{CH}_2=\text{CMeC}(\text{O})_2\text{Me}$	$(\text{CH}_2\text{C}^{\bullet}\text{MeCOOMe})_2$	55.0	9.30	8.26×10^2	1.87×10^{-24}
$\text{CH}_2=\text{CH}_2$	$\text{ClC}^{\bullet}\text{HCH}_2\text{CH}_2\text{C}^{\bullet}\text{HCl}$	60.4	9.60	3.90×10^2	1.24×10^{-23}
$\text{CH}_2=\text{CHCH}=\text{CH}_2$	$\text{ClC}^{\bullet}\text{HCH}_2\text{CH}_2\text{C}^{\bullet}\text{HCl}$	49.9	9.60	6.45×10^3	2.06×10^{-22}
$\text{CH}_2=\text{CHPh}$	$\text{ClC}^{\bullet}\text{HCH}_2\text{CH}_2\text{C}^{\bullet}\text{HCl}$	46.0	9.30	9.15×10^3	2.92×10^{-22}
$\text{CH}_2=\text{CHCl}$	$\text{ClC}^{\bullet}\text{HCH}_2\text{CH}_2\text{C}^{\bullet}\text{HCl}$	57.8	9.30	3.91×10^2	1.25×10^{-23}

^a Hereinafter, the parameter Kk has the dimension litre² mol^{−2} s^{−1}.

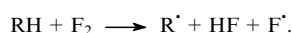
Table 9. The activation energies and rate constants for the reaction $(\text{RC}^{\bullet}\text{HCH}_2)_2 + \text{CH}_2=\text{CRCH}_3 \longrightarrow \text{RC}^{\bullet}\text{HCH}_2\text{CH}_2\text{CH}_2\text{R} + \text{CH}_2=\text{CRC}^{\bullet}\text{H}_2$ calculated within the framework of the parabolic model.¹⁵

$(\text{RC}^{\bullet}\text{HCH}_2)_2$	$\text{CH}_2=\text{CRCH}_3$	E	$\log A$	k (450 K)	Kk (450 K)
$(\text{MeC}^{\bullet}\text{HCH}_2)_2$	$\text{CH}_2=\text{CHMe}$	50.4	9.78	8.51×10^3	1.02×10^{-24}
$(\text{MeC}^{\bullet}\text{HCH}_2)_2$	$\text{CH}_2=\text{CHEt}$	42.7	9.60	4.42×10^4	5.30×10^{-24}
$(\text{MeC}^{\bullet}\text{HCH}_2)_2$	$\text{CH}_2=\text{CMePh}$	45.7	8.78	2.97×10^3	3.56×10^{-25}
$(\text{MeC}^{\bullet}\text{HCH}_2)_2$	$\text{CH}_2=\text{CMeCO}_2\text{Me}$	46.9	8.78	2.16×10^3	2.59×10^{-26}
$(\text{EtC}^{\bullet}\text{HCH}_2)_2$	$\text{CH}_2=\text{CHMe}$	49.3	9.78	1.14×10^3	8.39×10^{-25}
$(\text{EtC}^{\bullet}\text{HCH}_2)_2$	$\text{CH}_2=\text{CHEt}$	41.7	9.60	5.78×10^4	4.25×10^{-24}
$(\text{EtC}^{\bullet}\text{HCH}_2)_2$	$\text{CH}_2=\text{CMePh}$	44.7	8.78	3.89×10^3	2.86×10^{-25}
$(\text{EtC}^{\bullet}\text{HCH}_2)_2$	$\text{CH}_2=\text{CMeCO}_2\text{Me}$	45.9	8.78	2.82×10^3	2.07×10^{-25}
$(\text{PhMeC}^{\bullet}\text{CH}_2)_2$	$\text{CH}_2=\text{CHMe}$	80.0	9.78	3.10	1.69×10^{-15}
$(\text{PhMeC}^{\bullet}\text{CH}_2)_2$	$\text{CH}_2=\text{CHEt}$	70.8	9.60	24.2	1.32×10^{-18}
$(\text{PhMeC}^{\bullet}\text{CH}_2)_2$	$\text{CH}_2=\text{CMePh}$	74.4	8.78	1.39	7.57×10^{-20}
$(\text{PhMeC}^{\bullet}\text{CH}_2)_2$	$\text{CH}_2=\text{CMeCO}_2\text{Me}$	75.9	8.78	0.93	5.07×10^{-20}
$[\text{MeOC}(\text{O})\text{C}^{\bullet}\text{HCH}_2]_2$	$\text{CH}_2=\text{CHMe}$	56.3	9.78	1.75×10^3	8.40×10^{-24}
$[\text{MeOC}(\text{O})\text{C}^{\bullet}\text{HCH}_2]_2$	$\text{CH}_2=\text{CHEt}$	48.2	9.60	1.02×10^4	4.90×10^{-27}
$[\text{MeOC}(\text{O})\text{C}^{\bullet}\text{HCH}_2]_2$	$\text{CH}_2=\text{CMePh}$	51.4	8.78	6.48×10^2	3.11×10^{-26}
$[\text{MeOC}(\text{O})\text{C}^{\bullet}\text{HCH}_2]_2$	$\text{CH}_2=\text{CMeCO}_2\text{Me}$	52.7	8.78	4.58×10^2	2.20×10^{-24}

VI. Reactions involving halogen molecules

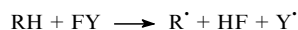
Molecular fluorine reacts with organic molecules at very fast rates even at low (200 K and lower) temperatures.^{1, 39, 43} High reactivity of the fluorine molecule is due to the low degree of binding between the atoms [$D(\text{F}-\text{F}) = 159 \text{ kJ mol}^{-1}$], whereas the C–F and F–H bonds in the fluorination products are strong [$D(\text{F}-\text{H}) = 570 \text{ kJ mol}^{-1}$ and $D(\text{H}_3\text{C}-\text{F}) = 464 \text{ kJ mol}^{-1}$].⁴⁴ Therefore, radical generation reactions involving molecular fluorine are exothermic and proceed at fast rates. Two radical generation reactions involving fluorine were predicted by N N Semenov¹ and are widely known.

One of them includes abstraction of the hydrogen atom from the C–H bond by the fluorine molecule resulting in the formation of the HF molecule and the fluorine atom:⁴⁵



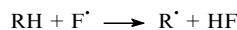
This reaction is exothermic even for isobutane [$D(\text{R}-\text{H}) = 400 \text{ kJ mol}^{-1}$]; its enthalpy is $\Delta H = 400 + 159 - 570 = -11 \text{ kJ mol}^{-1}$.

Other fluorine-containing molecules react analogously:



The values of enthalpies for such reactions are given in Table 10.

The reaction centres of the transition state ($\text{F} \cdots \text{H} \cdots \text{R}$) of the reaction indicated above and those involving $\text{F}^\cdot$:



are similar.

The kinetic parameters which characterise, in the framework of the parabolic model, the reactions involving fluorine- and chlorine-containing molecules are given in Tables 11 and 12; the results of the calculation of the activation energies and rate

Table 10. The enthalpies of reactions of hydrogen abstraction by fluorine-containing molecules $\text{RH} + \text{FY} \longrightarrow \text{R}^\cdot + \text{HF} + \text{Y}^\cdot$.

RH	<i>D</i>	ΔH					
		F_2	FCI	FBr	FI	FOH	CFOF
EtMeHC–H	413.0	1.4	98.9	92.9	114.3	57.2	24.7
Me ₃ C–H	400.0	–11.6	85.9	79.9	101.3	44.2	11.7
	418.5	6.9	104.4	98.4	119.8	62.7	30.2
	408.4	–3.2	94.3	88.3	109.7	52.6	20.1
	395.5	–16.1	81.4	75.4	96.8	39.7	7.2
<i>cis</i> -Decalin	387.6	–24.0	73.5	67.5	88.9	31.8	–70.0
H ₂ (CH ₂ =CH)C–H	368.0	–43.6	53.9	47.9	69.3	12.2	–20.3
H(CH ₂ =CH)C(Me)–H	349.8	–61.8	35.7	29.7	51.1	–6.0	–38.5
Me ₂ (CH ₂ =CH)C–H	339.6	–72.0	25.5	19.5	40.9	–16.2	–48.7
<i>cis</i> -MeCH=CHC(H)(Me)–H	344.0	–67.6	29.9	23.9	45.3	–11.8	–44.3
H(Me ₂ C=CH)C(Me)–H	332	–79.6	17.9	11.9	33.3	–23.8	–56.3
Me ₂ (Me ₂ C=CMe)C–H	322.8	–88.8	8.7	2.7	24.1	–33.0	–65.5
H(CH ₂ =CMe)(CH ₂ =CH)C–H	307.2	–104.4	–6.9	–12.9	8.5	–48.6	–81.1
	341.5	–70.1	27.4	21.4	42.8	–14.3	–46.8
	330.9	–80.7	16.8	10.8	32.2	–24.9	–57.4
	312.6	–99.0	–1.50	–7.5	13.9	–43.2	–75.7
	301.0	–110.6	–13.1	–19.1	2.3	–54.8	–87.3
Me ₂ (MeC≡C)C–H	329.4	–82.2	15.3	9.3	30.7	–26.4	–58.9
PhMeHC–H	364.1	–47.5	50.0	44.0	65.4	8.3	–24.2
PhMe ₂ C–H	354.7	–56.9	40.6	34.6	56.0	–1.1	–33.6
	345.6	–66.0	31.5	25.5	46.9	–10.2	–42.7
	322.0	–89.6	7.9	1.9	23.3	–33.8	–66.3
Me ₂ (NH ₂)C–H	379.5	–32.1	65.4	59.4	80.8	23.7	–88.0
[CH ₂ =CHC(H)–H] ₃ N	345.6	–66.0	31.5	25.5	46.9	–10.2	–42.7
Me ₂ C(OH)–H	390.5	–21.1	76.4	70.4	91.8	34.7	2.2
	329.7	–81.9	15.6	9.6	31.0	–26.1	–58.6

Table 10 (continued).

RH	<i>D</i>	ΔH					
		F ₂	FCI	FBr	FI	FOH	CFOF
HO(MeCH=CMe)C(Me)–H	325.2	–86.4	11.1	5.1	26.5	–30.6	–63.1
PhC(O)–H	348.0	–63.6	33.9	27.9	49.3	–7.8	–40.3
	394.1	–17.5	80.0	74.0	95.4	38.3	5.8
Ph ₂ C(OMe)–H	354.2	–57.4	40.1	34.1	55.5	–1.6	–34.1
Ph(COOH)C(H)–H	367.0	–44.6	52.9	46.9	68.3	11.2	–21.3
Bu ^o OO–H	358.6	–53.0	44.5	38.5	59.9	2.8	–29.7
Bu ₃ Si–H	351.0	–60.6	36.9	30.9	52.3	–4.8	–37.3

Table 11. The kinetic parameters of reactions involving fluorine- and chlorine-containing molecules.²²

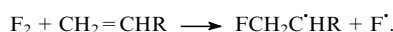
Reaction	α	$10^{-11} b$	$0.5 hN_{AVi}$	$0.5 hN_A$ ($v_i - v_f$)	$(r^{\neq}/r_e)_0$
RCH=CH ₂ +YF	1.422	5.389	9.9	3.6	0.413
RCH=CHCH=CH ₂ + +YF	1.678	5.389	11.7	5.4	0.373
RC≡CH+YF	1.824	6.912	12.7	6.4	0.354
RCH=CH ₂ +YCl	1.639	5.389	9.9	5.0	0.379
RCH=CHCH=CH ₂ + +YCl	1.934	5.389	11.7	6.8	0.341
RC≡CH+YCl	2.102	6.912	12.7	7.8	0.322
HR+XF	0.694	3.743	17.4	–7.4	0.590
HNR ₂ +XF	0.798	4.306	20.0	–4.8	0.556
HOR+XF	0.871	4.701	21.7	–3.1	0.534
HOOR+XF	0.853	4.600	21.2	–3.6	0.540
HSiR ₃ +XF	0.511	2.756	12.6	–12.2	0.662
HSR+XF	0.561	3.026	13.8	–11.0	0.641
RH+XCl	0.951	3.743	17.4	–0.5	0.513
H ₂ NR+XCl	1.094	4.306	20.1	2.1	0.478
HOR+XCl	1.194	4.701	21.7	3.8	0.456
HOOR+XCl	1.169	4.600	21.2	3.3	0.461
HSiR ₃ +XCl	0.700	2.756	12.6	–5.3	0.588
HSR+XCl	0.769	3.026	13.8	–4.1	0.565

constants are given in Table 13. The calculated and experimental values are very similar. For example, the experimental rate constant for the reaction:



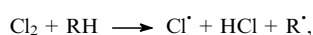
is equal to $2.0 \times 10^9 \exp(-47.0/RT) = 1.5 \times 10^3 \text{ litre mol}^{-1} \text{ s}^{-1}$ (400 K),⁴⁵ whereas the calculated rate constant is equal to $1.8 \times 10^{10} \exp(-51.0/RT) = 3.9 \times 10^3 \text{ litre mol}^{-1} \text{ s}^{-1}$.

Generation of radicals in yet another fluorine-induced reaction, which was also predicted by N N Semenov,¹ is the addition of fluorine to the double bond:

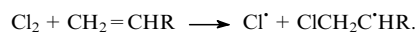


The activation energies and rate constants for this type of reaction were calculated within the framework of the parabolic model and using kinetic parameters of the given reaction (see Tables 11 and 12) (Table 14). The calculated rate constant for the reaction of F₂ with ethylene is equal to $1.69 \times 10^4 \text{ litre mol}^{-1} \text{ s}^{-1}$ (300 K), *i.e.*, is similar to the experimental values of *k*, *viz.*, $k = 2.04 \times 10^4$ (for 298 K),⁴⁶ 1.81×10^4 (for 298 K)⁴⁷ and $4.16 \times 10^4 \text{ litre mol}^{-1} \text{ s}^{-1}$ (for 315 K).⁴⁸

It may be assumed that analogous reactions occur with molecular chlorine:

Table 12. The kinetic and thermodynamic parameters of reactions involving fluorine- and chlorine-containing molecules.²²

HY	<i>br_e</i>	<i>E_{e0}</i>	$10^{-10} A_0$	$\Delta H_{e\text{max}}$
XF + HY $\longrightarrow$ X [·] + HF + Y [·] (gas phase) ³²				
R ¹ H	12.85	57.5	2.2	63.4
R ² H	13.73	65.7	0.25	80.7
R ³ H	13.20	60.7	0.25	70.1
NH ₃	14.40	64.1	7.5	83.9
H ₂ NR	14.67	66.6	75	89.6
HNR ₂	14.86	68.3	75	93.7
HOR	13.53	52.3	1.2	59.7
HOOR	14.00	57.1	1.2	70.3
HSiR ₃	11.00	53.0	2.2	47.4
HSR	12.18	60.9	7.5	63.3
XCl + HY $\longrightarrow$ X [·] + HCl + Y [·] (gas phase) ³²				
R ¹ H	9.90	25.7	1.0	16.6
R ² H	11.10	32.4	1.0	32.2
R ³ H	10.25	27.6	1.0	20.9
NH ₃	10.52	25.2	1.6	16.8
H ₂ NR	11.05	27.8	0.16	23.3
HNR ₂	10.38	24.6	0.16	15.2
HOR	15.28	48.5	4.2	86.7
HOOR	14.90	47.2	1.6	81.3
HSiR ₃	9.25	29.6	2.5	21.6
HSR	9.85	31.0	1.0	25.6
XF + CH ₂ =CHR $\longrightarrow$ X [·] + FCH ₂ C [·] HR (see Ref. 33)				
CH ₂ =CHR	19.30	63.5	2.5	240.0
CH ₂ =CHCH=CHR	21.20	76.6	2.5	303.3
CH ₂ =CHPh	20.55	72.0	2.5	280.8
XCl + CH ₂ =CHR $\longrightarrow$ X [·] + ClCH ₂ C [·] HR (see Ref. 33)				
CH ₂ =CHR	18.47	49.0	0.9	215.4
CH ₂ =CHCH=CHR	20.35	59.5	0.9	274.7
CH ₂ =CHPh	19.73	55.9	0.9	254.5



The enthalpies of these reactions are much lower than the dissociation energy of the Cl–Cl bond, but it is these reactions that seem to be the main radical sources in chain chlorination reactions in the absence of external initiators. Among chlorine-containing molecules, nitrosyl chloride ClNO has proved to be the most active hydrogen acceptor. The abstraction of the hydrogen atom by YCl molecules occurs with an activation energy similar to the reaction enthalpy [see formula (6)]. The rate constants for some of these reactions (Tables 11 and 12) calculated within the framework of the parabolic model are given in Table 15.

Table 13. The enthalpies, activation energies and rate constants for the reactions $F_2 + RH \longrightarrow F^\bullet + HF + R^\bullet$ calculated within the framework of the parabolic model.²²

RH	D	n	ΔH_e	E	$\log A$	k (300 K)
H_3C-H	440.0	4	21.0	51.0	10.26	24.0
$EtMeHC-H$	413.0	4	-6	36.5	10.94	8.02×10^3
Me_3C-H	400.0	1	-19	31.5	10.34	1.60×10^4
	418.5	8	-0.5	38.7	11.25	6.60×10^3
	408.4	10	-10.6	33.0	11.34	8.60×10^4
	395.5	1	-23.5	28.2	10.34	6.38×10^4
<i>cis</i> -Decalin	387.6	2	-31.4	25.4	10.64	4.12×10^5
$H_2(CH_2=CH)C-H$	368.0	3	-51	26.7	10.82	3.62×10^5
$H(CH_2=CH)C(Me)-H$	349.8	2	-69.2	21.1	10.64	2.53×10^6
$Me_2(CH_2=CH)C-H$	339.6	1	-79.4	18.1	10.34	4.57×10^6
<i>cis</i> - $MeCH=CHC(H)(Me)-H$	344.0	2	-75	23.5	10.64	9.19×10^5
$H(Me_2C=CH)C(Me)-H$	332.0	2	-87	20.1	10.64	3.88×10^6
$Me_2(Me_2C=CMe)C-H$	322.8	1	-96.2	17.6	10.34	5.66×10^6
$Me(CH_2=CH)_2C-H$	307.2	1	-111.8	13.7	10.34	3.06×10^7
	341.5	4	-77.5	22.8	10.94	2.46×10^6
	330.9	4	-88.1	19.8	10.94	8.80×10^6
	312.6	4	-106.4	15.0	10.94	6.92×10^7
	301.0	2	-118	12.2	10.64	1.18×10^8
$Me_2(MeC\equiv C)C-H$	329.4	1	-89.6	19.4	10.34	2.62×10^5
$MePhHC-H$	364.1	2	-54.9	24.8	10.64	5.31×10^5
Me_2PhC-H	354.7	1	-64.3	21.9	10.34	9.05×10^5
	345.6	4	-73.4	19.3	10.94	1.09×10^7
	322.0	4	-97	13.0	10.94	1.66×10^8
$Me_2(NH_2)C-H$	379.5	1	-39.5	26.7	10.34	1.20×10^5
$[CH_2=CHC(H)-H]_3N$	345.6	6	-73.4	23.9	11.12	2.35×10^6
$Me_2C(OH)-H$	390.5	1	-28.5	30.5	10.34	2.44×10^4
	329.7	1	-89.3	19.5	10.34	2.51×10^6
$PhC(O)-H$	348.0	1	-71	20.0	10.34	2.03×10^6
	394.1	4	-24.9	31.8	10.94	5.64×10^4
$Me_2CHOC(Me_2)-H$	390.8	2	-28.2	30.6	10.64	4.68×10^4
$Ph_2C(OMe)-H$	354.2	1	-64.8	21.8	10.34	9.45×10^5
$Ph(COOH)C(H)-H$	367.0	2	-52	25.7	10.64	3.64×10^5
Bu^tOO-H	358.6	1	-56	18.4	10.34	4.02×10^6
Bu_3Si-H	351.0	1	-72.8	16.8	10.34	7.98×10^6

Table 14. The enthalpies, activation energies and rate constants for the reactions of YF with alkenes calculated within the framework of the parabolic model.²⁸

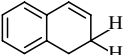
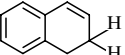
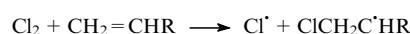
Alkene	ΔH_c	E	$\log A$	k (300 K)	Alkene	ΔH_c	E	$\log A$	k (300 K)
Fluorinating reagent F_2					Fluorinating reagent CF_3OF				
$CH_2=CH_2$	-29.1	38.6	11.00	1.69×10^4	$CH_2=CH_2$	-5.8	51.4	10.70	5.63×10
$Me_2C=CH_2$	-32.3	36.9	10.70	1.88×10^4	$Me_2C=CH_2$	-9.0	49.6	10.40	5.81×10
$EtHC=CH_2$	-27.7	39.3	10.70	7.20×10^3	$EtHC=CH_2$	-4.4	52.2	10.40	2.05×10
	-33.7	36.2	11.00	4.98×10^4		-10.4	48.8	10.70	1.60×10^2
$CH_2=CHCH=CH_2$	-74.5	13.4	11.00	4.64×10^7	$CH_2=CHCH=CH_2$	-51.6	24.6	10.70	2.61×10^6
$CH_2=CHCH=CMe_2$	-80.1	11.0	10.70	6.09×10^8	$CH_2=CHCH=CMe_2$	-56.8	21.8	10.40	4.02×10^6
$Me_2C=C(Me)C(Me)=CMe_2$	-109.5	0.03	11.00	9.88×10^{10}	$Me_2C=C(Me)C(Me)=CMe_2$	-86.2	8.4	10.70	1.73×10^9
	-91.3	6.4	11.00	7.68×10^9		-68.0	16.4	10.70	6.99×10^7
$PhCH=CH_2$	-70.0	26.7	10.70	1.12×10^6	$PhCH=CH_2$	-46.7	37.8	10.40	6.58×10^3
$PhCH=CHMe$	-66.2	28.4	10.70	5.69×10^5	$PhCH=CHMe$	-42.9	39.7	10.40	3.07×10^3
$Ph_2C=CH_2$	-137.2	1.9	10.70	2.34×10^{10}	$Ph_2C=CH_2$	-114.1	9.1	10.40	6.54×10^8
	-66.2	28.4	10.70	5.69×10^5		-42.9	39.7	10.40	3.07×10^3

Table 15. The enthalpies, activation energies and rate constants for the reactions $RH + Cl_2 \rightarrow R^\cdot + HCl + Cl^\cdot$ calculated within the framework of the parabolic model.

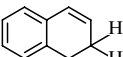
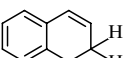
RH	D	n	ΔH	$\log A$	k (400 K)	RH	D	n	ΔH	$\log A$	k (400 K)
$EtMeHC-H$	413.0	4	224.0	11.95	2.94×10^{-19}	$Me_2(MeC \equiv C)C-H$	329.4	1	140.4	11.00	3.39×10^{-9}
Me_3C-H	400.0	1	211.0	11.33	3.62×10^{-19}	$MePhHC-H$	364.1	2	175.1	11.52	2.95×10^{-13}
	418.5	8	229.5	12.26	1.12×10^{-19}	Me_2PhC-H	354.7	1	165.7	11.19	2.40×10^{-12}
	408.4	10	219.4	12.34	2.87×10^{-18}		345.6	4	156.6	11.77	1.45×10^{-10}
	395.5	1	206.5	11.32	1.37×10^{-17}		322.0	4	133.0	11.7	1.61×10^{-7}
<i>cis</i> -Decalin	387.6	2	198.6	11.61	4.88×10^{-16}	$Me_2(NH_2)C-H$	379.5	1	190.5	11.29	1.40×10^{-15}
$H_2(CH_2=CH)C-H$	368.0	3	179.0	11.59	9.85×10^{-13}	$[CH_2=CHC(H)-H]_3N$	345.6	6	156.6	11.83	1.67×10^{-10}
$H(CH_2=CH)C(Me)-H$	349.8	2	160.8	11.37	1.61×10^{-11}	$Me_2C(OH)-H$	390.5	1	201.5	11.31	6.08×10^{-17}
$Me_2(CH_2=CH)C-H$	339.6	1	150.6	11.03	1.64×10^{-10}		329.7	1	140.7	11.00	3.10×10^{-9}
<i>cis</i> - $MeCH=CHC(H)(Me)-H$	344.0	2	155.0	11.35	8.95×10^{-11}	$HO(MeCH=CMe)C(Me)-H$	325.2	1	136.2	10.98	1.16×10^{-8}
$H(Me_2C=CH)C(Me)-H$	332.0	2	143.0	11.31	3.14×10^{-9}	$PhC(O)-H$	348.0	1	159.0	11.18	1.80×10^{-11}
$Me_2(Me_2C=CMe)C-H$	322.8	1	133.8	10.97	2.36×10^{-8}		394.1	4	205.1	11.92	8.31×10^{-17}
$Me(CH_2=CH)_2C-H$	307.2	1	118.2	10.90	2.33×10^{-6}	$Me_2(Pr^iO)C-H$	390.8	2	201.8	11.61	1.11×10^{-16}
	341.5	4	152.5	11.60	3.40×10^{-10}	$Ph_2C(OMe)-H$	354.2	1	165.2	11.19	2.08×10^{-12}
	330.9	4	141.9	11.60	8.53×10^{-9}	$Ph(COOH)C(H)-H$	367.0	2	178.0	11.52	1.22×10^{-13}
	312.6	4	123.6	11.53	1.91×10^{-6}	Bu^iOO-H	358.6	1	169.6	10.63	2.02×10^{-13}
	301.0	2	112.0	11.17	2.86×10^{-5}	Bu_3Si-H	351.0	1	162.0	10.92	3.98×10^{-12}

The addition of chlorine to the double bond:



is a slow endothermic process. The rate constants for some reactions of this type are given in Table 16.

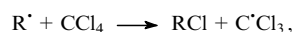
Table 16. The enthalpies, activation energies and rate constants of the reactions $YCl + CH_2=CHR \longrightarrow Y^\cdot + ClCH_2C^\cdot HR$ calculated within the framework of the parabolic model.

$RCH=CH_2$	ΔH_c	E	$\log A$	k (300 K)
Chlorinating reagent Cl_2				
$CH_2=CH_2$	168.2	169.3	10.56	2.96×10^{-13}
$Me_2C=CH_2$	165.0	166.5	10.26	3.46×10^{-13}
$EtCH=CH_2$	169.6	170.5	10.26	1.02×10^{-13}
	155.6	158.3	10.56	8.23×10^{-12}
$HC\equiv CH$	183.7	205.5	10.86	7.91×10^{-18}
$MeC\equiv CMe$	199.4	218.8	10.86	1.38×10^{-19}
$CH_2=CHCH=CH_2$	122.8	131.3	10.56	3.90×10^{-15}
$CH_2=CHCH=CMe_2$	118.2	127.5	10.26	4.38×10^{-9}
$Me_2C=C(Me)C(Me)=CMe_2$	88.8	103.4	10.56	9.29×10^{-6}
	98.0	110.8	10.56	1.09×10^{-6}
$PhCH=CH_2$	128.3	140.8	10.26	9.07×10^{-10}
$PhCH=CHMe$	123.1	136.6	10.26	3.27×10^{-9}
$Ph_2C=CH_2$	67.9	93.8	10.26	1.52×10^{-3}
	124.6	137.8	10.26	2.26×10^{-9}
Chlorinating reagent $ClNO_2^-$				
$CH_2=CH_2$	67.4	86.8	10.26	1.21×10^{-2}
$Me_2C=CH_2$	64.2	84.4	9.95	1.26×10^{-2}
$EtHC=CH_2$	68.8	87.9	9.95	4.37×10^{-3}
	54.8	77.5	10.26	2.12×10^{-1}
$HC\equiv CH$	82.9	123.8	10.56	2.54×10^{-7}
$MeC\equiv CMe$	98.6	136.0	10.56	6.08×10^{-9}
$CH_2=CHCH=CH_2$	22.0	52.6	10.26	10.3
$CH_2=CHCH=CMe_2$	17.4	49.4	9.95	13.1
$Me_2C=C(Me)C(Me)=CMe_2$	-12.4	29.6	10.26	8.50×10^3
	-2.8	35.8	10.26	1.39×10^3
$PhCH=CH_2$	26.1	61.3	9.95	6.59
$PhCH=CHMe$	20.9	57.8	9.95	19.2
$Ph_2C=CH_2$	-34.3	24.4	9.95	6.54×10^5
	22.4	58.8	9.95	1.53×10^2

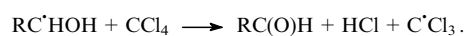
VII. Generation of radicals by ozone-induced bimolecular reactions

Ozone reacts very rapidly with alkenes and organoelement compounds without the formation of free radicals.^{49–53} However, it reacts with the C–H bonds of hydrocarbons and other organic compounds to generate free radicals.³ Evidence for this assumption can be derived from the following facts. Ozone initiates the chain oxidation of hydrocarbons in both gas and liquid phases.^{54–57} The peroxy radicals produced in the oxidation of hydrocarbons and polymers by an O_3-O_2 mixture were identified by EPR.^{58,59} The formation of peroxy radicals is confirmed by chemiluminescence induced by oxidation of hydrocarbons with the above mixture due to disproportionation of the peroxy radicals.^{55,60} Deuterated hydrocarbons are oxidised by ozone more slowly, which suggests that the ozone attack at the C–H and C–D bonds is a limiting step of the oxidation.^{53,61–65} The

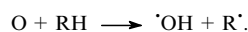
oxidation of hydrocarbons by ozone in carbon tetrachloride yields alkyl chlorides:^{60,66,67}



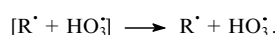
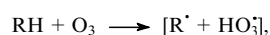
whereas the oxidation of alcohols yields hydrogen chloride:⁶⁸



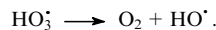
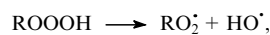
Ozone is decomposed in the gas phase at elevated temperatures to generate molecular and atomic oxygen; the latter initiates the formation of radicals:



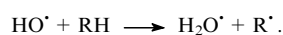
Hydrogen abstraction concomitant with cage radical processes is the most feasible reaction in the liquid phase:



The labile compounds $ROOOH$ and $HO_3^\cdot$ are rapidly decomposed to generate the radicals:



The reactive hydroxyl radical reacts rapidly with RH :



This mechanism is consistent with the high probability (p) of the exit of radicals to the bulk:

$$p = \frac{k_i}{2k_d},$$

where k_i and k_d are the rate constants determined experimentally for radical generation and ozone consumption, respectively (Table 17).^{69–72}

Table 17. The values of k_i , k_d (litre mol⁻¹ s⁻¹) and e for the oxidation reactions by ozone.

RH	k_i	k_d	p	Ref.
cyclo- C_6H_{12}	1.1×10^{-3}	1.8×10^{-3}	0.30	69
Me_2PhCH	1.6×10^{-2}	0.32	2.5×10^{-2}	70
$Me_2PhCOOH$	1.5×10^{-1}	0.1	0.68	71
$PhCHO$	2.0	2.0	0.50	72
$MeCHO$	1.6	2.7	0.30	72

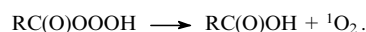
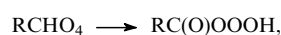
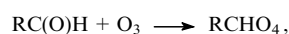
Table 18. The kinetic parameters of the reactions involving ozone and oxygen.

Oxygen acceptor	α	$10^{-11} b$	$0.5 h N_A v_i$	$0.5 h N_A (v_i - v_f)$ ($r^\cdot/r_c$) ₀	
$O_2(O_3) + HY \longrightarrow HO_2^\cdot (HO_3^\cdot) + Y^\cdot$					
RH	0.814	3.743	17.4	-3.8	0.551
HNR_2	0.936	4.306	20.0	-1.2	0.516
ROH	1.022	4.701	21.7	0.5	0.495
ROOH	1.000	4.600	21.2	0.0	0.500
$HSiR_3$	0.624	2.871	13.1	-8.1	0.616
RSH	0.658	3.026	13.8	-7.4	0.603
$HGeR_3$	0.608	2.796	12.6	-8.6	0.622
$HSnR_3$	0.586	2.695	12.1	-9.1	0.630
$O_2 + CH_2=CHR \longrightarrow ^\cdot OCH_2C^\cdot HR$					
$CH_2=CHR$	1.737	5.389	9.9	4.6	0.366

Table 19. The kinetic and thermodynamic parameters of the reactions involving ozone and oxygen.^{14–21}

Oxygen acceptor	br_e	E_{e0}	$10^{-9} A_0$	$\Delta H_{e\max}$
$O_2 + HY \longrightarrow HO_2^* + Y^*$ (see Refs 16 and 18)				
R ¹ H	13.61	56.3	5.0	76.1
R ² H	15.20	70.2	5.0	110.1
R ³ H	14.32	62.3	5.0	90.6
NH ₃	9.36	23.4	4.0	4.3
H ₂ NR	10.80	31.1	4.0	20.9
HNR ₂	11.73	36.7	4.0	33.9
ROH	14.45	51.1	5.0	73.7
ROOH	13.13	43.1	5.0	51.5
HSiR ₃	12.41	58.4	5.0	69.7
RSH	10.39	39.3	5.0	33.0
HGeR ₃	12.74	62.8	5.0	77.6
HSnR ₃	12.35	60.6	5.0	72.0
$O_2 + CH_2=CHR \longrightarrow ^\bullet O OCH_2C^*HR$ (see Ref. 19)				
CH ₂ =CHR	26.04	90.5	2.0	408.5
CH ₂ =CHPh	27.23	99.0	0.2	540.3
$O_3 + HY \longrightarrow HO_3^* + Y^*$ (see Refs 20 and 21)				
R ¹ H	13.61	56.3	0.2	76.1
R ² H	15.20	70.2	0.02	110.1
R ³ H	14.32	62.3	0.02	90.6
NH ₃	9.36	23.4	0.2	4.3
H ₂ NR	10.80	31.1	0.2	20.9
HNR ₂	11.73	36.7	0.2	33.9
ROH	14.45	51.1	0.2	73.7
ROOH	13.13	43.1	0.2	51.5
HSiR ₃	12.41	58.4	0.2	69.7
RSH	10.39	39.3	0.06	33.0
HGeR ₃	12.74	62.8	0.1	77.6
HSnR ₃	12.35	60.6	0.1	72.0

The low value of p for cumene is due to the fact that ozone reacts simultaneously with the C–H bond and with the π -bonds of the benzene ring without the formation of free radicals.⁷⁰ A similar situation takes place in the reaction of ozone with carbonyl compounds. Ozone reacts with both the C–H bond with the formation of radicals and the carbonyl group to yield a labile tetraoxide. The latter is rapidly decomposed to yield singlet oxygen.⁶⁶

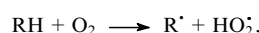


Since the reaction centres of the reactions $RH + O_3$ and $RO_2^* + RH$ are similar, this has been used to calculate the kinetic and thermodynamic parameters of ozone-mediated reactions (Tables 18–20).^{14, 20}

The experimental data for the reaction $RH + O_3$ can be found elsewhere.^{3, 8, 51, 52}

VIII. Chain generation in reactions with molecular oxygen

Chains are generated in the early steps of the oxidation of hydrocarbons in the absence of a hydroperoxide:³



which was proposed by Bolland and Gee.⁷³ The fact that this reaction occurs for oxidisable aldehydes was proved by Cooper and Melville.⁷⁴ The main experimental evidence in favour of this mechanism can be summarised as follows.^{7, 9}

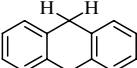
1. The rate of the radical formation in an $RH + O_2$ system measured by the free radical acceptor method for different compounds is directly proportional to the product of the concentrations $[RH] \times [O_2]$.

2. The rate constant for the reaction $RH + O_2$ increases with the decrease in stability of the weakest C–H bond in the molecule

Table 20. The enthalpies, activation energies and rate constants for the reactions $2RH + O_3 \longrightarrow R^* + HO_3^*HR$ calculated within the framework of the parabolic model.¹⁴

RH	D	n	ΔH_e	E	$\log A$	k (300 K)
EtMeHC–H	413.0	4	66.2	74.9	9.60	3.62×10^{-4}
Me ₃ C–H	400.0	1	53.2	67.2	9.00	1.99×10^{-3}
	418.5	8	71.7	78.3	9.90	1.85×10^{-4}
	408.4	10	61.6	72.1	10.00	2.80×10^{-3}
	395.5	1	48.7	64.7	9.00	5.43×10^{-3}
cis-Decalin	387.6	2	40.8	60.3	9.30	6.32×10^{-2}
H ₂ (CH ₂ =CH)C–H	368.0	3	21.2	63.9	8.48	2.26×10^{-3}
H(CH ₂ =CH)C(Me)–H	349.8	2	3.0	55.4	8.30	4.51×10^{-2}
Me ₂ (CH ₂ =CH)C–H	339.6	1	–7.2	50.8	8.00	0.14
cis-MeCH=CHC(H)(Me)–H	344.0	2	–2.8	52.8	9.30	1.28
H(Me ₂ C=CH)C(Me)–H	332.0	2	–14.8	47.6	8.30	1.03
Me ₂ (Me ₂ C=CMe)C–H	322.8	1	–24.0	43.7	8.00	2.46
H(CH ₂ =CMe)(CH ₂ =CH)C–H	307.2	1	–39.6	37.6	8.00	28.4
	341.5	4	–5.3	51.7	9.60	3.97
	330.9	4	–15.9	47.1	9.60	25.1
	312.6	4	–34.2	39.6	9.60	5.07×10^2

Table 20 (continued).

RH	<i>D</i>	<i>n</i>	ΔH_e	<i>E</i>	log <i>A</i>	<i>k</i> (300 K)
	301.0	2	−45.8	35.2	9.30	1.47×10^3
Me ₂ (MeC≡C)C−H	329.4	1	−17.4	46.5	8.00	0.80
MePhHC−H	364.1	2	17.3	54.2	8.30	7.31×10^{-2}
Me ₂ PhC−H	354.7	1	7.9	49.7	8.00	0.22
	345.6	4	−1.2	45.6	9.60	45.7
	322.0	4	−24.8	35.6	9.60	2.52×10^3
Me ₂ (NCH ₂)−H	379.5	1	32.7	56.0	9.00	0.18
[CH ₂ =CHC(H)−H] ₃ N	345.6	6	−1.2	53.5	8.78	0.29
Me ₂ C(OH)−H	390.5	1	4.4	61.9	9.00	1.67×10^{-2}
	329.7	1	−17.1	32.7	9.00	2.02×10^3
HO(MeCH=CMe)C(Me)−H	325.2	1	−21.6	44.7	8.00	1.65
PhC(O)−H	348.0	1	1.2	54.5	9.00	0.32
	394.1	4	47.3	63.9	9.60	2.98×10^{-2}
Me ₂ (Pr ⁱ O)C−H	390.8	2	44.0	62.0	9.30	3.21×10^{-2}
Ph ₂ C(OMe)−H	354.2	1	7.4	49.5	8.00	0.24
Ph(COOH)C(H)−H	367.0	2	20.2	55.6	8.30	4.17×10^{-2}
Bu ^t COO−H	358.6	1	15.6	31.2	9.00	3.69×10^3
Bu ₃ Si−H	351.0	1	−1.0	46.5	9.00	8.01

to be oxidised. Substitution of deuterium for the hydrogen atom in the RH molecule lowers the reaction rate, *e.g.*, the k_H/k_D ratio for diethyl sebacate is equal to 5.2 (413 K).⁷⁵

3. In polar solvents, the reaction $RH + O_2$ proceeds more rapidly, which is consistent with the polar nature of the transition state $R(\delta^+) \cdots H \cdots (\delta^-)O_2$.⁷⁵

4. The polarity causes a multidipole effect, *viz.*, the rate constant for a reaction increases with an increase in the number of polar groups in the molecule to be oxidised.⁷⁶

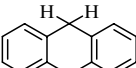
The values of rate constants for the reaction $RH + O_2$ can be found in numerous reviews and reference books (see, *e.g.*, Refs. 3, 7–9).

The structures of the transition states of the reactions $RH + O_2$ and $RO_2^* + RH$ are similar. The kinetic and thermodynamic parameters of the reaction $RH + O_2$, which characterise this reaction within the framework of the parabolic model, coincide with the corresponding parameters of the reaction $RH + O_3$ (see Tables 18 and 19). As the H–O bond in the radical $H-O_2^*$ formed is weak (220 kJ mol^{-1}), the activation energy of this reaction is close to its enthalpy; the pre-exponential factor A_0 depends on enthalpy.^{7,11} The values of the activation energy and the rate constant for this reaction calculated within the framework of the parabolic model are given in Table 21.

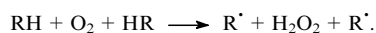
Table 21. The enthalpies, activation energies and rate constants for the reactions $RH + O_2 \longrightarrow R^* + HO_2^*$ calculated within the framework of the parabolic model.¹⁶

RH	<i>D</i>	<i>n</i> (C–H)	ΔH	$\Delta H_{\max}$	log <i>A</i>	<i>k</i> (450 K)
Bu ^t H ₂ C−H	422.0	12	202.0	76.1	12.508	8.17×10^{-12}
EtMeHC−H	413.0	4	193.0	76.1	12.06	2.68×10^{-11}
Me ₃ C−H	400.0	1	180.0	76.1	11.38	1.86×10^{-10}
	418.5	8	198.5	76.1	12.39	1.32×10^{-11}
	408.4	10	188.4	76.1	12.43	2.16×10^{-10}
	395.5	1	175.5	76.1	11.35	5.68×10^{-10}
<i>cis</i> -Decalin	387.6	2	167.6	76.1	11.60	8.31×10^{-9}
H ₂ (CH ₂ =CH)C−H	368.0	3	148.0	110.1	11.12	5.25×10^{-7}
H(CH ₂ =CH)C(Me)−H	349.8	2	129.8	110.1	10.58	1.96×10^{-5}

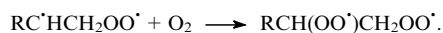
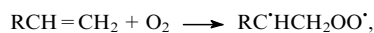
Table 21 (continued).

RH	<i>D</i>	<i>n</i> (C–H)	ΔH	$\Delta H_{\max}$	log <i>A</i>	<i>k</i> (450 K)
Me ₂ (CH ₂ =CH)C–H	339.6	1	119.6	110.1	9.96	4.47×10^{-4}
<i>cis</i> -MeCH=CHC(H)(Me)–H	344.0	2	124.0	110.1	10.41	6.27×10^{-5}
H(Me ₂ C=CH)C(Me)–H	332.0	2	112.0	110.1	9.89	4.70×10^{-4}
Me ₂ (Me ₂ C=CMe)C–H	322.8	1	102.8	110.1	8.63	3.02×10^{-4}
H(CH ₂ =CMe)(CH ₂ =CH)C–H	307.2	1	87.2	110.1	9.47	1.34×10^{-1}
	341.5	4	121.5	110.1	10.63	2.02×10^{-4}
	330.9	4	110.9	110.1	10.12	1.06×10^{-3}
	312.6	4	92.6	110.1	9.48	3.27×10^{-2}
	301.0	2	81.0	110.1	10.17	3.55
Me ₂ (MeC≡C)C–H	329.4	1	109.4	110.1	9.41	3.09×10^{-4}
PhH ₂ C–H	375.0	3	155.0	90.6	11.02	6.47×10^{-8}
PhMeHC–H	364.1	2	144.1	90.6	11.21	1.81×10^{-6}
PhMe ₂ C–H	354.7	1	134.7	90.6	10.79	8.59×10^{-6}
	345.6	4	125.6	90.6	11.25	2.82×10^{-4}
	322.0	4	102.0	90.6	10.66	3.94×10^{-2}
H ₂ (Me ₂ N)C–H	379.5	1	159.5	76.1	11.24	3.16×10^{-8}
[CH ₂ =CHC(H)–H] ₃ N	345.6	6	125.6	110.1	10.94	1.38×10^{-4}
Me ₂ C(OH)–H	390.5	1	170.5	76.1	11.32	2.00×10^{-9}
	329.7	1	109.7	76.1	10.66	5.08×10^{-3}
HO(MeCH=CMe)C(Me)–H	325.2	1	105.2	110.1	9.00	3.72×10^{-4}
PhC(O)–H	348.0	1	128.0	90.6	9.69	4.02×10^{-6}
	394.1	4	174.1	76.1	11.94	3.24×10^{-9}
Ph ₂ C(OMe)–H	354.2	1	134.2	90.6	10.78	9.60×10^{-6}
Bu ^t OO–H	358.6	1	138.6	51.5	11.39	1.21×10^{-5}
Bu ₃ ⁱ Si–H	351.0	1	131.0	69.7	11.02	3.92×10^{-5}

For compounds with weak C–H bonds [$D(\text{C–H}) < 330 \text{ kJ mol}^{-1}$], the chain generation follows a trimolecular mechanism:^{7,9}



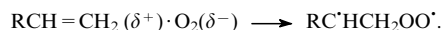
In the oxidation of unsaturated compounds, the chains appear in the reaction of O₂ addition to the double bond:^{5,7,9}



This process was suggested by Farmer⁷⁷ and experimentally proved for styrene by Miller and Mayo.⁷⁸ The reaction is endothermic, but its activation energy significantly exceeds ΔH .⁵

Monomer	$\Delta H / \text{kJ mol}^{-1}$	$E / \text{kJ mol}^{-1}$
CH ₂ =CH ₂	80.8	—
CH ₂ =CH ₂ Et	80.4	—
CH ₂ =CHPh	20.4	118
CH ₂ =CHC(O)OMe	84.8	117
CH ₂ =C(Me)C(O)OMe	86.9	115

With an increase in the solvent polarity, the rate of this reaction increases. For example, the reaction of O₂ addition to butyl methacrylate at 363 K is described by the rate constants equal to $8.1 \times 10^{-7} \text{ litre mol}^{-1} \text{ s}^{-1}$ in *N,N*-dimethylformamide and $3.4 \times 10^{-7} \text{ litre mol}^{-1} \text{ s}^{-1}$ in chlorobenzene.⁵ This may be preceded by the formation of a charge transfer complex:

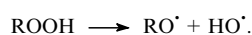


For some unsaturated compounds, chain generation follows a trimolecular mechanism, most probably, with the simultaneous formation of a biradical containing a peroxide bridge.⁵



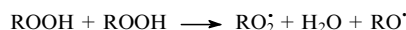
IX. Bimolecular reactions of hydroperoxides

The O–O bond of hydroperoxides is weak; the cleavage of this bond occurs with the formation of radicals:^{2,7}

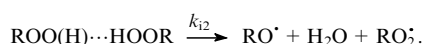
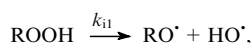


This reaction is responsible for the autoacceleration of the gas phase oxidation of hydrocarbons. In the case of liquid-phase oxidation of organic compounds, the autoacceleration of the chain reaction is due to diverse bimolecular reactions involving ROOH which proceed much faster than the monomolecular decomposition of the hydroperoxide.

The bimolecular reaction of hydroperoxide decomposition:



was discovered by Bateman *et al.*^{79,80} in the study of kinetics of autoxidation of unsaturated acid esters. It was found that the rate of radical generation in the developed oxidation reaction is proportional to the square of the ROOH concentration. Later, this reaction was studied by the free radical acceptor method over a broad range of ROOH concentrations. The following kinetic scheme for radical generation was proposed:⁸¹



According to this scheme, the rate of radical generation is equal to:

$$v_i = k_{i1}[\text{ROOH}] + k_{i2}K[\text{ROOH}]^2(1 + K[\text{ROOH}])^{-1}$$

For Me₃COOH (see Ref. 81) and PhMe₂COOH (see Ref. 82), the following parameters were determined (363 K):

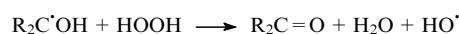
Hydroperoxide	<i>K</i> /litre mol ⁻¹	10 ⁷ <i>k</i> _{i2} /litre mol ⁻¹ s ⁻¹	10 ⁶ <i>k</i> _{i2} <i>K</i> /litre mol ⁻¹ s ⁻¹
Me ₃ COOH	1.9	8.61 (Ref. 81)	1.64
PhMe ₂ COOH	1.3	1.23 (Ref. 82)	0.16

The experimental data on bimolecular decomposition of hydroperoxides can be found in the reference books.^{3,8}

Table 22. The kinetic parameters of the reactions involving peroxides.^{25–27}

Second reactant	α	10 ⁻¹¹ <i>b</i>	0.5 <i>hN_Av_i</i>	0.5 <i>hN_A(v_i – v_f)</i> (<i>r</i> ≠ <i>r_e</i>) ₀	
ROOH + HY → RO* + HOH + Y*					
HR	0.788	3.743	17.4	–4.8	0.559
HNR ₂	0.907	4.306	20.0	–2.2	0.524
HOR	0.990	4.701	21.7	–0.5	0.502
HOOR	0.969	4.600	21.2	–1.0	0.508
HSiR ₃	0.604	2.871	13.1	–9.1	0.623
HSR	0.637	3.026	13.8	–8.4	0.611
HGeR ₃	0.589	2.796	12.6	–9.6	0.629
HSnR ₃	0.567	2.695	12.1	–10.1	0.638
ROOR + HY → RO* + ROH + Y*					
HR	0.796	3.743	17.4	–4.3	0.557
HNR ₂	0.916	4.306	20.0	–1.7	0.522
HOR	1.000	4.701	21.7	0.0	0.500
HOOR	0.978	4.600	21.2	–0.5	0.505
HSiR ₃	0.611	2.871	13.1	–8.6	0.621
HSR	0.644	3.026	13.8	–7.9	0.608
HGeR ₃	0.595	2.796	12.6	–9.1	0.627
HSnR ₃	0.573	2.695	12.1	–9.6	0.636
ROOH + CH₂=CHR → RO* + HOCH₂C*HR					
CH ₂ =CHR	0.889	3.238	5.1	–1.1	0.529
ROOR + CH₂=CHR → RO* + ROCH₂C*HR					
CH ₂ =CHR	0.849	3.238	5.1	–1.5	0.541

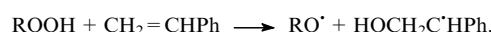
In the bimolecular ROOH decomposition reaction, the hydroxy group of one molecule attacks the O–O bond of another molecule and results in its cleavage. The reaction centres of this reaction and of the reaction of hydrogen peroxide reduction by the ketyl radical:



are similar.

The bimolecular decomposition of hydroperoxides is described well in terms of the kinetic parameters of the reaction of the ketyl radical with hydrogen peroxide,^{25,27} these parameters are given in Tables 22 and 23, and the activation energies and rate constants for these reactions calculated within the framework of the parabolic model are given in Table 24.

The formation of radicals in a bimolecular reaction of a hydroperoxide with an alkene was proved experimentally using the reaction of styrene with cumyl hydroperoxide as an example:⁸³



The rate of radical generation in this reaction is calculated by the formula:⁸⁴

$$v_i = k_i[\text{ROOH}][\text{CH}_2=\text{CHPh}],$$

where:

$$k_i = 1.2 \times 10^4 \exp\left(-\frac{72.0}{RT}\right) \text{ litre mol}^{-1} \text{ s}^{-1}.$$

Table 23. The kinetic and thermodynamic parameters for the reactions involving peroxides.^{25–27}

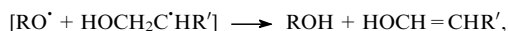
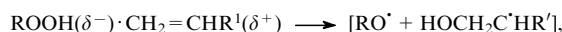
Second reagent	<i>br_e</i>	<i>E_{e0}</i>	10 ⁻⁹ <i>A₀</i>	$\Delta H_{e \max}$
ROOH + HY → RO* + H₂O + Y*				
R ¹ H	19.85	123.2	1.0	239.7
R ² H	21.15	139.9	0.1	283.5
R ³ H	20.35	129.5	0.1	256.2
H ₂ NR	17.33	82.6	10	149.7
HNR ₂	18.48	93.9	10	181.2
HOR	19.94	101.4	10	213.0
HOOR	20.45	107.9	10	228.6
HSiR ₃	15.80	97.0	1.0	145.6
HSR	18.40	126.3	1.0	214.9
HGeR ₃	16.71	110.6	1.0	172.0
HSnR ₃	17.15	119.8	1.0	187.4
ROOR + HY → RO* + ROH + Y*				
R ¹ H	21.34	141.2	2.0	289.2
R ² H	22.64	158.9	0.2	336.7
R ³ H	21.84	147.9	0.2	307.1
H ₂ NR	18.82	96.5	20	190.2
HNR ₂	19.97	108.6	20	225.0
HOR	21.43	114.8	20	259.6
HOOR	21.94	123.0	20	280.5
HSiR ₃	18.37	130.0	2.0	219.3
HSR	18.63	128.4	2.0	222.6
HGeR ₃	18.80	138.9	2.0	235.2
HSnR ₃	19.24	149.6	2.0	252.9
HOOR' + RCH=CH₂ → R'O* + RC*HCH₂OH				
CH ₂ =CHR	18.93	100.4	1.0	273.2
CH ₂ =CHCH=CHR	19.92	111.2	1.0	307.3
CH ₂ =CHPh	19.32	104.6	1.0	286.4
R'OOR' + RCH=CH₂ → R'O* + RC*HCH₂OR'				
CH ₂ =CHR	19.82	114.9	2.0	304.5
CH ₂ =CHCH=CHR	20.82	126.8	2.0	340.8
CH ₂ =CHPh	19.21	107.9	2.0	283.4

Table 24. The enthalpies, activation energies and rate constants for the reactions $2\text{ROOH} \longrightarrow \text{RO}_2^* + \text{H}_2\text{O} + \text{RO}^*$ calculated within the framework of the parabolic model.^{25–27}

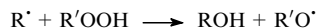
ROOH	<i>n</i>	ΔH_e	<i>E</i>	log <i>A</i>	<i>k</i> (350 K)
HOOH	2	50.0	114.1	8.93	7.97×10^{-9}
Pr ⁱ CHOOH	1	46.5	112.2	8.63	7.68×10^{-9}
	1	46.5	112.2	8.63	7.68×10^{-9}
Bu ^t OOH	1	39.6	108.4	8.64	2.90×10^{-8}
PhMe ₂ COOH	1	39.6	108.4	8.64	2.90×10^{-8}
Me ₂ C(OH)OOH	1	52.6	115.5	8.63	2.47×10^{-9}
Cl ₃ COOH	1	88.2	135.8	8.60	2.15×10^{-12}
Br ₃ COOH	1	88.0	135.7	8.60	2.23×10^{-12}
CCl ₃ CCl ₂ OOH	1	88.2	135.8	8.60	2.15×10^{-12}

This reaction is similar to the thermally neutral reaction, since $\Delta H = 9.7 \text{ kJ mol}^{-1}$.

Later, such reactions were studied for some other monomers.⁵ Thus studies of reactions with esters of polyatomic alcohols revealed the effect of the multidipole interaction.^{84,85} Presumably, this reaction is preceded by the formation of a charge transfer complex.

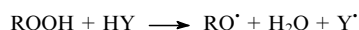


The reaction centres of this reaction and the substitution reaction involving alkyl radicals:⁸⁶



are similar. This circumstance can be used to calculate activation energies and rate constants of peroxides reactions. The kinetic and thermodynamic parameters are given in Tables 22, 23 and 25.

The condition $\Delta H < D(\text{O}-\text{O})$ [$D(\text{O}-\text{O}) = 175 \text{ kJ mol}^{-1}$] must be met to ensure successful competition of bimolecular reactions of the type:



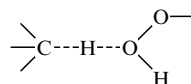
with monomolecular decomposition of the hydroperoxide. This condition is fulfilled for the majority of reactions of organic compounds, since $D(\text{Y}-\text{H}) < D(\text{HO}-\text{H})$ [$D(\text{HO}-\text{H}) = 498 \text{ kJ mol}^{-1}$]. For example, the enthalpy of the reaction of a hydroperoxide with cumene is equal to 41 kJ mol^{-1} . However,

Table 25. The enthalpies, activation energies (kJ mol^{-1}) and rate constants ($\text{litre mol}^{-1} \text{ s}^{-1}$) for the reactions $\text{Me}_3\text{COOH} + \text{CH}_2=\text{CHR} \longrightarrow \text{Me}_3\text{CO}^* + \text{HOCH}_2\text{C}^*\text{HR}$ calculated within the framework of the parabolic model.²⁵

$\text{CH}_2=\text{CHR}$	<i>n_C</i> (see ^a)	ΔH_e	<i>E</i>	log <i>A</i>	<i>k</i> (350 K)
$\text{CH}_2=\text{CH}_2$	2	53.5	124.0	9.00	6.23×10^{-10}
$\text{CH}_2=\text{CHMe}$	1	55.2	124.9	9.00	2.29×10^{-10}
$\text{CH}_2=\text{CMe}_2$	1	50.3	122.3	9.00	5.60×10^{-10}
$\text{CH}_2=\text{CHEt}$	1	54.9	124.8	9.00	2.37×10^{-10}
	2	55.2	124.9	9.00	2.29×10^{-10}
	2	52.2	123.3	9.00	3.97×10^{-10}
$\text{HC}\equiv\text{CH}$	2	33.2	113.3	9.30	4.91×10^{-8}
$\text{HC}\equiv\text{CMe}$	1	36.9	115.2	9.30	1.28×10^{-8}
$\text{MeC}\equiv\text{CMe}$	2	48.9	121.5	9.30	2.93×10^{-9}
$\text{CH}_2=\text{CHCH}=\text{CH}_2$	2	63.0	110.8	9.00	5.81×10^{-8}
$\text{CH}_2=\text{CHCMe}=\text{CH}_2$	1	54.0	110.4	9.00	3.34×10^{-8}
$\text{CH}_2=\text{CHCH}=\text{CMe}_2$	1	-0.3	107.7	9.00	8.45×10^{-8}
	2	-13.4	101.1	9.00	8.16×10^{-7}
$\text{CH}_2=\text{CHPh}$	1	13.6	107.7	9.00	8.45×10^{-8}
$\text{CH}_2=\text{CMePh}$	1	13.1	107.5	9.00	9.05×10^{-8}
$\text{MeCH}=\text{CMePh}$	1	3.0	102.6	9.00	4.87×10^{-7}
$\text{Me}_2\text{C}=\text{CMePh}$	1	3.0	102.6	9.00	4.87×10^{-7}
$\text{CH}_2=\text{CPh}_2$	1	-45.7	80.5	9.00	9.69×10^{-4}
	1	12.9	107.4	9.00	9.37×10^{-8}

^a The number of carbon atoms subject to the attack.

within the framework of the parabolic model^{25–27} the activation energy of this reaction is rather high (the calculated value for the reaction of *tert*-butyl hydroperoxide with cumene is $135.6 \text{ kJ mol}^{-1}$), which may be attributed to high repulsion energy in a non-linear transition state complex.



The kinetic parameters for the reactions involving C–H, N–H and O–H bonds (hydrocarbons, amines, alcohols, acids) are given in Tables 22 and 23; the results of calculations within the framework of the parabolic model are given in Table 26.

Table 26. The enthalpies, activation energies and rate constants for the reactions $\text{ROOH} + \text{HR} \longrightarrow \text{RO}^* + \text{H}_2\text{O} + \text{R}^*$ calculated within the framework of the parabolic model.²⁵

RH	<i>D</i>	<i>n</i> (R–H)	ΔH_1	<i>E</i>	log <i>A</i>	<i>k</i> (400 K)
EtMeHC–H	413.0	4	90.2	151.3	9.60	8.38×10^{-12}
Me ₃ C–H	400.0	1	77.2	140.6	9.00	5.41×10^{-11}
	418.5	8	95.7	150.4	9.90	2.16×10^{-11}
	408.4	10	85.6	145.0	10.00	1.41×10^{-10}
	403.9	14	81.1	142.6	10.15	4.06×10^{-10}
	395.5	1	72.7	138.2	9.00	1.10×10^{-10}

Table 26 (continued).

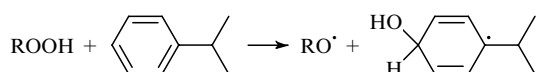
RH	<i>D</i>	<i>n</i> (R–H)	ΔH_1	<i>E</i>	log <i>A</i>	<i>k</i> (400 K)
<i>cis</i> -Decalin	387.6	2	64.8	134.2	9.30	7.57×10^{-10}
H ₂ (CH ₂ =CH)C–H	368.0	3	45.2	141.0	9.48	1.44×10^{-10}
H(CH ₂ =CH)C(Me)–H	349.8	2	27.0	132.3	9.30	1.32×10^{-9}
Me ₂ (CH ₂ =CH)C–H	339.6	1	16.8	139.0	9.00	8.84×10^{-11}
<i>cis</i> -MeCH=CHC(H)(Me)–H	344.0	2	21.2	141.0	9.30	9.59×10^{-11}
H(Me ₂ C=CH)C(Me)–H	332.0	2	9.2	135.5	9.30	5.04×10^{-10}
Me ₂ (Me ₂ C=CMe)C–H	322.8	1	0.0	131.4	9.00	8.75×10^{-10}
H(CH ₂ =CMe)(CH ₂ =CH)C–H	307.2	1	–15.6	124.7	9.00	6.88×10^{-9}
	341.5	4	18.7	139.8	9.60	2.72×10^{-10}
	330.9	4	8.1	135.0	9.60	1.17×10^{-9}
	312.6	4	–10.2	127.0	9.60	1.36×10^{-8}
	301.0	2	–21.8	122.0	9.30	3.07×10^{-8}
Me ₂ (MeC≡C)C–H	329.4	1	6.6	134.3	9.00	3.59×10^{-10}
MePhHC–H	364.1	2	41.3	150.4	9.30	5.46×10^{-12}
Me ₂ PhC–H	354.7	1	31.9	135.6	9.00	2.46×10^{-10}
	345.6	4	22.8	131.3	9.60	3.59×10^{-9}
	322.0	4	–0.8	120.7	9.60	9.22×10^{-8}
Me ₂ (NH ₂)C–H	379.5	1	56.7	141.4	9.00	4.21×10^{-11}
[CH ₂ =CHC(H)–H] ₃ N	345.6	6	22.8	131.3	9.78	5.39×10^{-9}
Me ₂ C(OH)–H	390.5	1	67.7	147.0	9.00	7.75×10^{-12}
	329.7	1	6.9	134.5	9.00	3.44×10^{-10}
HO(MeCH=CMe)C(Me)–H	325.2	1	2.4	124.8	9.00	6.61×10^{-9}
	337.5	1	14.7	119.9	9.00	2.91×10^{-8}
PhC(O)–H	348.0	1	25.2	124.7	9.00	6.68×10^{-9}
	394.1	4	71.3	141.1	9.60	1.83×10^{-10}
(Me ₂ C–H) ₂ O	390.8	2	68.0	139.4	9.30	1.53×10^{-10}
[CH ₂ =CHC(H)–H] ₂ O	360.0	4	37.2	140.7	9.60	2.05×10^{-10}
Ph ₂ C(OMe)–H	354.2	1	31.4	127.7	9.00	2.75×10^{-9}
Ph(COOH)C(H)–H	367.0	2	44.2	133.8	9.30	8.57×10^{-10}
Bu ₃ ^t Si–H	351.0	1	23.9	95.2	9.00	5.54×10^{-5}
Ph ₃ Ge–H	322.5	1	–5.1	97.0	9.00	3.17×10^{-5}
Ph ₃ Sn–H	296.9	1	–31.2	98.2	9.00	2.17×10^{-5}
H ₂ NN(H)–H	366.1	4	45.9	139.3	9.60	3.16×10^{-10}
HEtN–H	418.4	2	98.2	173.8	9.30	4.02×10^{-14}
Et ₂ N–H	382.8	1	62.6	160.9	9.00	1.12×10^{-13}
EtO–H	440.0	1	121.5	205.7	9.00	1.39×10^{-19}
Pr ⁱ O–H	443.0	1	124.5	207.8	9.00	7.40×10^{-20}
Bu ⁱ O–H	446.0	1	127.5	209.9	9.00	3.93×10^{-20}
	437.1	1	118.6	203.6	9.00	2.65×10^{-19}
ONO–H	327.6	1	9.1	134.2	9.00	3.77×10^{-10}
MeC(O)O–H	442.7	1	124.2	207.6	9.00	7.86×10^{-20}
PhCH ₂ C(O)O–H	443.5	1	125.0	208.1	9.00	6.76×10^{-20}

Table 27. The experimental and calculated rate constants of the reactions $\text{RH} + \text{O}_2 \longrightarrow \text{R}^\bullet + \text{HO}_2^\bullet$ and $\text{RH} + \text{ROOH} \longrightarrow \text{R}^\bullet + \text{H}_2\text{O} + \text{RO}^\bullet$.

Reaction	T /K	k		Ref.
		experi- mental	calcul- ated	
$\text{Me}_2\text{Pr}^\text{i}\text{C}-\text{H} + \text{O}_2$	800	1.0×10^{-1}	5.14×10^{-2}	24
 + O_2	400	3.47×10^{-7}	3.48×10^{-6}	11
 + O_2	600	7.2×10^{-1}	3.5×10^{-1}	27
$\text{PhMe}_2\text{C}-\text{H} + \text{O}_2$	400	1.95×10^{-7}	9.41×10^{-8}	12
$\text{HOOH} + \text{HOOH}$	350	4.76×10^{-9}	5.81×10^{-9}	5
$\text{Bu}^\text{i}\text{OOH} + \text{Bu}^\text{i}\text{OOH}$	350	4.99×10^{-7}	2.04×10^{-8}	3
$\text{Me}_2\text{EtCOOH} +$ $+ \text{Me}_2\text{EtCOOH}$	350	7.52×10^{-8}	2.04×10^{-8}	6
$\text{Me}_2\text{PhCOOH} +$ $+ \text{Me}_2\text{PhCOOH}$	350	2.71×10^{-9}	2.04×10^{-8}	9
$\text{Me}_2\text{PhCOOH} +$ $+ \text{Me}_2\text{PhCOOH}$	350	6.55×10^{-8}	2.04×10^{-8}	82
$\text{CH}_2=\text{CHPh} + \text{Bu}^\text{i}\text{OOH}$	350	2.21×10^{-7}	8.45×10^{-8}	12
$\text{PhMe}_2\text{CH} + \text{Me}_2\text{PhCOOH}$	400	2.92×10^{-7}	2.03×10^{-10}	9
$\text{EtMe}_2\text{COH} + \text{EtMe}_2\text{COOH}$	400	2.27×10^{-4}	3.02×10^{-19}	6

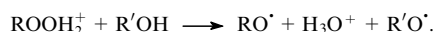
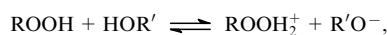
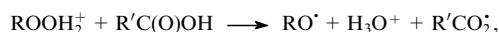
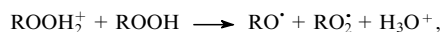
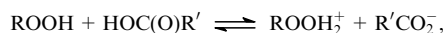
A comparison of the experimental and calculated values of the rate constants revealed that the former exceed the latter by several orders of magnitude (Table 27). Presumably, under the given experimental conditions the investigators deal with other, more efficient mechanisms of radical generation from the same reactants.

A comparison of rate constants and activation energies for the reactions $\text{ROOH} + \text{RH}$ and $\text{ROOH} + \text{C}=\text{C}$ revealed that the latter reaction proceeds faster and with lower activation energies (see Table 27). Probably, reactions of hydroperoxides with alkylaromatic hydrocarbons, *e.g.*, cumenes, of the type:

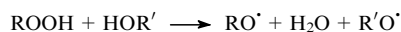


proceed faster.

The generation of radicals in the reaction of a hydroperoxide with a carboxylic acid follows, most probably, the mechanism of an acid-catalysed reaction as this takes place in an $\text{ROOH} + \text{mineral acid system}$ where the formation of radicals is preceded by the protonation of the hydroperoxide.⁷



In the reaction of alcohols with hydroperoxides



the radicals are also formed much faster (by 4–5 orders of magnitude) than in the bimolecular reaction of hydroperoxide decomposition (see Table 27).

Apparently, in these systems, too, a more rapid acid-catalysed hydroperoxide cleavage takes place.

X. Conclusion

Bimolecular reactions leading to radical generation are extremely diverse. Very often, they proceed much faster than monomolecu-

lar dissociation of molecules involving the weakest bond. Presumably, the fulfilment of the condition $E(\text{a bimolecular reaction}) < D(\text{a weak bond})$ depends on the enthalpy ratio of these reactions, *viz.*, $E(\text{a bimolecular reaction}) < D(\text{a weak bond})$, if $\Delta H(\text{a bimolecular reaction}) < D(\text{a weak bond})$. However, judging from the activation energies of individual reactions, this condition is insufficient.

First, for the dissociation reaction:

$$E_d = D + RT \approx D,$$

whereas for the bimolecular endothermic reaction:

$$E = \Delta H + \Delta E,$$

ΔE being dependent on the type of the reaction and ΔH (see Fig. 1). Therefore, a concrete analysis of the reactions that are compared is necessary.

Second, the pre-exponential factor A in the Arrhenius equation for the monomolecular decomposition reaction is $\sim 10^{13} - 10^{16} \text{ s}^{-1}$, while that for the bimolecular reaction (due to a negative activation enthalpy) is equal to $\sim 10^8 - 10^{10} \text{ litre mol}^{-1} \text{ s}^{-1}$. Moreover, proper allowance must be made for the fact that in the case of endothermic processes with $\Delta H_c > \Delta H_{e \text{ max}}$ the pre-exponential factor increases with the enthalpy of the reaction. The parabolic model takes proper account of all these factors and allows the estimation of activation energies and rate constants for any bimolecular homolytic reaction for which an analogous bimolecular radical reaction exists.

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^e — *Theor. Exp. Chem. (Engl. Transl.)*

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

Phase equilibria, phases and chemical compounds in the Ti–C system

A I Gusev

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Abstract. The results of experimental and theoretical investigations of the phase equilibria in the titanium–carbon system are generalised. The generalised thermodynamic characteristics of disordered titanium carbide, TiC_y , are reported. Peculiarities of the crystal structures of all the known and hypothetical compounds of titanium with carbon are considered in detail. The X-ray diffraction patterns which allow identification of all these compounds are presented. The phase diagrams of the Ti–C system constructed with allowance for atomic ordering of nonstoichiometric carbide, TiC_y , and for the existence of the molecular cluster-like compounds Ti_8C_{12} and $\text{Ti}_{13}\text{C}_{22}$ (TiC_2) are discussed. The bibliography includes 142 references.

I. Introduction

Carbides of Group IV and V transition *d*-metals belong to strongly nonstoichiometric interstitial compounds.^{1–3} A typical representative of strongly nonstoichiometric compounds is cubic titanium monocarbide TiC_y ($0.48 \leq y \leq 1.00$) with the *B1*-type structure, which has found wide practical applications and has been the subject of intensive experimental and theoretical research.

In 1823, Wollaston reported the discovery of pure crystalline titanium in metallurgic slags. However, after a lapse of 33 years Wöhler (Germany) showed that these crystals were titanium carbide containing nitrogen impurity. More recently in the 19th century contaminated titanium carbide was extracted from titanium-containing cast iron.^{4,5} Some attempts at obtaining pure titanium carbide by carbothermal reduction of titanium dioxide, TiO_2 , were also made (see Ref. 6).

The history of studies of titanium carbide and the Ti–C system can arbitrarily be divided into three periods.

In the first period (from the middle 1850s up to 1940), titanium carbide as well as the carbides and nitrides of other transition metals (zirconium, hafnium, vanadium, niobium, tantalum) were treated as ordinary chemical compounds of stoichiometric com-

position. Most studies carried out in this period were related to the establishment of the types of crystal structure and to the determination of the unit cell parameters of the titanium carbide samples obtained in one way or another. Titanium carbide was assumed to have a stoichiometric composition TiC . By the end of the first period, investigations of the thermodynamic and various physical properties of carbides and nitrides began and massive discrepancies between the results of different studies of the properties of titanium carbide were revealed. These discrepancies could not be rationalised by the measurement errors or by differences in the experimental methods. Detailed crystal-chemical studies showed that the discrepancies were due to the different content of carbon atoms in the carbide. It was found that, in contrast to other compounds, the composition of titanium carbide and, broadly, of the Group IV and V transition metal carbides and nitrides can vary over a very wide range while their crystal structure remains unchanged. In particular, the composition of titanium monocarbide TiC_y can vary from $\text{TiC}_{0.48}$ to $\text{TiC}_{1.00}$.

In the second period (from 1940 to 1970s), emphasis was mainly placed on investigations of the composition–property correlations for strongly nonstoichiometric compounds (in particular, interstitial phases). Interest in the carbides peaked in the 1960s, when thousands of communications were reported, concerning the effect of composition on the crystal-chemical, thermodynamic, thermal-physical, electrical, magnetic, optical, mechanical and other properties of these substances. By this time, the main qualitative concepts of the nature of chemical bonding in nonstoichiometric carbides have been developed. In the 1970s, the number of publications concerning basic problems relating to nonstoichiometric carbides reduced considerably; however, this time was characterised by increasing interest in applied studies. Titanium carbide had found wide use in production of hard alloys for metal-cutting tools. Most of the researchers erroneously concluded that there was almost nothing left to study in nonstoichiometric carbides. The first (tentative) variants of the phase diagram of the Ti–C system were reported,^{7,8} which reflected the existence of the only compound, *viz.*, cubic titanium monocarbide, TiC_y , with a broad homogeneity region. These phase diagrams remained nearly unchanged up to the mid-1990s.

For a long time after nonstoichiometric compounds were shown to have broad homogeneity regions, it was assumed that non-metal interstitial atoms and structural vacancies (unoccupied interstices of the metal sublattice) were randomly distributed over the lattice. However, crystallographic studies reported in 1967 (see Ref. 9) and more recently revealed that under particular condi-

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tions the interstitial atoms and vacancies can be redistributed over the sites of the crystal lattice, thus forming different types of ordered structures. The ordering of carbon atoms and structural vacancies was first observed in nonstoichiometric titanium carbide.⁹

In the late 1960s, the third period began of studies of nonstoichiometric compounds, which is mainly related to investigations into the ordering and its influence on the properties of these systems. Currently, one can say with certainty that at temperatures below 1000 K nonstoichiometric carbides and nitrides exist in the thermodynamically equilibrium ordered state, whereas their disordered state is metastable in the same temperature range.

In the 1980s, research into correlations between the properties of strongly nonstoichiometric compounds and the character of distribution of the interstitial atoms and vacancies began. It was shown that the effect of atomic and vacancy ordering on changes in the properties of a nonstoichiometric compound is comparable with the effect of varying the composition of the same system within the homogeneity region of the ordered phase. Therefore, varying the composition and redistribution of the atoms and vacancies in the crystal lattice of strongly nonstoichiometric compounds are two ways of controlling the properties of these compounds that possess equal rights.

A large number of ordered phases of strongly nonstoichiometric compounds was found during the decade from 1990 to 2000. The results of experimental studies and calculations of the phase equilibria allowed construction of the phase diagrams of the M–C and M–N (M = Ti, Zr, Hf, V, Nb, Ta) systems with allowance for both the presence of strongly nonstoichiometric carbides (MC_y) and nitrides (MN_y) and their ordering at temperatures below 1300 K (see Refs 1–3 and 10–27).

In 1992, a novel class of molecular metal–carbon nanoclusters was discovered.^{28–38} Three stable molecular clusters — Ti₈C₁₂, Ti₁₃C₁₄ and Ti₁₃C₂₂ — were obtained in the Ti–C system. Some experimental and theoretical studies on titanium dicarbide, TiC₂, were also reported.

Thus, the last two decades are characterised by avalanche-like growth of the body of information on the phase equilibria and compounds in the Ti–C system. The phase diagram of this system was found to be much more intriguing and complicated than it was assumed previously. The aim of this review was to generalise the results of recent (reported between 1980 and 2000) experimental and theoretical investigations of chemical compounds and phases in the Ti–C system taking into account all available information. The emphasis is placed on the phase equilibria in this binary system and on the crystal structure of both the known and theoretically possible (model) phases and compounds of carbon and titanium.

II. Phase diagrams of the Ti–C system at temperatures above 1000 K and thermodynamic properties of disordered titanium monocarbide TiC_y

1. Phase diagrams

No phase diagrams of the Ti–C system constructed with allowance for the ordering of nonstoichiometric carbide TiC_y were reported until the mid-1990s. In the text below we will consider the principal results of investigations into the phase equilibria in the Ti–C system at temperatures above the ordering temperature of nonstoichiometric titanium carbide (*i.e.*, at $T > 1000$ K).

Detailed studies of phase equilibria in binary carbide-forming M–C (M is a transition metal) systems were mostly carried out in 1961–1965.³⁹ Up to now, the experimental results [including those for the Ti–C system at temperatures above 1800 K (see Ref. 7)] obtained at that time are the most reliable and accurate.

The phase diagram of the Ti–C system is presented in Fig. 1. In this system, cubic titanium carbide TiC_y with the B1-type

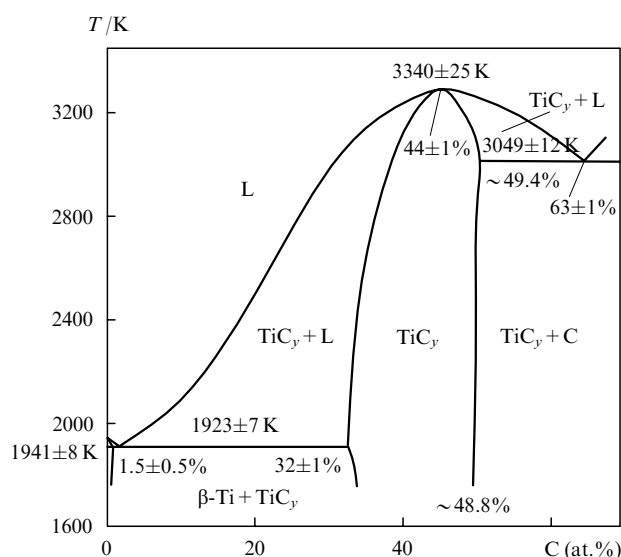


Figure 1. Experimental phase diagram of the Ti–C system at $T > 1800$ K.⁷

structure is in equilibrium with β -Ti (bcc structure) or α -Ti (hcp structure).

The melting temperature of pure metallic β -Ti is 1941 ± 8 K (see Ref. 7). The addition of carbon to titanium reduces the melting temperature of Ti down to the eutectic temperature [1918 ± 5 ,⁴⁰ 1923 ± 7 ,⁷ 1921 ± 5 ,^{41–43} 1925 K (see Ref. 44)]. The eutectic $L \rightleftharpoons \beta\text{-Ti} + \text{TiC}_y$ was reported to contain 4.4 at.% of carbon,⁴⁰ however, metallographic tests⁷ showed that the content of carbon in the eutectic is 1.5 ± 0.5 at.%. Difficulties in determination of the eutectic composition by metallographic tests have been pointed out.^{7,39}

Allotropic transformation $\alpha\text{-Ti} \rightleftharpoons \beta\text{-Ti}$ occurs at 1155 ± 5 K (see Ref. 8). The addition of carbon to titanium causes an increase in the temperature of this transformation up to the temperature of the $\beta\text{-Ti} + \text{TiC}_y \rightleftharpoons \alpha\text{-Ti}$ peritectoid transformation, which equals 1193 ± 3 K (see Refs 41–43) or 1205 K (see Ref. 44).

At temperatures above 1000 K, there is only one nonstoichiometric compound in the binary system Ti–C, *viz.*, cubic titanium carbide TiC_y with a very broad homogeneity region from TiC_{0.47} to TiC_{0.96} at $T \approx 1920$ K.^{7,39} Raising the temperature up to 3000 K causes a shift of both the lower and upper bounds of the homogeneity region of TiC_y towards a higher content of carbon. At $T \approx 3000$ K, the upper bound of the homogeneity region corresponds to a TiC_{0.998} composition (see Ref. 8). The highest melting temperature, 3340 ± 15 K (see Refs 7, 39, 41–43) or 3341 K (see Ref. 44), has carbide TiC_{0.80} which undergoes congruent melting. The temperature of the $L \rightleftharpoons \text{TiC}_y + C$ eutectic containing ~ 63 at.% of carbon is 3049 ± 12 K,⁷ 3049 ± 6 K (see Refs 39, 41, 42) or 3048 K (see Ref. 44).

Figure 2 presents the phase diagram of the Ti–C system constructed by Murray^{41,42} for $T > 800$ K. The same phase diagram was also reported in a reference guide.⁴³ Most of the phase equilibria in this diagram were shown tentatively. Murray supplemented the phase diagram shown in Fig. 1 with some essential details by indicating the regions of allotropic transformation $\alpha\text{-Ti} \rightleftharpoons \beta\text{-Ti}$ and peritectoid transformation $\beta\text{-Ti} + \text{TiC}_y \rightleftharpoons \alpha\text{-Ti}$. On the other hand, the phase diagram of this system (see Fig. 2) contained a tentatively shown existence region of ordered Ti₂C phase that was thought to exist and be stable at temperatures below 2170 K.^{9,45} However, the first report⁹ on the stability of the ordered Ti₂C phase at $T \leq 2170$ K was found to be erroneous: more recently, numerous studies of the ordering of nonstoichiometric carbide TiC_y revealed that cubic ordered Ti₂C phase (space group C_{4h}^5) is formed at temperatures below 1000 K (see, *e.g.*, Refs 12, 21, 46–56). At $T < 1000$ K,

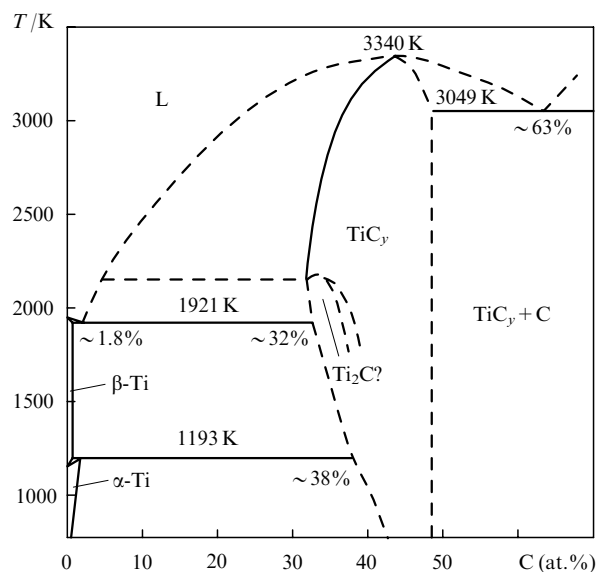


Figure 2. Phase equilibria in the Ti–C system at $T > 800$ K.^{41–43} Ti_2C is the ordered phase of nonstoichiometric titanium carbide TiC_y .

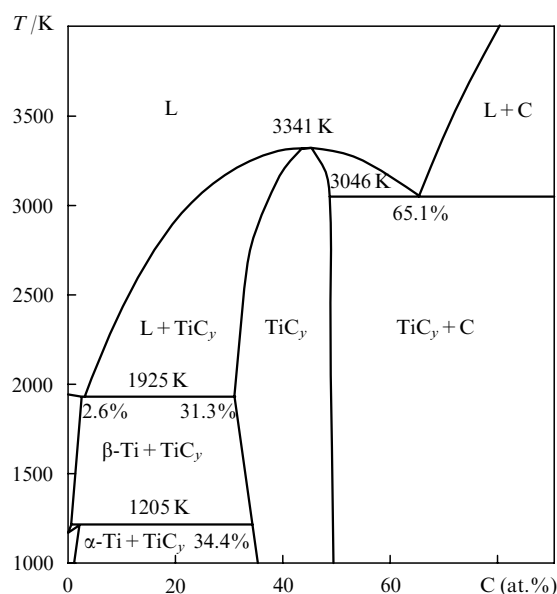


Figure 3. Phase diagram of the Ti–C system at $T > 1000$ K calculated⁴⁴ taking into account the results of experimental studies.^{7, 8, 39}

there are several ordered phases in the homogeneity region of carbide TiC_y that are not shown in this phase diagram.

Phase equilibria in the system under study at temperatures above 1000 K have most reliably been shown in the phase diagram calculated by Jonsson⁴⁴ taking into account the experimental data reported by Rudy *et al.*^{7, 39} Jonsson's phase diagram is shown in

Table 1. Crystal structure of phases that exist in the Ti–C system at $T > 1000$ K.

Phase	Existence region [C (at.%)]	Space group	Pearson notation	Lattice type
β -Ti	0–0.6	$Im\bar{3}m (O_h^9)$	<i>cI2</i>	<i>A2</i> (W)
α -Ti	0–1.6	$P6_3/mmc (D_{6h}^4)$	<i>hP2</i>	<i>A3</i> (Mg)
TiC_y	~32.0–49.8	$Fm\bar{3}m (O_h^3)$	<i>cF8</i>	<i>B1</i> (NaCl)
C	100	$P6_3/mmc (D_{6h}^4)$	<i>hP4</i>	<i>A9</i> (graphite)

Table 2. Characteristics of special points in the phase diagram of the Ti–C system at $T > 1000$ K.

Phase transformation	Composition of phases involved in reaction [C (at.%)]			T /K	Phase transformation type
$L \rightleftharpoons \beta\text{-Ti} + \text{TiC}_y$	1.8	0.6	32	1918 ± 5	eutectic transformation
$L \rightleftharpoons \text{TiC}_y$	—	44.4	—	3340 ± 15	congruent melting
$L \rightleftharpoons \text{TiC}_y + \text{C}$	65.1	48.5	~100	3050 ± 6	eutectic transformation
$\beta\text{-Ti} + \text{TiC}_y \rightleftharpoons \alpha\text{-Ti}$	0.4	34.4	2.1	1193 ± 3	peritectoid transformation
$L \rightleftharpoons \beta\text{-Ti}$	—	0	—	1941 ± 8	melting
$\beta\text{-Ti} \rightleftharpoons \alpha\text{-Ti}$	—	0	—	1155 ± 5	allotropic transformation

Fig. 3. The results of investigations of the crystal structure of different phases and the characteristics of special points of the phase diagram of the Ti–C system at $T > 1000$ K are listed in Tables 1 and 2, respectively.

2. Structure and thermodynamic properties of disordered titanium carbide

a. Structure

Disordered cubic titanium monocarbide TiC_y with the *B1*-type structure is the most important chemical compound that exists in the Ti–C system at temperatures above 1000 K. The unit cell of TiC_y comprises two face-centred (metal and non-metal) sublattices displaced by half the lattice constant with respect to each other (Fig. 4). All sites in the metal sublattice of TiC_y are occupied by titanium atoms. The number of sites in the non-metal (carbon) sublattice is larger than that of interstitial atoms (*i.e.*, carbon atoms), which is typical of nonstoichiometric compounds. In the disordered state, which is in thermodynamic equilibrium only at $T > 1000$ K and is treated as a quenched metastable state at lower temperatures, carbon atoms are randomly distributed over the sites. The non-metal sublattice is characterised by the same site occupation probability equal to the value of y (the relative content of carbon in the carbide). This is responsible for the retention of cubic symmetry of the disordered non-metal sublattice and means that all sites in the carbon sublattice of disordered TiC_y are crystallographically equivalent. A typical X-ray diffraction pattern of homogeneous cubic titanium carbide is shown in Fig. 5. The lattice constant of TiC_y nonmonotonically increases as the content of carbon increases (Fig. 6).⁵⁷

Nonstoichiometric titanium carbide can possess quite different thermodynamic properties within the homogeneity region. Therefore, of particular value are those studies in which the

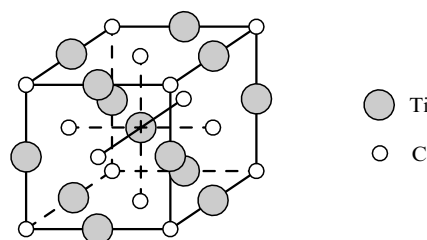


Figure 4. Unit cell of cubic disordered nonstoichiometric TiC_y with the *B1*(NaCl)-type structure. All sites in the metal sublattice are occupied by Ti atoms, while the sites in the non-metal sublattice are randomly occupied by C atoms.

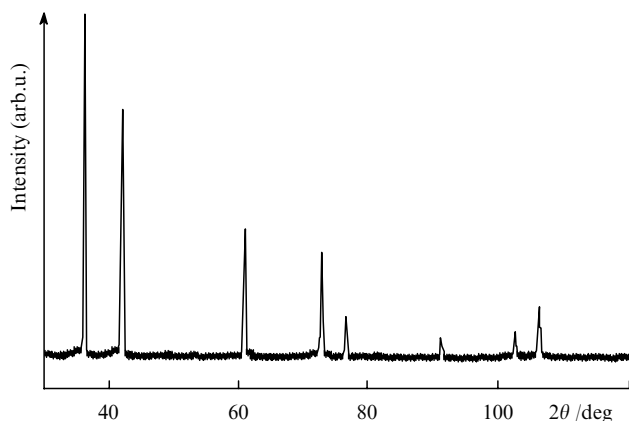


Figure 5. X-Ray diffraction pattern of disordered titanium carbide $\text{TiC}_{0.52}$ with cubic $B1$ -type structure ($a_{B1} = 0.4306$ nm, $\text{CuK}\alpha_{1,2}$ radiation).

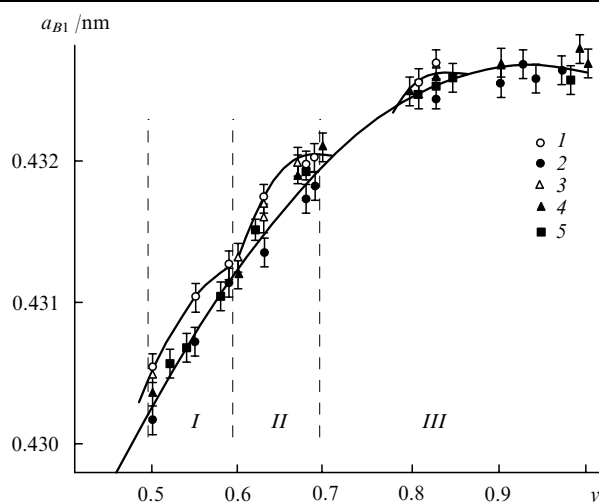


Figure 6. Lattice constant a_{B1} of the basic crystal lattice as a function of the composition of titanium carbide, TiC_y , in the quenched disordered (full circles) and annealed ordered (open circles) states.⁵⁷ Samples obtained by sintering Ti and $\text{TiC}_{0.94}$ (1, 2), by sintering Ti and C (3, 4) and by hot pressing Ti and $\text{TiC}_{0.98}$ (5). The existence regions of the ordered phases Ti_2C , Ti_3C_2 and Ti_6C_5 are labelled I, II and III, respectively.

measured thermodynamic characteristics were attributed to a certain composition of the carbide with the known (disordered or ordered) structural state. The presence of the temperature and concentration dependences of thermodynamic characteristics of disordered carbide allows quantitative description of high-temperature phase equilibria involving TiC_y ; however, of much greater importance is that using these data also provides the possibility of direct investigations into the disorder–order phase transformations. Unfortunately, the available experimental data on thermodynamic characteristics of nonstoichiometric titanium carbide are scarce.

b. Enthalpy (heat) of formation

Burning of a substance in oxygen in a calorimetric bomb is the main method of experimental determination of the formation enthalpy. Most of the data on the formation enthalpy of disordered TiC_y were obtained using this technique. The formation enthalpy can also be determined indirectly from the dependence of the partial pressure of the components of a compound on the evaporation temperature.

Calorimetric measurements of the standard formation enthalpy ($\Delta H_{f,298}^\circ$) of titanium carbide of a nearly stoichiometric

composition $\text{TiC}_{0.996}$ by burning of carbide in oxygen revealed⁵⁸ that $\Delta H_{f,298}^\circ = -183.8 \pm 1.7$ kJ mol⁻¹. Calculations using the refined value of the formation enthalpy of titanium dioxide gave a more correct value: $\Delta H_{f,298}^\circ = -184.6 \pm 1.7$ kJ mol⁻¹.⁸

Morozova *et al.*⁵⁹ determined the formation enthalpies of disordered cubic carbides of compositions $\text{TiC}_{0.79}$, $\text{TiC}_{0.91}$ and $\text{TiC}_{1.00}$ by burning them in oxygen and calorimetrically measuring the heat effect. The $\Delta H_{f,298}^\circ$ values for these carbides were found to be -183.0 ± 2.1 , -206.8 ± 0.8 and -192.6 ± 2.1 kJ mol⁻¹, respectively. The dependence of the formation enthalpy (in kJ mol⁻¹) determined by burning technique⁵⁹ on the composition of TiC_y can be described by the following formula:^{1–3,27}

$$\Delta H_{f,298}^\circ(y) = -91.07 - 186.7y + 89.0y^2.$$

The formation enthalpies of carbides $\text{TiC}_{0.63}$, $\text{TiC}_{0.72}$, $\text{TiC}_{0.80}$ and $\text{TiC}_{0.91}$ (-108.0 ± 7.0 , -135.0 ± 7.0 , -157.0 ± 7.0 and -184.0 ± 7.0 kJ mol⁻¹, respectively) were determined from the data on vacuum evaporation of TiC_y in the temperature range from 1873 to 2673 K.^{60,61} The dependence of $\Delta H_{f,298}^\circ$ (in kJ mol⁻¹) on the composition of TiC_y calculated using these values has the form⁶¹

$$\Delta H_{f,298}^\circ(y) = 135.6 - 467.8y + 128.3y^2.$$

Comparison of the $\Delta H_{f,298}^\circ(y)$ dependences obtained from calorimetric and evaporation measurements showed that these results are in satisfactory agreement for carbides with $y > 0.9$ but disagree at lower content of carbon. These dependences cannot be combined since the discrepancies between them seem to be due to the systematic errors of the methods employed. However, one can assume that the formation enthalpy of carbides TiC_y ($y < 0.9$) lies between the values found from calorimetric and evaporation measurements.

Analysis of the experimental data on the formation enthalpy of titanium monocarbide taking into account the position of the lower bound of the homogeneity region of TiC_y suggested¹⁸ that the dependence of $\Delta H_{f,298}^\circ$ (in kJ mol⁻¹) on the carbide composition has the form

$$\Delta H_{f,298}^\circ(y) = 16.75 - 304.49y + 89.04y^2. \quad (1)$$

Mention may be made that dependence (1) is close to the average between the experimental dependences $\Delta H_{f,298}^\circ(y)$ obtained from the results of calorimetric⁵⁹ and evaporation⁶¹ measurements.

c. Enthalpy (heat content)

High-temperature enthalpy ($H_T^\circ - H_{298}^\circ$) measurements are usually carried out by a mixing technique using an adiabatic-shell calorimeter. The high-temperature enthalpy of titanium carbide was measured^{62–65} and the following expressions for description of the temperature dependences of the enthalpy (in kJ mol⁻¹) were proposed.

For carbide of composition $\text{TiC}_{0.99}$ in the temperature range from 400 to 1800 K (see Ref. 62):

$$H_T^\circ - H_{298}^\circ = -19.95 + 49.53 \times 10^{-3}T + 1.67 \times 10^{-6}T^2 + 1499T^{-1}. \quad (2)$$

For carbide of composition $\text{TiC}_{0.95}$ (the measurement error was $\pm 1.4\%$) in the temperature range from 1300 to 2700 K (see Ref. 63)

$$H_T^\circ - H_{298}^\circ = -13.68 + 41.13 \times 10^{-3}T + 4.48 \times 10^{-6}T^2. \quad (3)$$

Storms⁸ found the following formula for calculating the enthalpy (in kJ mol⁻¹) of stoichiometric compound $\text{TiC}_{1.0}$ in the temperature range from 300 to 3000 K

$$H_T^\circ - H_{298}^\circ = -22.19 + 55.67 \times 10^{-3}T - 4.07 \times 10^{-6}T^2 + 1763.6T^{-1} + 16.1 \times 10^{-10}T^3. \quad (4)$$

The enthalpies of disordered carbides $\text{TiC}_{0.64}$, $\text{TiC}_{0.71}$, $\text{TiC}_{0.82}$ and $\text{TiC}_{0.99}$ were measured in the temperature range 1300–2500 K by a mixing technique.^{64,65} The authors suggested a polynomial description of the temperature dependence of the enthalpy; however, the polynomials did not fulfil the obvious normalisation condition:

$$H_T^\circ - H_{298}^\circ \equiv 0 \text{ at } T = 298 \text{ K.}$$

Because of this, we calculated the temperature dependences of the enthalpy (in kJ mol^{-1}) of these carbides taking into account the normalisation condition^{1,27} using the experimental data reported by Fesenko *et al.*⁶⁴ and the following expression

$$H_T^\circ - H_{298}^\circ = A + BT + CT^2 + DT^{-1}.$$

The corresponding formulae are as follows:
for carbide of composition $\text{TiC}_{0.64}$

$$H_T^\circ - H_{298}^\circ = -2.42 + 24.54 \times 10^{-3} T + 7.47 \times 10^{-6} T^2 - 1657.1 T^{-1}, \quad (5)$$

for carbide of composition $\text{TiC}_{0.71}$

$$H_T^\circ - H_{298}^\circ = -2.03 + 24.46 \times 10^{-3} T + 8.12 \times 10^{-6} T^2 - 1780.9 T^{-1}, \quad (6)$$

for carbide of composition $\text{TiC}_{0.82}$

$$H_T^\circ - H_{298}^\circ = -5.75 + 30.90 \times 10^{-3} T + 6.54 \times 10^{-6} T^2 - 1204.9 T^{-1} \quad (7)$$

and for carbide of composition $\text{TiC}_{0.99}$

$$H_T^\circ - H_{298}^\circ = -12.97 + 36.61 \times 10^{-3} T + 6.79 \times 10^{-6} T^2 + 431.1 T^{-1}. \quad (8)$$

These equations can be combined to derive a common function

$$\begin{aligned} (H_T^\circ - H_{298}^\circ)_{\text{TiC}_y} = & (15.86 + 12.03 \times 10^{-3} T + 9.67 \times 10^{-6} T^2 - 6051.5 T^{-1}) + \\ & (-22.80 + 6.17 \times 10^{-3} T - 3.09 \times 10^{-6} T^2 + 6328.2 T^{-1})y + \\ & (-5.680 + 19.06 \times 10^{-3} T)y^2 \quad (\text{kJ mol}^{-1}), \end{aligned} \quad (9)$$

which allows estimation of the enthalpy of disordered monocarbide TiC_y with any content of carbon in the temperature range from 300 to 2000 K.

d. Heat capacity and entropy

The heat capacity, C_p , of titanium carbides of compositions $\text{TiC}_{0.95}$ and $\text{TiC}_{0.99}$ was measured using the adiabatic technique in the temperature range from 12 to 300 K.⁶⁶ A decrease in the content of carbon in the TiC_y carbide is accompanied by a decrease in C_p . Lorenzelli *et al.*⁶⁷ measured the heat capacity of samples of disordered and ordered carbide of composition $\text{TiC}_{0.625}$ between 0.5 and 5.0 K; however, they presented only the difference between the heat capacities of the samples.

Since

$$C_p = \frac{d(H_T^\circ - H_{298}^\circ)}{dT},$$

the high-temperature heat capacity is usually determined using the results of experimental enthalpy measurements. This allows the functions (5)–(9) to be used for estimating the heat capacity of disordered TiC_y .

The entropy, S_{298}° , of stoichiometric titanium monocarbide $\text{TiC}_{1.0}$ is $24.24 \text{ J mol}^{-1} \text{ K}^{-1}$ (see Ref. 8). No experimental data on changes in entropy within the homogeneity region of cubic carbide TiC_y are available so far. To a first approximation, the dependence of entropy on the composition of carbide MC_y can be

represented by the additive sum of the entropies of the components normalised to the entropy of stoichiometric carbide $\text{MC}_{1.0}$, *i.e.*,

$$S_{298}^\circ(y) = k(S_{298}^\circ \text{M} + yS_{298}^\circ \text{C}), \quad (10)$$

where $k = S_{298}^\circ \text{MC}_{1.0} / (S_{298}^\circ \text{M} + S_{298}^\circ \text{C})$ is the normalisation constant and $S_{298}^\circ \text{M}$ and $S_{298}^\circ \text{C}$ are the entropies of the metal and carbon, respectively. The entropies of α -Ti and carbon are 30.72 (see Ref. 68) and $5.39 \text{ J mol}^{-1} \text{ K}^{-1}$ (see Ref. 69), respectively. Taking into account these values and the value $S_{298}^\circ \text{TiC}_{1.0} = 24.24 \text{ J mol}^{-1} \text{ K}^{-1}$ (see Ref. 8), the normalisation constant, k , was found to be 0.671 . To a first approximation, the dependence of entropy (in $\text{kJ mol}^{-1} \text{ K}^{-1}$) on the composition, TiC_y , has the form

$$S_{298}^\circ(y) = 20.62 + 3.62 y. \quad (11)$$

e. The free energy

The free energy of disordered carbide can be calculated using the dependences (1), (9) and (11).

Indeed, thermodynamic properties of solids are usually described assuming a constant pressure (usually, p is set to 0 or 1). Under isobaric conditions, the internal energy (configuration energy of a crystal), E , equals the enthalpy H . At 298 K, the enthalpy of a compound is equal to the formation enthalpy of this compound from corresponding elements, *i.e.*, $H_{298}^\circ \equiv \Delta H_{f,298}^\circ$. Taking into account the temperature dependence of the enthalpy of nonstoichiometric compound MX_y , from here it follows that

$$\begin{aligned} E(y, T) = H(y, T) = H_{298}^\circ(y) + (H_T^\circ - H_{298}^\circ)_{\text{MX}_y} \equiv & (12) \\ \equiv \Delta H_{f,298}^\circ(y) + (H_T^\circ - H_{298}^\circ)_{\text{MX}_y}. \end{aligned}$$

The free energy (F) of a disordered nonstoichiometric compound MX_y is given by the following expression^{1–3, 14, 17, 20, 22, 70}

$$\begin{aligned} F(y, 0, T) = E(y, T) - T[S(y, 0, T) + S_c(y, 0)] \equiv & (13) \\ \equiv F_0(T) + yF_1(T) + y^2F_2(T) - TS_c(y, 0), \end{aligned}$$

where $S(y, 0, T)$ is the non-configurational entropy, which is an explicit function of temperature; $S_c(y, 0)$ is the combinatorial (configurational) entropy, which is independent of temperature; and $F_0(T)$, $F_1(T)$ and $F_2(T)$ are the free energy parameters.

Using the standard entropy, the temperature dependence of entropy can be written as follows

$$S(T) = S_{298}^\circ + \int_{298}^T \frac{d(H_T^\circ - H_{298}^\circ)}{T}.$$

In this case

$$S(y, 0, T) = S_{298}^\circ(y) + \int_{298}^T \frac{d(H_T^\circ - H_{298}^\circ)_{\text{MX}_y}}{T}. \quad (14)$$

The free energy of a disordered compound MX_y minus the term responsible for the contribution of configuration entropy, $S_c(y, 0)$, is given by the expression

$$F_0(T) + yF_1(T) + y^2F_2(T) \equiv E(y, T) - TS(y, 0, T) \quad (15)$$

or, taking into account Eqns (12) and (14),

$$\begin{aligned} F_0(T) + yF_1(T) + y^2F_2(T) = \Delta H_{f,298}^\circ(y) + & (16) \\ + (H_T^\circ - H_{298}^\circ)_{\text{MX}_y} - T \left[S_{298}^\circ(y) + \int_{298}^T \frac{d(H_T^\circ - H_{298}^\circ)_{\text{MX}_y}}{T} \right]. \end{aligned}$$

The expression for a fraction of the free energy (in kJ mol^{-1}) of disordered carbide TiC_y was derived^{1–3, 27} from Eqn (16) using the dependences (1), (9) and (11)

$$\begin{aligned}
 F_0(T) + yF_1(T) + y^2F_2(T) = & \quad (17) \\
 = (32.61 + 31.61 \times 10^{-3} T - 9.67 \times 10^{-6} T^2 - 3026 T^{-1} - \\
 - 12.03 \times 10^{-3} T \ln T) + (-327.29 + 71.49 \times 10^{-3} T + \\
 + 3.09 \times 10^{-6} T^2 + 3164 T^{-1} - 6.17 \times 10^{-3} T \ln T)y + \\
 + (83.36 + 127.65 \times 10^{-3} T - 19.06 \times 10^{-3} T \ln T)y^2,
 \end{aligned}$$

where the parameters $F_0(T)$, $F_1(T)$ and $F_2(T)$ of the free energy $F(y, 0, T)$ [see Eqn (13)] are given in explicit form. Knowledge of these parameters allows all types of thermodynamic calculations of the phase equilibria involving nonstoichiometric titanium carbide.

3. High-temperature evaporation of titanium carbide

Thermodynamic properties of nonstoichiometric carbides are often determined using measurements of the vapour pressure above the solid compounds. Of particular interest is the case of congruent evaporation.

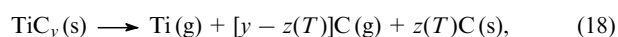
According to the kinetic theory of gases, the rate of evaporation from the surface that is in equilibrium with vapour equals the condensation rate, which is proportional to the equilibrium vapour pressure p . Under nonequilibrium conditions (in the case of, e.g., vacuum evaporation from the open surface) the evaporation rate is independent of the condensation rate and equals the equilibrium evaporation rate at a given temperature;⁷¹ this holds if the residual pressure in the vacuum chamber does not exceed 10 Pa. Therefore, knowledge of the rate of steady-state vacuum evaporation allows determination of the equilibrium parameter, namely, the saturated vapour pressure, and calculation of the thermodynamic characteristics. If transition from the condensed phase to the vapour phase is accompanied by dissociation of the former, the observed evaporation rate and the partial pressure are lower than the equilibrium values; this can be taken into account by introducing the evaporation coefficient $\alpha \leq 1.0$.

The kinetic and thermodynamic conditions for congruent evaporation of disordered nonstoichiometric interstitial compounds have been studied in detail in monograph.¹⁴ Thermodynamics of congruent evaporation of nonstoichiometric compounds was also developed.^{72, 73}

Evaporation of TiC_y at temperatures above 1800 K was studied by many authors. Mass spectrometric studies of the composition and the pressure measurements of the vapour above titanium carbide evaporated from a graphite effusion chamber (evaporation in the presence of excess of free carbon) at 2200–2500 K showed that the vapours contained elemental carbon and titanium and the C_2 and C_3 units; no molecular species TiC were found.^{74, 75} The vapour pressure of titanium above the titanium carbide–graphite system at 2383–2593 K measured⁷⁶ by the Knudsen effusion technique was found to be much higher than that determined by other authors. The value reported in this study seems to be overestimated, since evaporation of pure graphite through the effusion orifice was ignored. In the temperature range between 2518 and 2790 K, the vapours above the titanium carbide–carbon system contained Ti, TiC_2 , TiC_4 and C_3 units.⁷⁷ According to estimates,⁷⁸ the gas phase above this system contains elemental titanium and carbon as the major components at $T < 2500$ K and Ti, C and C_3 units at $T > 2500$ K. Titanium carbide was shown to undergo dissociation during evaporation at $2200 < T \leq 2500$ K in the presence of excess of free carbon; in this case, elemental titanium is released in the gaseous state while carbon is released in the solid state.^{74–76}

Studies of evaporation of carbide $\text{TiC}_{0.97}$ at 2773 K using Langmuir's technique revealed that under these conditions the compound undergoes congruent evaporation and that the vapours contain mostly elemental titanium and carbon.⁷⁹ The composition of carbide TiC_y affects the vapour pressure, namely, the vapour pressure of titanium monotonically increases from 1×10^{-4} Pa for $\text{TiC}_{0.91}$ to 0.2 Pa for $\text{TiC}_{0.55}$ as the content of carbon decreases (see Ref. 8). Evaporation and dissociation of

carbide $\text{TiC}_{0.91}$ in the temperature range between 1873 and 2673 K can be described by the reaction⁸⁰



where $z(T) = y$ at $T \leq 2100$ K; $z(T)$ decreases from y down to 0 as the temperature increases from 2100 to 2273 K; $z(T) = 0$ at $T \geq 2273$ K. The vapour pressure of titanium above carbide $\text{TiC}_{0.91}$ at 1900 K was found to be $\sim 6 \times 10^{-5}$ Pa,⁸⁰ which is close to the value reported by Storms.⁸

Evaporation of titanium carbide was mainly studied near the upper bound of the homogeneity region of the cubic phase taking the TiC_y samples with $y > 0.9$ as examples (see Refs 74–77, 79 and 80). The evaporation coefficient was assumed to be equal to unity, though if evaporation is accompanied by dissociation, this value is less than 1. The results of determination of the vapour pressure of titanium reported by different authors^{8, 74–77, 79, 80} are substantially different (from 2 to 40 times).

Vacuum evaporation (at 0.0013 Pa) of samples of cubic monocarbide TiC_y with different contents of carbon ($0.6 < y \leq 0.93$) was studied in the temperature range between 1873 and 2673 K.^{60, 61} The samples represented disordered titanium carbide, since only disordered nonstoichiometric carbides are in thermodynamic equilibrium at $T > 1300$ –1500 K.^{1–3, 14, 17, 70} All TiC_y samples were found to be homogeneous and contained one phase with the B1-type structure. Evaporation of titanium carbide was studied by Langmuir's technique. The evaporation rate

$$V = \frac{\Delta m}{S_{\text{ef}} t}$$

was determined from the mass loss (Δm) from the effective evaporation surface area, S_{ef} , of a vacuum heated sample over a period t . Due to the presence of the open surface pores the S_{ef} value was larger than the geometric evaporation surface area S

$$S_{\text{ef}} = S \left[1 + \left(\frac{9\pi P^2}{2} \right)^{1/3} \right],$$

where P is the relative porosity. The evaporation surface area was determined^{60, 61} with allowance for porosity which was determined as the average between the initial (before the experiment) and final (after heating) porosity. Evaporation was carried out until establishment of a constant total evaporation rate V (for a given temperature) and a constant crystal lattice parameter on the surface of the sample, i.e., until steady-state regime of the process.

The overall time of vacuum evaporation of titanium carbide samples varied from 2–8 h at 2673 K to 54 h at 1873 K. During evaporation the lattice constant on the surface of the samples remained virtually unchanged, which indicated a constant composition of TiC_y at $T < 2673$ K.

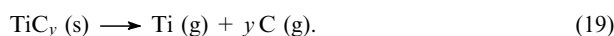
Evaporation of carbides TiC_y at $T < 2273$ K led to release of elemental carbon on the surface of the samples, whereas no elemental carbon was found on the surface of the TiC_y samples at higher evaporation temperatures ($T \geq 2273$ K). These data and the results of evaporation rate measurements suggest that at $T \leq 2273$ K evaporation of titanium carbide TiC_y is described by reaction (18). Indeed, at $T < 2100$ K the pressure and evaporation rate of metallic titanium are much higher than those of elemental carbon;⁶⁸ because of this, carbon is mainly released in the solid phase and can thus be found on the surface of the samples. As the content of carbon in TiC_y decreases (especially at $y \leq 0.8$), the amount of elemental carbon released on the surface rapidly decreases. Raising the temperature leads to an increase in the evaporation rate of carbon and no elemental carbon was found on the surface of TiC_y samples at $T > 2300$ K. At $T > 2273$ K, which corresponds to complete evaporation of carbon released on the surface, the $z(T)$ value equals zero, and the equilibrium in system (18) loses ambiguity. Since at temperatures below 2600 K (in the absence of excess elemental carbon) the vapour above titanium carbide contains mostly elemental

Table 3. Total evaporation rate V ($\text{kg m}^{-2} \text{s}^{-1}$) and partial pressure p_{Ti}° (Pa) in the temperature range between 2273 and 2673 K, evaporation coefficients α_{Ti} and α_{C} , atomisation enthalpy ($\Delta_{\text{at}}H_{298}^{\circ}$ / kJ mol^{-1}), formation enthalpy ($\Delta_{\text{f}}H_{298}^{\circ}$ / kJ mol^{-1}) and evaporation enthalpy ($\Delta_{\text{s}}H_{298}^{\circ}$ / kJ mol^{-1}) of TiC_y samples.⁶¹

TiC_y	$\ln V = a - b/T$		α_{Ti}	α_{C}	$\ln p_{\text{Ti}}^{\circ} = a - b/T$ (see ^a)		$\Delta_{\text{at}}H_{298}^{\circ}$		$\Delta_{\text{f}}H_{298}^{\circ}$	$\Delta_{\text{s}}H_{298}^{\circ}$
	a	b			a	b	see ^b	see ^c		
$\text{TiC}_{0.63}$	21.545 ± 0.091	72609 ± 225	0.80 ± 0.05	0.40 ± 0.05	29.538 ± 0.084	73836 ± 209	1028 ± 2	1025 ± 2	-108 ± 7	553 ± 70
$\text{TiC}_{0.72}$	21.882 ± 0.034	75111 ± 85	0.90 ± 0.05	0.45 ± 0.05	29.721 ± 0.035	76339 ± 87	1119 ± 2	1115 ± 2	-135 ± 7	644 ± 70
$\text{TiC}_{0.80}$	21.998 ± 0.129	77011 ± 322	0.90 ± 0.10	0.45 ± 0.10	29.987 ± 0.170	78601 ± 423	1198 ± 6	1193 ± 4	-157 ± 7	723 ± 70
$\text{TiC}_{0.91}$	21.700 ± 0.027	79115 ± 67	0.60 ± 0.05	0.30 ± 0.05	29.921 ± 0.023	80342 ± 57	1303 ± 1	1299 ± 1	-184 ± 7	828 ± 70

^a For carbide TiC_y , $\ln p_{\text{Ti}}^{\circ} = \ln p_{\text{Ti}}^{\circ} + \ln y$. ^b Found using the equation of the second law of thermodynamics (see below). ^c Found using the equation of the third law of thermodynamics (see below).

titanium and carbon and does not contain C_2 units and larger carbon molecular species and titanium carbide molecules,⁷⁸ one can suggest congruent evaporation of TiC_y in the temperature range between 2273 and 2673 K following the reaction



This character of evaporation of TiC_y has been confirmed experimentally.^{78–80}

An increase in the evaporation temperature causes a rapid increase in the evaporation rate: *e.g.*, the evaporation rate of $\text{TiC}_{0.92}$ increases by a factor of more than 20 000 as the temperature increases from 1873 to 2673 K. For TiC_y samples with different contents of carbon the temperature dependence of the evaporation rate has the form

$$\ln V = a - \frac{b}{T}.$$

In Table 3 we present the values of the coefficients a and b for some carbides. The evaporation rate of carbide of composition $\text{TiC}_{0.92}$ calculated using this dependence for 2773 K is $108 \times 10^{-5} \text{ kg m}^{-2} \text{s}^{-1}$. This is rather close to the estimate $(93–113) \times 10^{-5} \text{ kg m}^{-2} \text{s}^{-1}$ for the evaporation rate of $\text{TiC}_{0.97}$ at 2773 K.⁷⁹

If a compound MC_y undergoes congruent evaporation, the observed partial pressures of its components, p_{M} and p_{C} , are^{14, 71, 80}

$$p_{\text{M}} = \alpha_{\text{M}} p_{\text{M}}^{\circ} = \frac{V(2\pi RT A_{\text{M}})^{1/2}}{M}, \quad (20)$$

$$p_{\text{C}} = \alpha_{\text{C}} p_{\text{C}}^{\circ} = \frac{yV(2\pi RT A_{\text{C}})^{1/2}}{M}, \quad (21)$$

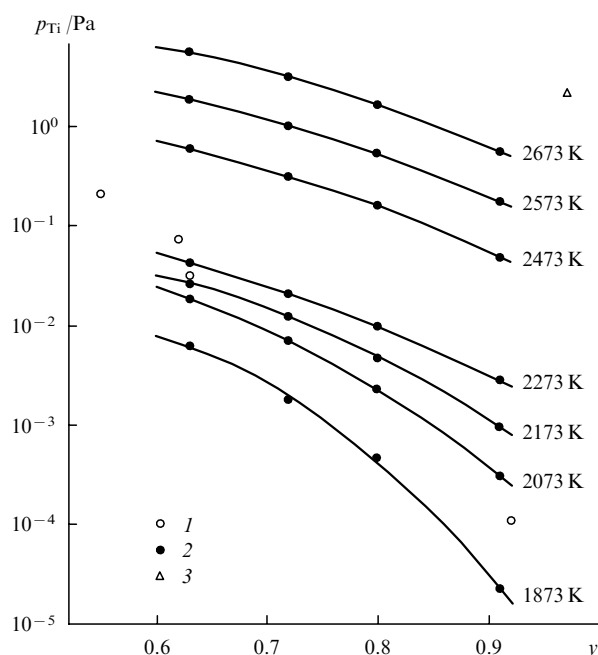
where α_{M} , α_{C} and p_{M}° , p_{C}° are the evaporation coefficients and the equilibrium partial pressures of the metal and non-metal components of condensed carbide MC_y ; V is the total evaporation rate; A_{M} and A_{C} are the atomic masses of the metal and carbon, respectively, and $M = A_{\text{M}} + yA_{\text{C}}$ is the molecular mass of carbide MC_y .

Under equilibrium congruent evaporation one gets $p_{\text{C}}^{\circ} = y p_{\text{M}}^{\circ}$; hence from Eqns (20) and (21) it follows¹⁴ that

$$\alpha_{\text{C}} = \alpha_{\text{M}} \left(\frac{A_{\text{C}}}{A_{\text{M}}} \right)^{1/2},$$

$$p_{\text{C}} = y \left(\frac{A_{\text{C}}}{A_{\text{M}}} \right)^{1/2} p_{\text{M}}.$$

In Fig. 7 we present the dependences of the partial pressure of titanium on the composition of carbide TiC_y . At any temperature, the larger the deviation of the carbide composition from the stoichiometric composition, the higher the p_{Ti} value. Earlier, an analogous type of change in p_{Ti} was reported for $T = 1900 \text{ K}$.⁸

**Figure 7.** Partial pressure of titanium, p_{Ti} , as a function of the composition of titanium carbide, TiC_y ; pressure p_{Ti} above the TiC_y carbide at 1900 K (1);⁸ data⁶¹ (2) and pressure p_{Ti} above the $\text{TiC}_{0.97}$ carbide at 2773 K (3).⁷⁹

Taking into account the relationship

$$p_{\text{C}} = y \left(\frac{A_{\text{C}}}{A_{\text{M}}} \right)^{1/2} p_{\text{M}},$$

the equilibrium constant, K , of reaction (19) is (when calculating K values, the partial pressure is given in atmospheres):

$$K = p_{\text{M}} p_{\text{C}} = p_{\text{M}}^{(1+y)} y y \left(\frac{A_{\text{C}}}{A_{\text{M}}} \right)^{y/2} = \alpha_{\text{M}}^{(1+y)} (p_{\text{M}}^{\circ})^{(1+y)} y^y \left(\frac{A_{\text{C}}}{A_{\text{M}}} \right)^{y/2}. \quad (22)$$

Knowledge of the equilibrium constant K allowed estimation of the enthalpy of process (19);⁶¹ in the case of evaporation accompanied by dissociation this is the atomisation enthalpy $\Delta_{\text{at}}H_{298}^{\circ}$. In accord with the second law of thermodynamics, the $\Delta_{\text{at}}H_{298}^{\circ}$ value was found using the available temperature dependences of K and by solving Van't Hoff's isobar equation

$$\frac{d \ln K}{dT} = \frac{\Delta_{\text{at}}H_{298}^{\circ}}{RT^2}. \quad (23)$$

Calculations of $\Delta_{\text{at}}H_{298}^{\circ}$ were carried out with inclusion of correction Δ for the temperature dependence of the enthalpy of the components of reaction (19):

$$\Delta = (H_T^\circ - H_{298}^\circ)_{\text{Ti(g)}} + y(H_T^\circ - H_{298}^\circ)_{\text{C(g)}} - (H_T^\circ - H_{298}^\circ)_{\text{TiC}_y(\text{s})}.$$

The $\Delta_{\text{at}}H_{298}^\circ$ values for carbides TiC_y under study were found by the least-squares minimisation of the expression

$$R \ln K(T) = c - \frac{\Delta_{\text{at}}H_{298}^\circ + \Delta}{T},$$

where c is a constant, using the experimental dependences $K(T)$. The heat effect of reaction (19), *i.e.*, the atomisation enthalpy of carbide TiC_y , was also determined using the equation of the third law of thermodynamics.

$$\Delta_{\text{at}}H_{298}^\circ = T\Delta\phi_T' - RT \ln K$$

with allowance for the calculated temperature and concentration dependence of the reduced potential $\Delta\phi_T'$.

The calculated standard atomisation enthalpies, $\Delta_{\text{at}}H_{298}^\circ$, of titanium carbides of different composition and the evaporation coefficients α_M and α_C are listed in Table 3. The parameters of the dependences $\ln V - T$ and $\ln p_{\text{Ti}}^\circ - T$ (see Table 3) correspond to the temperature range of congruent evaporation of TiC_y (from 2273 to 2673 K).

The dependence of the atomisation enthalpy on the composition of carbide TiC_y calculated by the least squares method using the $\Delta_{\text{at}}H_{298}^\circ$ values calculated from the equations of the second and third laws of thermodynamics has the form:

$$\Delta_{\text{at}}H_{298}^\circ(y)_{\text{TiC}_y} = 335.4 + 1177.8y - 128.3y^2 \pm 7. \quad (24)$$

For compounds MX_y , the atomisation enthalpy is given by the expression

$$\Delta_{\text{at}}H_{298}^\circ(y) = \Delta_s H_M^\circ + y\Delta_s H_X^\circ - \Delta H_{\text{f}298}^\circ(y), \quad (25)$$

where $\Delta_s H_M^\circ$ and $\Delta_s H_X^\circ$ are the evaporation enthalpies of the components M and X, respectively, and $\Delta H_{\text{f}298}^\circ(y)$ is the formation enthalpy of compound MX_y . The expression for the dependence of the heat of formation of carbide TiC_y on its composition derived using the relationships (24) and (25) and the reference data on the evaporation enthalpies of titanium and carbon, $\Delta_s H_{\text{Ti}}^\circ = 471$ and $\Delta_s H_{\text{C}}^\circ = 710 \text{ kJ mol}^{-1}$ (see Ref. 68) has the form^{60,61}

$$\Delta H_{\text{f}298}^\circ(y)_{\text{TiC}_y} = 135.6 - 467.8y + 128.3y^2 \pm 7. \quad (26)$$

The $\Delta H_{\text{f}298}^\circ$ values for carbides of compositions $\text{TiC}_{0.79}$, $\text{TiC}_{0.91}$ and $\text{TiC}_{1.00}$ were found to be -157 , -184 and -204 kJ mol^{-1} , respectively;⁶¹ this is in fairly good agreement with the results of earlier studies [*cf.* the $\Delta H_{\text{f}298}^\circ$ values of -183 , -207 (see Ref. 59) and -184 kJ mol^{-1} (see Ref. 58) for carbides of compositions $\text{TiC}_{0.79}$, $\text{TiC}_{0.91}$ and $\text{TiC}_{0.996}$, respectively]. The dissociation enthalpy of a gaseous titanium carbide molecule is $473 \pm 60 \text{ kJ mol}^{-1}$ (see Refs 68, 81). Using this value, the evaporation enthalpy of titanium carbide TiC_y was also roughly estimated^{60,61} as the difference between the atomisation and dissociation enthalpies (see Table. 3).

4. Nanocrystalline titanium carbide

Establishment of the fact that reduction of the grain or crystallite size down to and below a certain threshold value can cause substantial changes in the properties of solids^{82–86} gave a strong impetus to investigations of the nanocrystalline state of matter. Pioneering studies in this field were reported by Gleiter^{87–90} who developed a method for fabrication of compact nanomaterials from nanopowders (the so-called ‘compaction’). Ultradispersed and nanocrystalline transition metal carbides can be prepared by plasmachemical synthesis, mechanochemical synthesis, intense plastic deformation and structure ordering.^{91,92} Investigations of the nanocrystalline state of carbides are directed at making them less brittle and at improving their plasticity with simultaneous retention of high hardness typical of these compounds.

Ultradispersed transition-metal carbide powders are usually obtained by the interaction of chlorides of corresponding elements with dihydrogen and methane or other hydrocarbons in the low-temperature (4000–8000 K) argon plasma. The particles of such powders are single crystals 10 to 100–200 nm in size. Finely dispersed titanium, zirconium, niobium, tantalum, boron and silicon carbide powders were prepared by a plasmachemical technique.^{93,94}

Gas-phase synthesis involving laser heating of the mixture of reactant gases is a kind of plasmachemical synthesis.^{95–98} Laser heating allows control of homogeneous nucleation and excludes contamination. As the intensity of laser radiation increases, the size of nanoparticles decreases due to an increase in the temperature and in the heating rate of the reactant gases.

In the last decade, a mechanochemical technique has found wide use for the synthesis of nanocrystalline carbides. Mechanical milling is the most efficient method for production of large amounts of powders of different nanomaterials including carbides. Mechanochemical synthesis of nanocrystalline titanium carbide from a mixture of the metal and carbon powders was reported.⁹⁹ The mixture was ball milled. Formation of carbide occurred after pulverisation over a period of 4 to 12 h; the average particle size of the nanocrystalline powder after 48 h milling was $7 \pm 1 \text{ nm}$.

Nanocrystalline powder of cubic titanium carbide was also prepared by pulverising metallic titanium and graphite in a sapphire ball mill. The components were taken in a ratio that provided a $\text{Ti}_{44}\text{C}_{56}$ composition of the product.¹⁰⁰ The ball-to-powder mass ratio was 10:1. Milling was performed at room temperature in an argon atmosphere.

After pulverisation for 2000 s the X-ray diffraction pattern of the reactant mixture exhibited only broad reflections of elemental carbon and titanium (Fig. 8). Milling over a period of $1.1 \times 10^4 \text{ s}$ led to nearly complete disappearance of the graphite reflections. New reflections appeared after pulverisation for $1.5 \times 10^4 \text{ s}$ corresponded to a new cubic phase with the B1-type structure, *viz.*, titanium carbide. The lattice constant of titanium carbide pre-

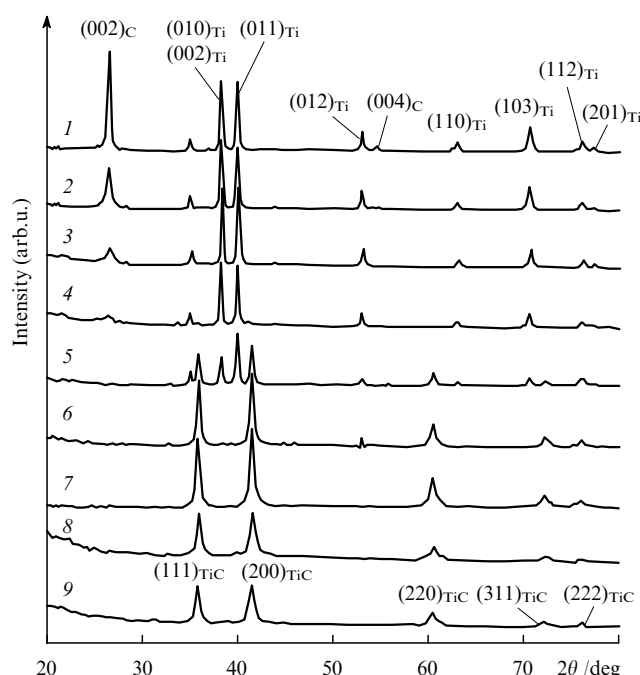


Figure 8. Changes in the X-ray diffraction patterns of a powder mixture $\text{Ti}_{44}\text{C}_{56}$ as a function of milling duration (t) in the mechanochemical synthesis of titanium carbide ($\text{CuK}\alpha_{1,2}$ radiation).¹⁰⁰ $t = 2 \times 10^3$ (1), 6×10^3 (2), 8×10^3 (3), 1.15×10^4 (4), 1.5×10^4 (5), 2.2×10^4 (6), 4×10^4 (7), 8×10^4 (8) and $7.2 \times 10^5 \text{ s}$ (9).

pared in this manner was 0.4326 nm. Prolonged milling (4×10^4 s) led to complete disappearance of the reflections of metallic titanium and to an increase in the intensity of titanium carbide reflections. After 8×10^4 s, mechanical deformation of the powder particles developed and the grain size reduced dramatically, which was manifested in substantial broadening of reflections in the X-ray diffraction pattern. Pulverisation for 72×10^4 s resulted in the formation of titanium carbide nanocrystals. No observable changes in the state of the carbide sample were detected upon further extension of milling duration to 10^6 s.

Figure 9 illustrates the changes in the powder grain size during pulverisation according to X-ray diffraction and electron microscopy studies. The formation of nanocrystalline titanium carbide involves four stages. The first stage (milling for no longer than 1.1×10^4 s) is characterised by the formation of Ti/C composite particles with an average size of ~ 1000 nm. Metallographic tests revealed an onion-like structure of these species comprised of titanium and carbon layers. In the second stage, which takes from 1.1×10^4 to 2×10^4 s, solid-phase interaction between titanium and carbon occurs, resulting in coarse-grained titanium carbide particles 800 to 1000 nm in size. The third stage takes from 2×10^4 to 8×10^4 s and involves intense milling of titanium carbide grains followed by the formation of finely dispersed powder with a rather broad grain size distribution (from 5 to 100 nm in diameter); in this stage, titanium carbide grains form agglomerates of size 5 to 10 μm . The last, fourth, stage takes 8×10^4 to 1×10^6 s and is characterised by ‘grain size homogenisation’ of the nanocrystalline powder. Carbide powder thus obtained had a particle size of $\sim 2 \pm 1$ nm while its grains were agglomerated into spherulites of size no greater than 300 nm.

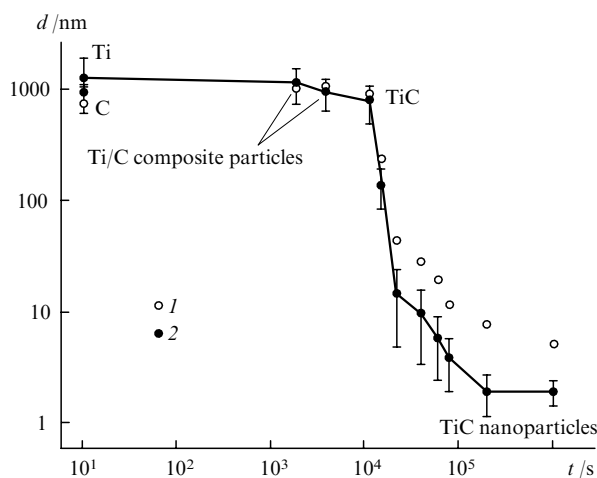


Figure 9. Grain size (d) of milled $\text{Ti}_{44}\text{C}_{56}$ powder as a function of milling duration t in the mechanochemical synthesis of titanium carbide.¹⁰⁰ The grain size was determined from broadening of X-ray diffraction reflections (1) and by electron microscopy (2).

Titanium carbide powders prepared¹⁰⁰ by milling over different periods of time (2.2×10^4 , 4×10^4 , 8×10^4 and 7.2×10^5 s) were sintered in activated plasma. This type of sintering is a kind of hot pressing. Salient features of the method are the use of pulsed voltage for plasma activation and combination of nonaxial torsion with pressure. Sintering for less than 8 min resulted in compact titanium carbide samples of high density (up to 5.2 g cm^{-3}) while the average grain size remained less than 70 nm. The microhardness of the sintered samples ($32 \pm 3 \text{ GPa}$) was no greater than that of conventional coarse-grained titanium carbide TiC_y ($0.9 \leq y \leq 1.0$).

The results obtained by El-Eskandarany *et al.*¹⁰⁰ pointed to high efficiency of mechanochemical synthesis for fabrication of nanocrystalline titanium carbide; however, no data on the chem-

ical composition of the carbide were reported in this study. The assumption¹⁰⁰ that the composition of mechanochemically synthesised titanium carbide is identical to that of the initial mixture ($\text{Ti}_{44}\text{C}_{56}$) seems to be doubtful. The reported lattice constant of titanium carbide is somewhat smaller, while the measured density is higher than the corresponding parameters of stoichiometric carbide $\text{TiC}_{1.0}$ (0.4328 nm and 4.91 g cm^{-3} , respectively). The reason for such a high density of titanium carbide obtained by El-Eskandarany *et al.*¹⁰⁰ is particularly incomprehensible. Even assuming that the synthesised carbide with the B1-type structure has the same composition as the charge [*i.e.*, $\text{Ti}_{0.44}\text{C}_{0.56}$ (or $\text{TiC}_{1.27}$?)], the metal sublattice of this carbide should contain defects, since for the B1-type structure the number of sites in the non-metal sublattice is the same as that in the metal sublattice and there are no possibilities of arranging any sort of excess atoms. If a particular sort of atom is in relative excess, the sublattice formed by the other sort of atom contains structural vacancies. In our case titanium carbide with the defect metal sublattice can have a composition $\text{Ti}_{0.79}\text{C}_{1.00}$; however, its density should be 20% lower than the calculated (theoretical) value. Noteworthy is that no vacancies were found so far in the metal sublattice of carbides; therefore, the metal sublattice of transition metal carbides is assumed to be perfect. Taking into account the aforesaid, the results obtained by El-Eskandarany *et al.*¹⁰⁰ should be thoroughly checked. We believe that titanium carbide synthesised in that study was highly contaminated with metal, which led to higher density of the material compared to the theoretical value.

A promising way of producing compact nanomaterials is to employ intense plastic deformation.^{85, 92, 101} Preparation of compact samples of nanocrystalline titanium carbide using this technique was reported.¹⁰² Milling and compacting experiments were carried out with coarse-grained ($d \approx 2\text{--}5 \mu\text{m}$) powder of nonstoichiometric carbide $\text{TiC}_{0.62}$. Intense plastic deformation was produced by applying torsion under quasi-hydrostatic pressure. X-Ray diffraction studies revealed retention of the B1-type cubic structure of all plastic deformed titanium carbide samples; however, the diffraction reflections were substantially broadened (Fig. 10). Evaluation of the grain size from the broadening magnitude showed that the compacted nanocrystalline samples of nonstoichiometric titanium carbide had an average grain size lying between ~ 30 and 50 nm. Contrary to metals, titanium carbide is very hard and brittle; therefore, it is of considerable interest that the grain size of titanium carbide was smaller than that of the metal samples after nearly identical plastic deformation.

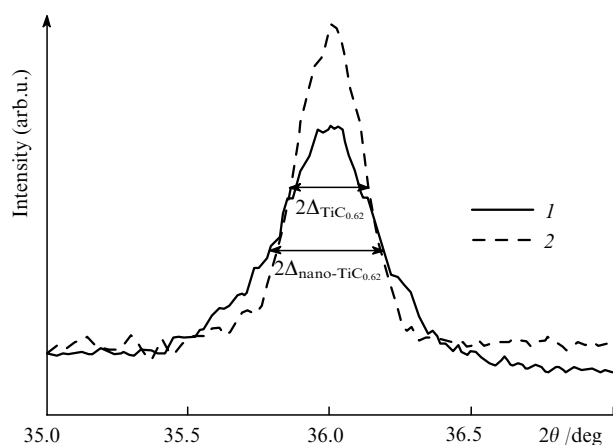


Figure 10. Broadening of the (111)_{B1} reflection of nanocrystalline titanium carbide of composition $\text{TiC}_{0.62}$ prepared by intense plastic deformation (1) and coarse-grained (grain size $\sim 5 \mu\text{m}$) carbide $\text{TiC}_{0.62}$ (2).¹⁰² 2Δ is the total width of the reflection at half-maximum ($\text{CuK}\alpha_{1,2}$ radiation).

III. New chemical compounds in the Ti–C system

The discovery of molecular clusters of carbon and the first observations of the C_{60} fullerene molecule^{103–105} gave an impetus to investigations into the synthesis, structure and properties of fullerenes (see, *e.g.*, Refs 106–108) and to an intensive search for methods of obtaining molecular clusters of other substances. By analogy with fullerenes, molecular clusters were expected to have unique physical and chemical properties that differ from the properties of the known polymorphous modifications of the same substances.

1. Molecular cluster Ti_8C_{12}

In 1992,²⁸ search for new molecular clusters led to the discovery of unusual, stable charged cluster $Ti_8C_{12}^+$ corresponding to a pentagondodecahedral molecule of stoichiometric composition Ti_8C_{12} (Fig. 11 *a*). In an ideal dodecahedral molecule, all atoms are arranged on a sphere whose surface is obtained by linking adjacent atoms and comprises twelve regular pentagons. In this molecule, all carbon and titanium atoms are tricoordinated (similarly to fullerene C_{60}), occupy identical sites and are distributed over the vertices of the dodecahedron in such a manner that the Ti atom is linked to carbon atoms only while six C_2 units alternate with eight Ti atoms. The dodecahedral structure of Ti_8C_{12} can be represented as a cube with eight titanium atoms at the vertices and a C_2 unit in each face. The point symmetry group, T_h , of this structure includes 24 symmetry elements (rotations and reflections). High symmetry of the met-car (metallocarbohedrene) molecule implies its stability.

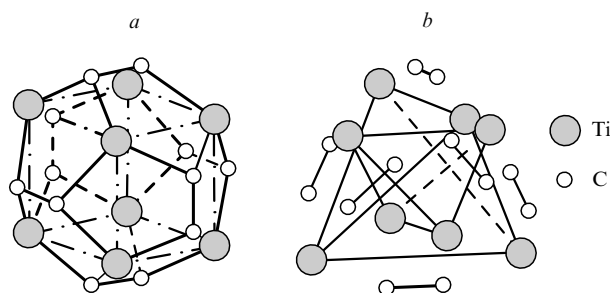


Figure 11. Dodecahedral structure of a Ti_8C_{12} molecular cluster of T_h symmetry (*a*) and a fragment of structure of T_d symmetry (*b*).²⁹

Yet another possible structure of the Ti_8C_{12} cluster is characterised by the point symmetry group T_d (see Fig. 11 *b*).²⁹ In this structure, titanium atoms occupy two types of lattice sites and each type of site forms a tetrahedron. The smaller tetrahedron is rotated by 90° about the larger tetrahedron. The sites in the titanium sublattice differ in arrangement with respect to the C_2 units. Indeed, six C_2 units are arranged parallel to the edges of the larger tetrahedron built of $Ti(1)$ atoms and perpendicular to the edges of the smaller tetrahedron formed by four $Ti(2)$ atoms. The $Ti(1)$ atoms are linked to three adjacent carbon atoms while the $Ti(2)$ atoms form bonds with six carbon atoms. The $Ti(1)$ –C and $Ti(2)$ –C distances are 0.193 and 0.219 nm, respectively.²⁹

The issue of which structural type is practically realised is still to be clarified since no molecular crystals of met-cars have been synthesised so far.

Clusters Ti_8C_{12} were synthesised using the gas-phase plasma-chemical technique with helium as inert gas, hydrocarbons (methane, ethylene, acetylene, propylene and benzene) and titanium vapours as reactants; the pressure of the gas mixture in the reactor was 93 Pa. A rotating metallic titanium rod was evaporated by exposing it to focussed radiation of a Nd laser operated at 532 nm, thus creating an ionised metal vapour beam. Neutral and ionised clusters were separated from other reaction products and

analysed mass spectrometrically. The mass spectra of the reaction products exhibited a sharp peak corresponding to the Ti_8C_{12} molecule. In addition to neutral molecules, the mixture of ionised gases also contained stable $Ti_8C_{12}^+$ ions.

The cluster Ti_8C_{12} was assumed²⁸ to be a member of a novel class of molecular clusters and called metallocarbohedrene or met-car (see Ref. 106). In met-cars, both the transition metal and carbon atoms form a cage-like structure. Indeed, other M_8C_{12} clusters of such transition metals as Zr, Hf, V,^{30,31} Cr, Mo and Fe³² were obtained after a short time. Met-cars have been reviewed.^{33,34}

The high stability of the cluster Ti_8C_{12} is thought to be due to peculiarities of its molecular and electronic structure; chemical bonds in the Ti_8C_{12} molecule are similar to those in the carbon fullerenes.²⁸ However, in contrast to C_{60} fullerene, both ionised and neutral M_8C_{12} molecules are comprised of five-membered rings only. The shape of the surface of stable cluster Ti_8C_{12} is similar to that of hypothetical unstable (and, hence, unfeasible) C_{20} fullerene. This fact shows that full similarity of chemical bonds in the clusters M_8C_{12} to those in carbon fullerene is hardly probable.

Indeed, calculations of the equilibrium crystal and electronic structure of the cluster Ti_8C_{12} with T_h symmetry (see Ref. 35) showed that the bonds between the titanium atoms and three adjacent carbon atoms differ from the bonds between carbon atoms in graphite or C_{60} fullerene. In particular, the Ti–C and C–C bond lengths in the Ti_8C_{12} molecule differ by nearly a factor of 1.5 and equal $3.76a_0$ and $2.63a_0$ ($a_0 = 0.052918$ nm is the radius of the first Bohr orbit), respectively. According to Reddy *et al.*,³⁶ the Ti–C bond is $\sim 30\%$ longer than the C–C bond. On the other hand, the distances from carbon and titanium atoms to the centre of the cluster are nearly equal. This means that the real dodecahedral structure of Ti_8C_{12} is strongly distorted. The bonding states of the cluster Ti_8C_{12} are thought to be composed of the Ti *d*-AOs and the C_2 MOs while the Fermi level lies between the bonding and antibonding states of titanium, thus providing stability for the cluster.³⁵ Analogous conclusions that clusters M_8C_{12} have a distorted rather than ideal pentagondodecahedron shape were obtained in calculations reported by other authors.

Comparative analysis of the electronic structure of the Ti_8C_{12} met-car of T_h and $T_d^\dagger$ symmetry showed³⁷ that in both structural types the highest occupied energy level corresponds to a sharp peak of the density of states (DOS) composed mainly of the $C2p$ - and $Ti3d$ -AOs. High chemical stability of compound Ti_8C_{12} is due to a combination of strong $Ti3d$ – $C2p$ interactions between the titanium atoms and C_2 unit on the one hand and to the C–C interactions in the carbon units on the other hand. In both structural types, Ti_8C_{12} has an open electron shell and can therefore be both electron acceptor and donor.

The atoms in met-car molecules are tightly bound. For instance, the bond energy in the Ti_8C_{12} molecule is 6.1–6.7 eV per atom.^{35,36,38} For comparison, this parameter is 7.4–7.6 eV per atom for C_{60} fullerene molecule (see Refs 109, 110) and 7.2 eV per atom for titanium carbide TiC with the *B1* (NaCl)-type fcc structure.³⁵

Modern concepts of the geometry and electronic structure of molecular clusters Ti_8C_{12} (see Refs 29, 35–38) provide good explanation for their chemical stability and specific features of the reactivity towards both polar and nonpolar compounds. Combination of high reactivity and stability of Ti_8C_{12} clusters was confirmed experimentally.¹¹¹

Molecular cluster Ti_8C_{12} has been the most detailed studied new compound in the Ti–C system; however, no macroscopic amounts of this substance were obtained so far.

[†] Calculations for T_h and T_d symmetry were carried out using the structure parameters and interatomic distances reported by Reddy *et al.*³⁶ and by Lin and Hall,²⁹ respectively.

2. Polymorphous modification of dicarbide TiC₂

Comparative analysis of the electronic structure of hypothetical metastable polymorphous modifications of carbide TiC_{1.0} with the *B2* (CsCl)-, *B8* (NiAs)-, *B3*- and *B4* (sphalerite and wurtzite ZnS)-type structures and that of the real carbide TiC_{1.0} with the *B1*-type structure showed¹¹² that search for new stable modifications of titanium carbide should be performed among those substances that are structurally similar to or derived from the *B1* type.

Titanium dicarbide, which can have several types of crystal structure, was studied as a representative of this group of substances.^{112, 113} The ThC₂-type monoclinic structure (space group *C2/c*) has a tetrahedral body-centred metal sublattice while the C₂ units occupy the octahedral interstices. In the CaC₂ (*C11a*)-type tetragonal body-centred structure [space group *I4/m* (*C*_{4h}⁵)] the C₂ units also occupy octahedral interstices. The *C11a* structural type can be derived from the *B1*-type lattice by extending it along the *c* axis; sites in the non-metal sublattice are occupied by the C₂ units oriented along the *c* axis. The unit cell of titanium dicarbide with this structural type comprises two formula units TiC₂ (Fig. 12). The atomic coordinates in the unit cell are listed in Table 4; the running coordinate of carbon atoms, *z/c* = 0.427, was determined assuming the same length of all Ti–C distances in the unit cell because each type of atom occupies sites of the same type. Figure 13 presents the X-ray diffraction pattern of tetragonal TiC₂ calculated using the atomic coordinates listed in Table 4.

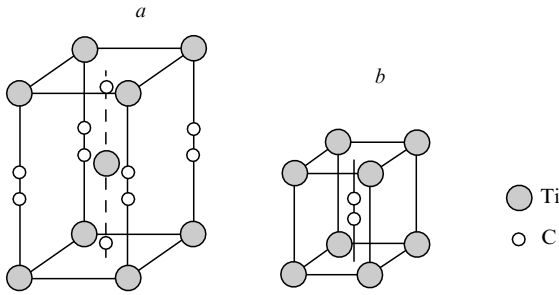


Figure 12. Unit cells of body-centred tetragonal TiC₂ with the CaC₂ (*C11a*)-type structure, space group *I4/m* (*C*_{4h}⁵) (a), and with the CsCl (*B2*)-type structure, space group *P4/mmm* (*D*_{4h}¹) (b).

The non-metal sublattice of titanium dicarbide with the *B2* (CsCl)-type tetragonal structure [space group *P4/mmm* (*D*_{4h}¹)] is built of C₂ units. The unit cell of this structure comprises one

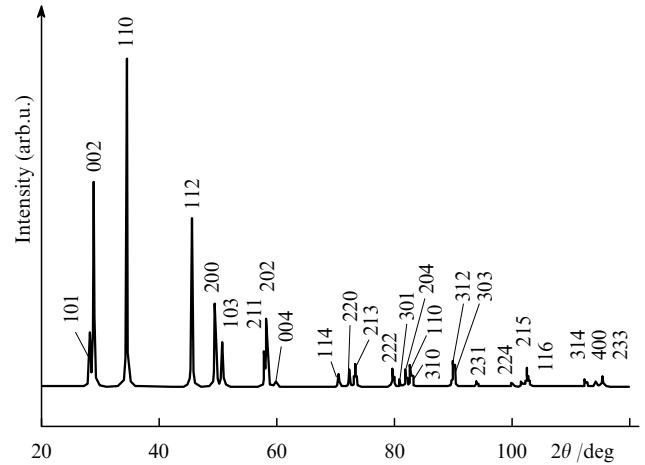


Figure 13. X-Ray diffraction pattern of tetragonal TiC₂ with the CaC₂ (*C11a*)-type structure, space group *I4/m* (*C*_{4h}⁵). Calculated for CuK_{α1,2} radiation.

formula unit TiC₂ (see Fig. 12). The atomic coordinates in the unit cell are listed in Table 4. The running coordinate, *z/c*, of carbon atoms remains unknown so far and can vary between 0 and 0.5. The C–C separation in the C₂ unit is 0.124 nm; in titanium dicarbide this distance should be somewhat longer due to titanium–carbon interatomic interactions. This suggests that the most probable *z/c* values lie between 0.25 and 0.31. Figure 14 presents the X-ray diffraction patterns of tetragonal titanium dicarbide TiC₂ (space group *P4/mmm*) calculated for several different positions of the carbon atom (*z* = 0.10, 0.25, 0.30 and 0.40). Position of the carbon atom has a strong effect on the intensity ratio of diffraction reflections, namely, an increase in *z* from 0.1 to 0.4 causes a decrease in the intensities of the (001) and (111) reflections and an increase in the intensity of the (101) reflection.

Similarly to cubic monocarbide TiC_y, in titanium dicarbide with the CaF₂ (*C1*)-type cubic structure [space group *Fm3m* (*O*_h⁵)] (Fig. 15) titanium atoms form a face-centred metal sublattice. However, carbon atoms occupy tetrahedral rather than octahedral (as in TiC_y) interstices. Naturally, the lattice constant of titanium dicarbide must be larger than that of titanium monocarbide, since only in this case is the size of the tetrahedral interstice sufficient to contain a carbon atom. Analysis of the crystal structure of cubic TiC₂ showed that it is a typical representative of interstitial phases. In the nondistorted crystal

Table 4. Crystal-chemical characteristics of possible (model) modifications of titanium dicarbides.

Dicarbide structure	Space group	Unit cell parameters /nm			Atomic coordinates in the unit cell					
		<i>a</i>	<i>b</i>	<i>c</i>	atom	position	<i>x/a</i>	<i>y/a</i>	<i>z/a</i>	<i>z/c</i>
Tetragonal CaC ₂ (<i>C11a</i>)	<i>I4/m</i> (<i>C</i> _{4h} ⁵)	0.3668	—	0.617	Ti	2 (<i>a</i>)	0	0	—	0
					C	4 (<i>e</i>)	0	0	—	0.427
Tetragonal (derived from CsCl-type structure)	<i>P4/mmm</i> (<i>D</i> _{4h} ¹)	0.2594	—	0.337	Ti	1 (<i>a</i>)	0	0	—	0
					C	2 (<i>h</i>)	1/2	1/2	—	—
Cubic of the CaF ₂ type (<i>C1</i>)	<i>Fm3m</i> (<i>O</i> _h ⁵)	0.487	—	—	Ti	4 (<i>a</i>)	0	0	0	—
					C	8 (<i>c</i>)	1/4	1/4	1/4	—
Monoclinic of the ThC ₂ type (see ^a)	<i>C2/c</i> (<i>C</i> _{2h} ⁶)	0.510	0.310	0.510	Ti	4 (<i>e</i>)	0	0.2	0.25	—
					C	8 (<i>f</i>)	0.30	0.13	0.05	—
Cubic	<i>F43m</i> (<i>T</i> _d ²)	0.588	—	—	Ti	4 (<i>a</i>)	0	0	0	—
					C1	4 (<i>b</i>)	1/2	1/2	1/2	—
					C2	4 (<i>d</i>)	3/4	3/4	3/4	—

^a The angle β in the unit cell is 103.9°.

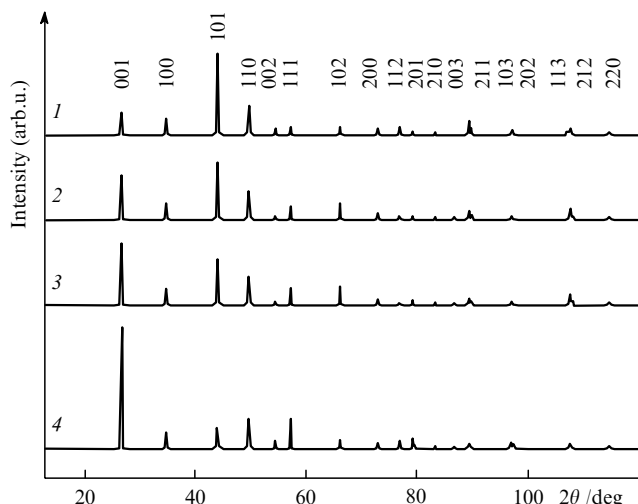


Figure 14. Effect of the position of carbon atom (z) in the unit cell of tetragonal TiC_2 with the CsCl -type structure (space group $P4/mmm$, $a = 0.2594$, $c = 0.337$ nm) on the intensity ratio of diffraction reflections (calculated for $\text{CuK}\alpha_{1,2}$ radiation). $z = 0.40$ (1); 0.30 (2); 0.25 (3) and 0.10 (4).

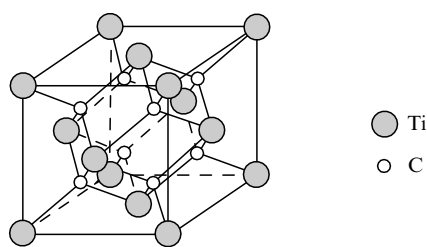


Figure 15. Unit cell of cubic TiC_2 with the CaF_2 ($C1$)-type structure, space group $Fm\bar{3}m$ (O_h^5).

lattice of this compound each carbon atom has a regular tetrahedral environment (four titanium atoms) while each titanium atom is surrounded by eight carbon atoms arranged at the cube vertices. The unit cell of cubic titanium dicarbide comprises four TiC_2 formula units. The calculated X-ray diffraction pattern of this dicarbide is shown in Fig. 16.

The electronic energy spectrum of hypothetical titanium dicarbide TiC_2 with the ThC_2 -type monoclinic structure [space group $C2/c$ (C_{2h}^6)] was calculated.^{112,113} The lattice constants of this compound are $a = c = 0.510$ and $b = 0.310$ nm.¹¹² The unit

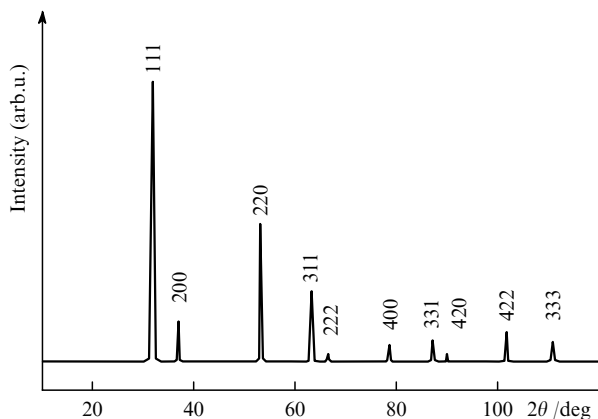


Figure 16. X-Ray diffraction pattern of cubic TiC_2 with the CaF_2 ($C1$)-type structure, space group $Fm\bar{3}m$ (O_h^5). Calculated for $\text{CuK}\alpha_{1,2}$ radiation.

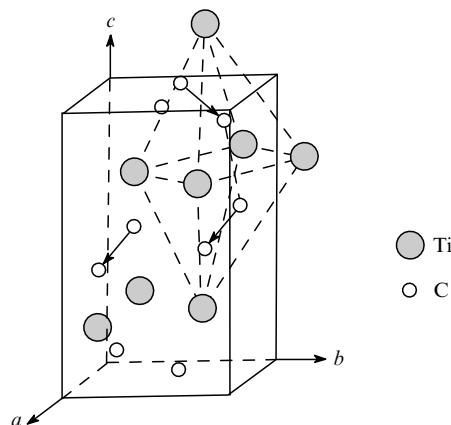


Figure 17. Unit cell of monoclinic TiC_2 with the ThC_2 -type structure, space group $C2/c$ (C_{2h}^6). The two Ti atoms and one C atom arranged beyond the unit cell are also shown.

cell of monoclinic titanium dicarbide constructed using the atomic coordinates for monoclinic ThC_2 (see Ref. 114) is shown in Fig. 17 (the atomic coordinates in the unit cell are listed in Table 4). The unit cell comprises four formula units TiC_2 . Distorted octahedra built of six titanium atoms contain two asymmetrically arranged carbon atoms (connected by a dashed line) separated by 0.251 nm. Atoms of the C_2 units are shared by two neighbouring octahedra while the C—C bonds pass through their common edges; the C—C distance in the C_2 units is 0.097 nm (in Fig. 17, the atoms of these units are shown connected by an arrow). The X-ray diffraction pattern calculated for polycrystalline dicarbide TiC_2 with this unit cell is shown in Fig. 18.

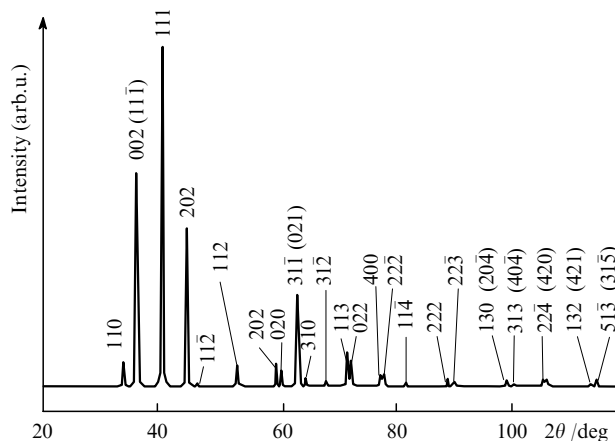


Figure 18. X-Ray diffraction pattern of monoclinic TiC_2 with the ThC_2 -type structure, space group $C2/c$ (C_{2h}^6). Calculated for $\text{CuK}\alpha_{1,2}$ radiation.

In polymorphous modifications of TiC_2 with the CaC_2 -, CsCl -, CaF_2 - and ThC_2 -type structures the Fermi level lies in the region of delocalised d -states of titanium;^{112,113} therefore, all the four TiC_2 modifications behave as metals. The most stable is dicarbide with the ThC_2 -type monoclinic structure. In dicarbide with the CaC_2 -type structure the C—C bonds in C_2 units are the strongest, whereas the Ti—C bonds are poorly populated and, hence, weaker. Calculations for cubic TiC_2 with the CaF_2 -type structure showed the absence of C—C bonds. According to calculations of the electronic structure of titanium dicarbides with the CaC_2 - and ThC_2 -type structures, the density of electron states at the Fermi level depends on the orientation of C_2 units in the crystal lattice. This implies the possibility of modifying the

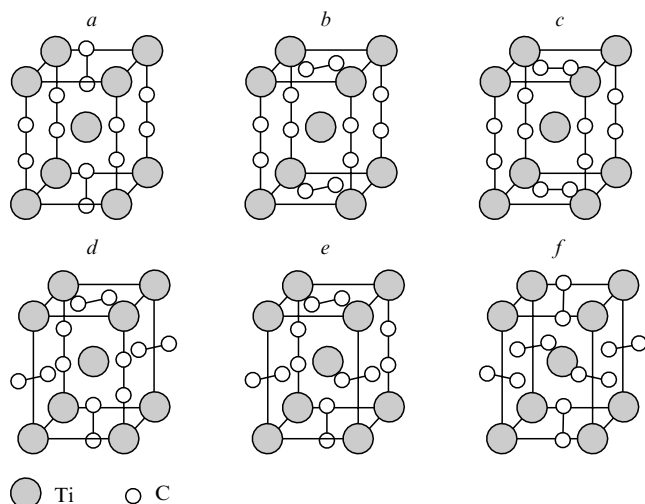


Figure 19. Arrangement of C_2 dimers in hypothetical titanium dicarbide with body-centred tetragonal structure of the CaC_2 (YC_2) type (a) and possible orientation disorder types of the carbon dimers (b–f).¹¹²

electronic structure and properties of titanium dicarbide by means of orientation ordering of the C_2 units.

Some of the possible types of orientation ordering of C_2 units are shown in Fig. 19.^{112, 113} The simplest form has the electronic spectrum of dicarbide TiC_2 with ordered CaC_2 -type structure (see Fig. 19 a). Changes in the orientation of a fraction of C_2 units are accompanied by complication of the DOS distribution profile and by the appearance of new peaks. The most probable orientation type of C_2 units is to some extent similar to the ThC_2 -type structure (Fig. 19 d).¹¹² The least probable is the orientation of a fraction of C_2 units along the edges of the unit cell (Fig. 19 c).

Experimental studies concerning the search for titanium dicarbide are scarce. A carbon–titanium compound with the concentration of bound carbon of greater than 50 at.% was first obtained in the high-temperature interaction of ethylene with titanium tetrachloride (gas-phase synthesis).¹¹⁵ The carbide thus obtained had a CsCl-type cubic lattice with a lattice constant of 0.313 nm and was thought to have a TiC_2 composition. However, attempts at reproducing these results¹¹⁵ failed.

A recent microdiffraction study¹¹⁶ on films prepared by ion sputtering of carbon and titanium followed by vapour deposition revealed the formation of a compound with a body-centred lattice and composition TiC_2 . The deposition temperature was varied from 330 to 770 K; thin films were deposited on fresh KCl cleavages, coatings 10 to 18 μm thick were obtained on glassy substrates. Films condensed at 330 K and annealed at 700 K for 3 h contained only titanium monocarbide. As the deposition (condensation) temperature increased from 330 to 620 K, the phase composition of the films remained unchanged; however, the fcc lattice constant of titanium carbide in these films reached ~ 0.455 nm at a carbon content of greater than 65 at.%. A gas-phase electron diffraction study also revealed a decrease in the intensity of reflections accompanied by an increase in the diffuse background at a carbon content of greater than 60 at.%. The electron diffraction patterns of the films containing ~ 65 at.% of carbon and deposited at 670 K exhibited three diffuse lines assigned to the body-centred lattice with a lattice constant of ~ 0.3 nm. A homogeneous film was prepared by condensation at 770 K; the partial pressure of reactants (gaseous carbon and titanium) was 8×10^{-8} Pa, the film growth rate was ~ 0.1 nm s^{-1} and the content of carbon in the vapours was ~ 66 at.%. The results obtained allowed one to suggest the formation of TiC_2 films, a body-centred lattice of this compound with a lattice constant of 0.294 nm and the structure of titanium dicarbide.

The results reported by Perekrestov and Pavlov¹¹⁶ and especially their interpretation provoke some objections. First of all, no direct determination of film composition was made (at best, the content of carbon in the gas flow was monitored indirectly). The proposed crystal lattice structure of TiC_2 is not body-centred. This is a cubic lattice [space group $F\bar{4}3m$ (T_d^2)] with a face-centred metal (titanium) sublattice and a diamond-like non-metal (carbon) sublattice [$A4$ type, *i.e.*, two face-centred lattices displaced by $(1/4, 1/4, 1/4)$ with respect to each other]. In the unit cell of this structure (Fig. 20) half of the carbon atoms occupy the octahedral interstices of the titanium sublattice, while the rest of the carbon atoms occupy half of the tetrahedral interstices of the titanium sublattice, so each of them is tetrahedrally surrounded by four titanium atoms and by four carbon atoms. This unit cell comprises four formula units TiC_2 and the lattice constant is 0.588 nm. The atomic coordinates in the cubic unit cell of TiC_2 (space group $F\bar{4}3m$) are listed in Table 4 and the calculated X-ray diffraction pattern is presented in Fig. 21.

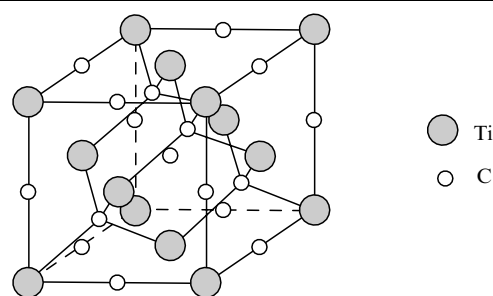


Figure 20. Unit cell of cubic TiC_2 , space group $F\bar{4}3m$ (T_d^2), $a = 0.588$ nm.

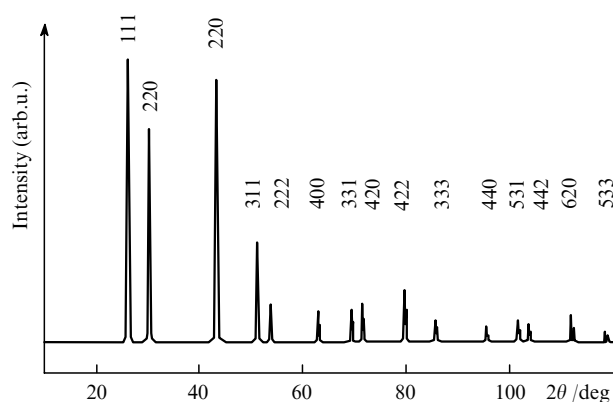


Figure 21. X-Ray diffraction pattern of polycrystalline cubic TiC_2 , space group $F\bar{4}3m$ (T_d^2), $a = 0.588$ nm. Calculated for $CuK_{\alpha 1,2}$ radiation.

In addition to clusters M_8C_{12} (see Section III.1), laser-assisted plasmachemical synthesis led to the formation of cluster-type nanoparticles M_mC_n ($M = Ti, Zr, Hf, V$; $m:n \approx 1:2$).^{28, 30, 31} For $M = Ti$, molecular clusters of composition $Ti_{13}C_{22}$ were usually formed (*i.e.*, the titanium : carbon ratio was close to the corresponding parameter in ideal TiC_2). Preferable formation of nano-clusters with a high content of carbon ($M:C \approx 1:2$) occurred at a high concentration of hydrocarbon in the gas phase and at an increased laser power, which led to an increase in the hydrogenation degree of the hydrocarbon and, correspondingly, to an increase in the content of carbon in the plasma.

Thus, analysis of the available data suggests that titanium dicarbide TiC_2 can belong to five structural types. These are the ThC_2 -type monoclinic structure [space group $C2/c$ (C_{2h}^6)]; CaC_2 ($C11a$)- and CsCl ($B2$)-type tetragonal structures with $I4/m$ (C_{4h}^5) and $P4/mmm$ (D_{4h}^1) space groups, respectively; CaF_2 ($C1$)-type cubic structure [space group $Fm\bar{3}m$ (O_h^h)] and a cubic structure

with a diamond-like carbon sublattice and the $F\bar{4}3m$ (T_d^2) space group.

3. Endohedral fullerene $\text{Ti}@\text{C}_{28}$ and rhombohedral titanium carbide

The discovery of C_n fullerenes ($n = 60-90$) (see Refs 70–73, 117, 118) and further studies of these compounds showed that the C_n clusters containing less than 60 carbon atoms are of low stability. Fullerenes with a small number of atoms (*e.g.*, C_{28} fullerene) can be stabilised by preparing endohedral complexes $\text{M}@\text{C}_{28}$ in which the dopant atom is placed inside the carbon sphere. A $\text{Ti}@\text{C}_{28}$ endohedral complex was also synthesised.¹¹⁹

The possibility of stabilising unstable C_{28} fullerene by intercalating it with both non-metal atoms of 2*p*-elements (B, C, N and O) and metals (3*d*-elements such as Sc, Ti, V, Cr, Fe and Cu) was studied theoretically.^{112, 120} When estimating the formation probability of endohedral $\text{M}@\text{C}_{28}$ complexes with 3*d*-metals, one can take into account the geometric, chemical and kinetic factors. In the case of C_{28} fullerene the maximum radius of a metal ion that can be placed inside the carbon sphere lies between 0.09 and 0.10 nm (see Ref. 121); all 3*d*-metals fulfil this geometric criterion. The chemical factor is favourable if electron density transfer as a result of intercalation favours an increase in the bonding character of the MOs. The kinetic factor includes the formation mechanism of endohedral complexes. They are prepared by rolling a graphene sheet around the metal atom adsorbed on the graphite surface. This can occur if the interaction between the metal and the graphite surface causes strengthening of the M–C bonds and weakening of the C–C bonds (especially of the interlayer bonds). Recent studies^{112, 120} showed that intercalation of metal atoms is accompanied by electron density transfer from these atoms to the atoms of the fullerene cage, by changes in the populations of the overlapping C–AOs, by the formation of the M–C bond and by a change in the pattern of the electronic energy spectrum.

The endohedral complex $\text{Ti}@\text{C}_{28}$ with the Ti atom at the centre of the C_{28} polyhedron was shown to be the most stable (with inclusion of the chemical and kinetic factors).¹²⁰ Probably, this complex can be considered as a possible molecular cluster-like compound that can be formed in the Ti–C system.

The results of a recent study¹²² on the electronic structure of hypothetical metastable polymorphous modifications of $\text{TiC}_{1.0}$ prompted us to mention a study by Dubrovinskaia *et al.*¹²² who experimentally found a rhombohedral modification of titanium carbide. The sample of cubic titanium carbide (no composition was reported) with a lattice constant of 0.4327 nm was subjected to quasi-hydrostatic pressure (~ 10 GPa) at 300 K. This resulted in broadening of the diffraction reflections of the $B1$ -type cubic structure and in splitting of the $(111)_{B1}$ reflection into two lines corresponding to the rhombohedral structure at a pressure of 18 and 38 GPa. The authors believed that rhombohedral distortion of the cubic unit cell is due to extension of its $[111]$ diagonal, which led to splitting of the $(111)_{B1}$ reflection into the (003) and (101) rhombohedral lines and to splitting of the $(200)_{B1}$ reflection into the (104) and (110) lines. Rhombohedral titanium carbide prepared at a pressure of 38 GPa has a unit cell with the lattice constants $a = 0.29442$ and $c = 0.73354$ nm (in a hexagonal setting).

IV. Ordered phases of nonstoichiometric titanium carbide TiC_y

The ordering of interstitial atoms was experimentally found for most of the nonstoichiometric transition metal carbides, nitrides and oxides. In disordered nonstoichiometric compounds the interstitial atoms and structural vacancies form a substitution solution in the non-metal sublattice, all sites of the non-metal sublattice being crystallographically equivalent. Ordering causes redistribution of the interstitial atoms and vacancies over sites of the non-metal sublattice, thus making the lattice sites inequivalent. The crystal lattice is divided into at least two sublattices

differing in site occupation probabilities by the atoms of the same sort. Ordering is accompanied by symmetry reduction of the crystal, since some of the symmetry elements of a disordered non-metal sublattice that match the occupied and vacant sites do not belong to the group of symmetry elements of the ordered crystal in which these sites become crystallographically inequivalent.

From the aforesaid it follows that the nonstoichiometry responsible for the fact that the number of interstitial sites is larger than that of atoms occupying these sites is a prerequisite to the ordering in defect carbides.

Description of different ordered phases of nonstoichiometric carbides, nitrides, oxides and their solid solutions can be found in reviews^{1, 22, 123–127} and monographs.^{2, 3, 14, 17, 27, 70}

Compared to other carbides (except for vanadium carbide VC_y), the ordering in nonstoichiometric titanium carbide TiC_y with the $B1$ -type cubic structure has been studied in most detail; however, the mechanism of this process is still to be clarified. A great body of experimental information on the chemical composition and structure of ordered phases of titanium carbide TiC_y , published earlier has not been confirmed later. The main characteristics of both experimentally observed and theoretically calculated ordered phases of nonstoichiometric titanium carbide are listed in Table 5.

As mentioned above, disordered titanium carbide TiC_y ($\text{TiC}_y\Box_{1-y}$) is characterised by an extremely broad homogeneity region from $\text{TiC}_{0.48}$ to $\text{TiC}_{1.00}$ (see Refs 2, 3, 14). Within this region, carbon atoms and structural vacancies $\Box$ form a substitution solution in the non-metal sublattice. Depending on the composition and the synthesis and heat treatment conditions, TiC_y can exist in a disordered or ordered state. The disordered state is in thermodynamic equilibrium at $T > 1100$ K, while the ordered state is in thermodynamic equilibrium at $T < 1000$ K. Due to the low diffusive mobility of the atoms, the disordered state of nonstoichiometric titanium carbide is retained upon quenching from $T > 1100$ K to rather low temperatures (~ 300 K) and exists as a metastable state at $T < 1000$ K.

Order-parameter functional (OPF) calculations^{1–3, 18, 20, 22} showed that monocarbide TiC_y can form three ordered phases of compositions Ti_2C , Ti_3C_2 and Ti_6C_5 . According to the inverse Monte Carlo calculations performed for a narrower composition range from $\text{TiC}_{0.55}$ to $\text{TiC}_{0.70}$ (see Ref. 12), the ordered phases Ti_2C and Ti_3C_2 are in thermodynamic equilibrium at $T < 950$ K, which is in agreement with the results of the above-mentioned calculations.^{1–3, 18, 20, 22} Experimental studies of carbide TiC_y in the composition range $0.5 \leq y < 0.7$ revealed the existence of ordered phases of the Ti_2C type with cubic (space group $Fd\bar{3}m$) and trigonal (space group $R\bar{3}m$ or $P3_121$, the former being more probable) symmetry (see Table 5), orthorhombic ordered phase Ti_3C_2 (space group $C222_1$) and hexagonal ordered phase Ti_6C_5 (see Ref. 130). The trigonal ordered phase Ti_8C_5 (space group $R\bar{3}m$) was reported erroneously. Virtually no studies of the ordering of TiC_y ($y > 0.7$) were performed until the mid-1990s.

Let us consider in more detail which ordered phases of the compositions Ti_2C and Ti_3C_2 can be formed in nonstoichiometric carbide TiC_y .

According to different studies of TiC_y , an ordered phase of composition Ti_2C with cubic (space group $Fd\bar{3}m$) (see Refs 9, 46–48, 50) or trigonal (space group $R\bar{3}m$) (see Refs 12, 49) symmetry is formed in the range $0.5 \leq y \leq 0.65$ at $T < 1100$ K.[‡] Cubic Ti_2C phase is thought to be metastable. Initially,^{49, 129} the cubic phase was assumed to have a higher T_{trans}

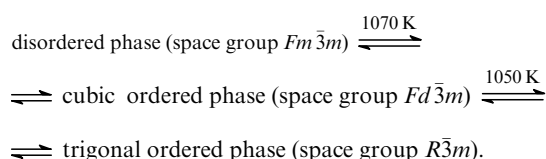
[‡] Information on the existence of the trigonal (space group $P3_121$) Ti_2C ($\text{Ti}_6\text{C}_{3+x}$) phase is erroneous: formation of a trigonal (space group $P3_121$) M_2C -type phase with the unit cell parameters $a = b = a_{B1}/\sqrt{2}$ ($\mathbf{a} = \{1/2, 1/2, 0\}_{B1}$) and $c = 3\sqrt{2} \times a_{B1}$ ($\mathbf{c} = \{222\}_{B1}$) based on the basic $B1$ -type structure is impossible, since in this case the sites of the metal and non-metal sublattices partially match one another.

Table 5. Characteristics of ordered phases of nonstoichiometric titanium carbide TiC_y with cubic $B1$ -type structure.

Com- position	Existence region	Symmetry (lattice type)	Space group	Unit cell parameters /nm	Ref.	Note ^a
Ti_2C	$\text{TiC}_{0.52} - \text{TiC}_{0.71}$	cubic	$Fd\bar{3}m$	$a = 2a_0$	9, 48	carbon sublattice is partially ordered; $T_{\text{trans}} \approx 950 - 1030$ K
Ti_2C	$\text{TiC}_{0.58} - \text{TiC}_{0.63}$	trigonal	$R\bar{3}m$	$a = b = c = (a_0\sqrt{6})/2$	12, 128	calculated; $T_{\text{trans}} < 900$ K; the homogeneity region corresponds to 750 K
Ti_3C_2	$\text{TiC}_{0.64} - \text{TiC}_{0.68}$	orthorhombic	$C222_1$	$a = a_0\sqrt{2}, b = 3a_0\sqrt{2},$ $c = 2a_0$	12, 129	calculated; $T_{\text{trans}} < 720$ K; the homogeneity region corresponds to 650 K
Ti_2C	$\text{TiC}_{0.49} - \text{TiC}_{0.54}$	cubic	$Fd\bar{3}m$	$a = 2a_0$	21	$T_{\text{trans}} < 1000$ K; the homogeneity region corresponds to ~ 600 K
Ti_2C	$\text{TiC}_{0.55} - \text{TiC}_{0.59}$	trigonal	$R\bar{3}m$	$a = b = c = (a_0\sqrt{6})/2$	21	$T_{\text{trans}} < 1010$ K; the homogeneity region corresponds to ~ 600 K
Ti_3C_2	$\text{TiC}_{0.63} - \text{TiC}_{0.67}$	orthorhombic	$C222_1$	$a = a_0\sqrt{2}, b = 3a_0\sqrt{2},$ $c = 2a_0$	21	$T_{\text{trans}} < 990$ K; the homogeneity region corresponds to ~ 600 K
Ti_6C_5	—	hexagonal	—	$a = b = (a_0\sqrt{6})/2 = 0.529,$ $c = (4a_0\sqrt{3})/3 = 0.996$	130	phase was found in thin films
Ti_2C	$\text{TiC}_{0.47} - \text{TiC}_{0.54}$	—	—	—	18, 20, 22	calculated; $T_{\text{trans}} < 950$ K; the homogeneity region corresponds to 600 K
Ti_3C_2	$\text{TiC}_{0.62} - \text{TiC}_{0.70}$	—	—	—	18, 20, 22	calculated; $T_{\text{trans}} < 930$ K; the homogeneity region corresponds to 600 K
Ti_6C_5	$\text{TiC}_{0.80} - \text{TiC}_{0.90}$	—	—	—	18, 20, 22	calculated; $T_{\text{trans}} < 920$ K; the homogeneity region corresponds to 600 K

^a T_{trans} is the disorder–order transformation temperature.

value than the trigonal phase, thus being an intermediate ordered high-temperature phase with respect to the disordered phase and low-temperature trigonal phase of composition Ti_2C . Tashmetov *et al.*¹³¹ reported a consecutive phase transformation



However, de Novion *et al.*¹² suggested that in TiC_y ($y \geq 0.58$) the cubic phase Ti_2C can exist as a metastable phase for which T_{trans} is ~ 10 K lower than for the trigonal ordered phase.

Analysis of the results of experimental structural studies^{9, 12, 46–50, 128, 131} showed that cubic superstructure Ti_2C is usually found in annealed TiC_y samples with $y < 0.55–0.56$, whereas the samples with $0.58 \leq y \leq 0.65$ are characterised by trigonal ordering. It should be noted that the X-ray diffraction patterns of both cubic and trigonal ordered phases of composition Ti_2C exhibit identical sets of superstructure reflections and can be distinguished only given trigonal distortions in the phase with the space group $R\bar{3}m$ and taking into account the directions of static atomic displacements.¹²⁶ Probably, this is the reason for attributing the observed superstructure reflections in annealed carbide TiC_y ($y \geq 0.59$) to the cubic phase Ti_2C in the studies^{46–48, 50} concerned with the cubic model of ordering.⁹ Other authors^{12, 49, 128, 129, 131} showed that trigonal phase Ti_2C is the major ordered phase of TiC_y ($y \geq 0.6$).

The assumption of the existence of ordered phase Ti_3C_2 in the composition range $\text{TiC}_{0.60} - \text{TiC}_{0.70}$ was confirmed by some experimental studies. An elastic neutron scattering study¹²⁹ of annealed single crystal $\text{TiC}_{0.61}$ revealed the presence of the $(2/3 \ 2/3 \ 0)$ superstructure reflections. The X-ray diffraction pattern of annealed carbide $\text{TiC}_{0.70}$ exhibited weak superstructure reflections with the reduced diffraction vector $|\mathbf{q}| \approx 2.03$ characteristic of the orthorhombic phase Ti_3C_2 (space group $C222_1$).¹³² Diffuse neutron scattering maxima corresponding to the $(2/3 \ 2/3 \ 0)$ reflections and due to short-range order in $\text{TiC}_{0.76}$ were detected.¹³³ Estimation of the short-range order parameters in a

single crystal of composition $\text{TiC}_{0.64}$ ¹² using the diffuse neutron scattering data showed that agreement between the calculated and experimental data is the best when annealed carbide $\text{TiC}_{0.64}$ contained a mixture of two ordered phases Ti_2C and Ti_3C_2 . The existence of a trigonal phase Ti_3C_2 was also confirmed by the OPF^{18, 20, 22} and Monte Carlo^{10, 12} calculations. A theoretical study¹⁸ also suggested the formation of an ordered phase Ti_6C_5 in carbide TiC_y ($0.78 < y < 0.88$). The calculated disorder–order transformation temperatures for the Ti_3C_2 and Ti_6C_5 phases did not exceed 950 K.^{18, 20, 22}

The structure of the ordered phases of nonstoichiometric carbide TiC_y has been studied in detail.²¹

Samples of nonstoichiometric titanium carbide TiC_y with different carbon content ($0.52 \leq y \leq 0.98$) were synthesised by hot pressing the mixtures of $\text{TiC}_{0.98}$ and metallic titanium powders ($T = 1773–2173$ K, $p = 20–30$ MPa) in highly pure argon atmosphere for 30 min or by solid-phase vacuum sintering the $\text{TiC}_{0.94}$, carbon black and metallic titanium powders ($T = 2000$ K, $p = 0.001$ Pa) for 6 h. The ordered state of the carbides obtained was achieved by annealing the samples with gradual lowering of the temperature from 1070 down to 770 K for 340 h. Annealing resulted in the appearance of superstructure reflections in the X-ray diffraction patterns of carbides $\text{TiC}_{0.50}$, $\text{TiC}_{0.52}$, $\text{TiC}_{0.54}$, $\text{TiC}_{0.55}$, $\text{TiC}_{0.58}$ and $\text{TiC}_{0.62}$.

The X-ray diffraction patterns of the annealed carbides $\text{TiC}_{0.50}$, $\text{TiC}_{0.52}$ and $\text{TiC}_{0.54}$ exhibited identical sets of superstructure reflections. The first superstructure reflection with the reduced wave vector $|\mathbf{q}| = (2a_B \sin \theta)/\lambda \approx 0.870$ in the region $2\theta \approx 17.8–17.9^\circ$ corresponds to the vector $\{1/2 \ 1/2 \ 1/2\}$ of length $|\mathbf{q}| \approx 0.866$. The next three superstructure reflections at $2\theta \approx 34.5, 45.9$ and 55.4° correspond to the vectors $\{3/2 \ 1/2 \ 1/2\}$, $\{3/2 \ 3/2 \ 1/2\}$ and $\{3/2 \ 3/2 \ 3/2\}$. The $\{3/2 \ 3/2 \ 1/2\}$ superstructure reflection is very weak. Taking into account the positions of the observed superstructure reflections and the absence of trigonal splitting of the $(331)_{B1}$, $(420)_{B1}$ and $(422)_{B1}$ lines, one can suggest that annealing led to the formation of the ordered cubic phase Ti_2C (space group $Fd\bar{3}m$) in carbides $\text{TiC}_{0.50}$, $\text{TiC}_{0.52}$ and $\text{TiC}_{0.54}$. The channel of disorder–order structural phase transformation TiC_y (space group $Fm\bar{3}m$) $\rightleftharpoons$ Ti_2C (space group

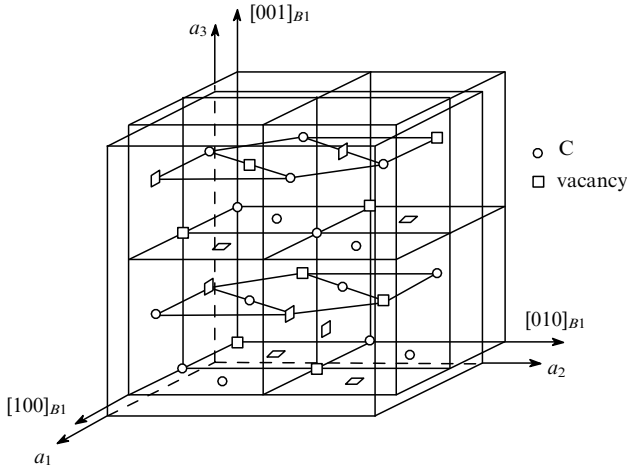


Figure 22. Cubic unit cell (space group $Fd\bar{3}m$) of the Ti_2C superstructure in the lattice with the $B1$ -type structure (Ti atoms are not shown).^{17, 27, 126}

$Fd\bar{3}m$) includes all four arms of the $\{\mathbf{k}_9\}$ Lifshitz star: $\mathbf{k}_9^{(1)} = (\mathbf{b}_1 + \mathbf{b}_2 + \mathbf{b}_3)/2$, $\mathbf{k}_9^{(2)} = \mathbf{b}_1/2$, $\mathbf{k}_9^{(3)} = \mathbf{b}_2/2$ and $\mathbf{k}_9^{(4)} = \mathbf{b}_3/2$.[§]

The unit cell of cubic superstructure M_2C (space group $Fd\bar{3}m$) is shown in Fig. 22. The translation vectors of and the atomic and vacancy coordinates in the unit cell are listed in Table 6. In completely ordered, ideal cubic superstructure M_2C all metal atoms occupy sites of the M_3^4 type (the subscript and superscript denote the number of vacancies in the first and second coordination sphere of the metal atom, respectively). The non-metal sublattice of this superstructure is characterised by alternation of the $(111)_{B1}$ atomic planes in which $1/3$ and $2/3$ of the total number of sites are vacant.

Table 6. Characteristics of cubic [space group $Fd\bar{3}m (O_h^7)$] M_2C superstructure: $\mathbf{a}_1 = \langle 200 \rangle_{B1}$, $\mathbf{a}_2 = \langle 020 \rangle_{B1}$, $\mathbf{a}_3 = \langle 002 \rangle_{B1}$.^{16, 27, 126}

Atom	Position	Atomic coordinates in ideal ordered structure		
		x/a_1	y/a_2	z/a_3
C1 (vacancy)	16 (c)	1/8	1/8	1/8
C2	16 (d)	5/8	5/8	5/8
M1	32 (e)	3/8	3/8	3/8

The X-ray diffraction pattern of annealed carbide $\text{TiC}_{0.58}$ exhibited the $\{1/2 \ 1/2 \ 1/2\}$, $\{3/2 \ 1/2 \ 1/2\}$ and $\{3/2 \ 3/2 \ 3/2\}$ superstructure reflections at $2\theta \approx 17.9^\circ$, 34.4° and 55.4° (see Ref. 21). No $\{3/2 \ 3/2 \ 1/2\}$ reflection was observed. An important distinction of the X-ray diffraction pattern of annealed carbide $\text{TiC}_{0.58}$ from those of annealed carbides of compositions $\text{TiC}_{0.50}$, $\text{TiC}_{0.52}$ and $\text{TiC}_{0.54}$ is the presence of trigonal splitting of the $(220)_{B1}$, $(311)_{B1}$, $(222)_{B1}$, $(331)_{B1}$, $(420)_{B1}$ and $(422)_{B1}$ lines. This is an indication of the trigonal ordered phase Ti_2C (space group $R\bar{3}m$) formed in carbide $\text{TiC}_{0.58}$ upon annealing.

The unit cell of the trigonal phase is shown in Fig. 23. Its translation vectors and the atomic and vacancy coordinates in ideal trigonal structure M_2C are listed in Table 7. The TiC_y (space group $Fm\bar{3}m$) $\rightleftharpoons$ Ti_2C (space group $R\bar{3}m$) disorder – order phase transition channel involving the formation of this superstructure includes one arm, $\mathbf{k}_9^{(3)} = \mathbf{b}_2/2$, of the $\{\mathbf{k}_9\}$ Lifshitz star.

[§] For a detailed description of all stars $\{\mathbf{k}_s\}$ of the wave vectors of the first Brillouin zone and their arms for a crystal with a fcc lattice, see Refs 2, 3 and 70.

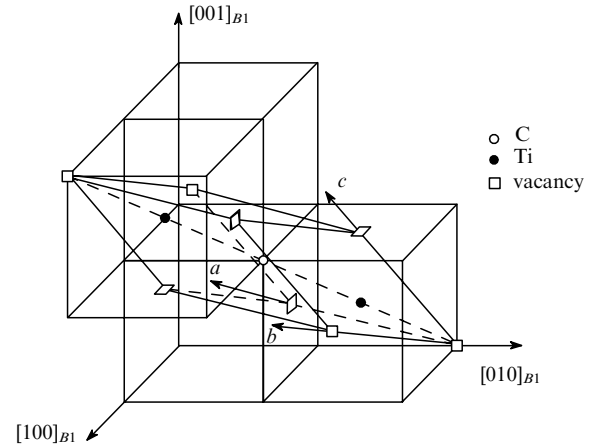


Figure 23. Trigonal unit cell (space group $R\bar{3}m$) of the Ti_2C superstructure in the lattice with the $B1$ -type structure.^{17, 27, 126}

Table 7. Characteristics of trigonal space group $[R\bar{3}m (D_{3d}^5)]$ M_2C superstructure: $\mathbf{a}_{tr} = \frac{1}{2}\langle 121 \rangle_{B1}$, $\mathbf{b}_{tr} = \frac{1}{2}\langle 211 \rangle_{B1}$, $\mathbf{c}_{tr} = \frac{1}{2}\langle 1\bar{1}2 \rangle_{B1}$.^{16, 27, 126}

Atom	Position	Atomic coordinates in ideal ordered structure		
		x/a_{tr}	y/b_{tr}	z/c_{tr}
C1 (vacancy)	1 (a)	0	0	0
C2	1 (b)	1/2	1/2	1/2
M1	2 (c)	1/4	1/4	1/4

The non-metal sublattice of completely ordered trigonal structure M_2C (space group $R\bar{3}m$) is characterised by alternation of the $(1\bar{1}1)_{B1}$ atomic planes with completely occupied (by interstitial atoms) and completely vacant sites along the $[1\bar{1}1]_{B1}$ direction. This superstructure must have a highly distorted metal sublattice. In completely ordered, ideal trigonal superstructure M_2C all metal atoms occupy identical sites of the M_3^4 type with three vacancies in the first and four vacancies in the second coordination sphere.

The X-ray diffraction pattern of annealed carbide $\text{TiC}_{0.62}$ exhibited both the $\{1/2 \ 1/2 \ 1/2\}$ ($2\theta \approx 18.0^\circ$) and $\{3/2 \ 3/2 \ 3/2\}$ ($2\theta \approx 55.2^\circ$) superstructure reflections from the trigonal ordered phase Ti_2C (space group $R\bar{3}m$) and some other superstructure reflections that were absent in the X-ray diffraction patterns of the carbides of compositions $\text{TiC}_{0.50}$, $\text{TiC}_{0.52}$, $\text{TiC}_{0.54}$, $\text{TiC}_{0.55}$ and $\text{TiC}_{0.58}$ (see Ref. 21). These are the reflections in the ranges $2\theta \approx 30.6 - 30.7^\circ$, 41.2° , 42.6° and $55.4 - 55.5^\circ$ with reduced wave vectors of lengths $|\mathbf{q}| \approx 1.488$, 1.970 , 2.038 and 2.607 , respectively. The first two reflections are associated with the $\mathbf{k}_4^{(1)} = \{2/3 \ 2/3 \ 0\}$ and $\mathbf{k}_4^{(2)} = -\mathbf{k}_4^{(1)}$ arms of the $\{\mathbf{k}_4\}$ star, while the other two reflections are associated with the $\mathbf{k}_3^{(3)} = \{1/3 \ -2/3 \ -1/2\}$, $\mathbf{k}_3^{(4)} = -\mathbf{k}_3^{(3)}$, $\mathbf{k}_3^{(5)} = \{-1/3 \ 2/3 \ -1/2\}$ and $\mathbf{k}_3^{(6)} = -\mathbf{k}_3^{(5)}$ arms of the $\{\mathbf{k}_3\}$ star. This set of superstructure reflections can correspond only to the orthorhombic ordered phase Ti_3C_2 (space group $C222_1$). The transition channel involving the formation of this phase includes two arms of the $\{\mathbf{k}_4\}$ star and four arms of the $\{\mathbf{k}_3\}$ star (see Ref. 126). Characteristic of this superstructure are the $\{1/3 \ -2/3 \ -1/2\}$ and $\{2/3 \ 2/3 \ 0\}$ reflections which should be observed in the regions $2\theta \approx 18.4^\circ$ and 19.4° , respectively. The experimental X-ray diffraction pattern in this interval of angles exhibited a slightly ‘swollen’ slope of the $\{1/2 \ 1/2 \ 1/2\}$ superstructure reflection of the trigonal phase Ti_2C .²¹

The orthorhombic unit cell of the M_3C_2 superstructure is shown in Fig. 24. Its translation vectors and the atomic and

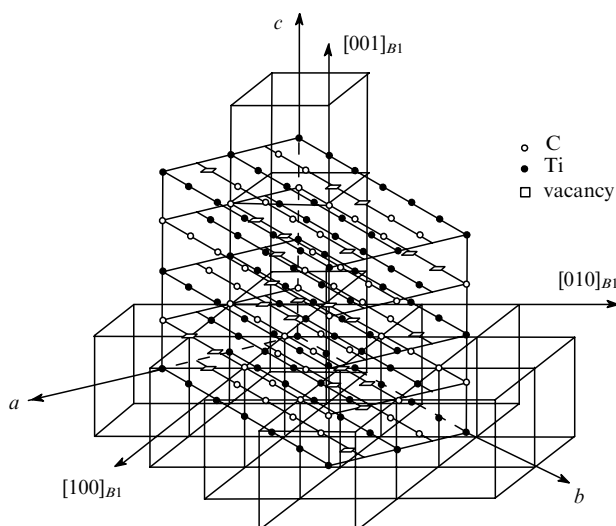


Figure 24. Orthorhombic unit cell (space group $C222_1$) of the Ti_3C_2 superstructure in the lattice with the $B1$ -type structure.^{2, 3, 17, 27, 126}

vacancy coordinates in this superstructure are listed in Table 8. The existence of orthorhombic ordered phase M_3C_2 (space group $C222_1$) of titanium carbide $TiC_{0.64}$ was suggested¹² based on the results of Monte Carlo simulations. In completely ordered orthorhombic structure M_3C_2 two thirds of all metal atoms occupy the sites of the type M_2^3 while the rest metal atoms occupy the sites of the type M_2^2 .

Metallographic tests of annealed carbides $TiC_{0.50}$ and $TiC_{0.55}$ in reflected polarised white light showed that the former exhibited neither grain interference from the disordered phase nor surface precipitate interference from the ordered phase.²¹ This can occur if both phases belong to the cubic crystal system. Particular grains of annealed carbide $TiC_{0.55}$ were coated with plate-like and prismatic precipitates of the ordered phase. The symmetry of these precipitates was different from that of the disordered phase while their shape was typical of the crystals that belong to the trigonal crystal system and, unlike the crystals of the disordered cubic phase, exhibit an interference pattern (*i.e.*, are anisotropic). Therefore, the results of diffraction studies of the ordered phases of non-

Table 8. Characteristics of orthorhombic [space group $C222_1 (D_2^5)$] M_3C_2 superstructure: $\mathbf{a}_{rh} = \langle 110 \rangle_{B1}$, $\mathbf{b}_{rh} = \langle 330 \rangle_{B1}$, $\mathbf{c}_{rh} = \langle 002 \rangle_{B1}$.^{17, 27, 126}

Atom	Position	Atomic coordinates in ideal ordered structure		
		x/a_{rh}	y/b_{rh}	z/c_{rh}
C1 (vacancy)	4 (b)	0	1/6	1/4
C2 (vacancy)	4 (b)	0	1/3	1/4
C3 (vacancy)	8 (c)	1/4	5/12	0
C4	4 (b)	0	0	1/4
C5	4 (b)	0	1/2	1/4
C6	4 (b)	0	2/3	1/4
C7	4 (b)	0	5/6	1/4
C8	8 (c)	1/4	1/12	0
C9	8 (c)	1/4	1/4	0
M1	4 (a)	0	0	0
M2	4 (a)	1/2	0	0
M3	8 (c)	1/4	1/12	1/4
M4	8 (c)	1/4	1/4	1/4
M5	8 (c)	1/4	5/12	1/4
M6	8 (c)	0	1/6	1/2
M7	8 (c)	0	1/3	1/2

stoichiometric carbide TiC_y were confirmed by the results of metallographic tests.

Thus, low-temperature annealing of carbide TiC_y leads to the formation of some ordered phases. These are the cubic phase Ti_2C (space group $Fd\bar{3}m$) in the composition range $TiC_{0.50}$ – $TiC_{0.54}$, the trigonal phase Ti_2C (space group $R\bar{3}m$) for $TiC_{0.55}$ – $TiC_{0.58}$ and the orthorhombic phase Ti_3C_2 (space group $C222_1$) in the range $TiC_{0.63}$ – $TiC_{0.68}$.

Figure 25 presents the calculated X-ray diffraction patterns of the cubic and trigonal ordered phases Ti_2C formed in carbides of composition $TiC_{0.50}$ ($a_{B1} = 0.4305$ nm) and $TiC_{0.55}$ ($a_{B1} = 0.4310$ nm), respectively. The X-ray diffraction patterns were calculated assuming the maximum degree of long-range order characterised by the parameter η equal to 1.00 and 0.90 for the ordered carbides $TiC_{0.50}$ and $TiC_{0.55}$, respectively. The X-ray diffraction patterns of the cubic and trigonal ordered phases Ti_2C exhibit identical sets of superstructure reflections; however, distortion of the ideal lattice of the trigonal phase [slight extension along the $(1 - 1 1)_{B1}$ axis] leads to splitting of the $(311)_{B1}$, $(222)_{B1}$, $(420)_{B1}$ and $(422)_{B1}$ reflections. Trigonal splitting of the $(222)_{B1}$ reflection into two lines, *viz.*, the $(0 0 12)$ and $(0 2 4)$ lines, is shown in the inset in Fig. 25 *b* as an example; the doublet $\alpha_{1,2}$ is due to the use of $CuK_{\alpha 1,2}$ radiation. The superstructure reflections are of rather high intensity: for instance, the intensity of the first superstructure reflection is 30 times lower than that of the $(111)_{B1}$ reflection and only 3 times lower than the intensity of the $(222)_{B1}$ reflection. This makes the ordered phase Ti_2C readily detectable.

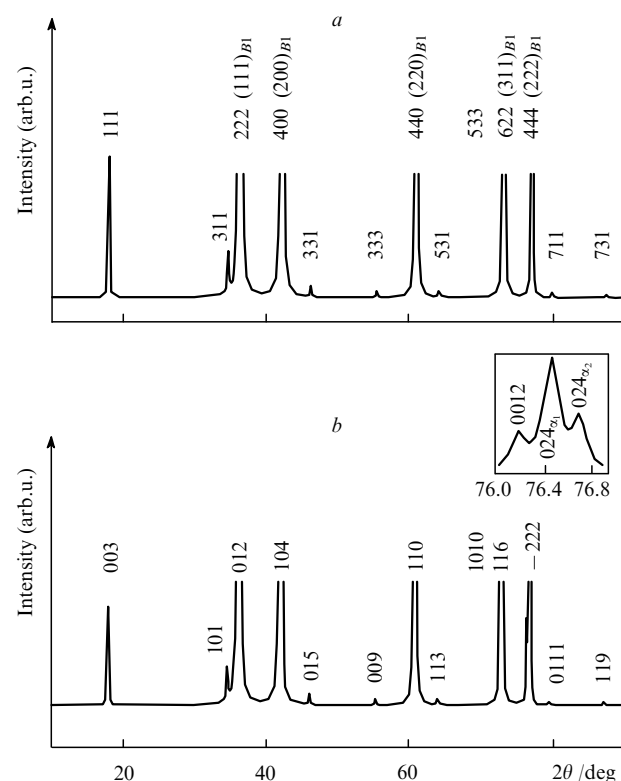


Figure 25. X-Ray diffraction patterns of cubic (space group $Fd\bar{3}m$, $a = 0.861$ nm) (a) and trigonal (space group $R\bar{3}m$, the lattice constants for hexagonal setting are $a = b = 0.3048$ and $c = 1.4982$ nm) (b) ordered Ti_2C phases formed in titanium carbide of the compositions $TiC_{0.50}$ ($a_{B1} = 0.4305$ nm) and $TiC_{0.55}$ ($a_{B1} = 0.4310$ nm), respectively. The long-range order parameter, $\eta = \eta_{max}$, equals 1 (a) and 0.90 (b). The inset demonstrates trigonal splitting of the $(222)_{B1}$ reflection into the $(0 0 12)$ and $(0 2 4)$ lines due to slight extension of the basic cubic lattice along the $(1 - 1 1)_{B1}$ axis (lattice constant, $c = 1.4982$ nm, is increased compared to the value $c = 1.4930$ nm for the ideal trigonal cell). Calculated for $CuK_{\alpha 1,2}$ radiation.

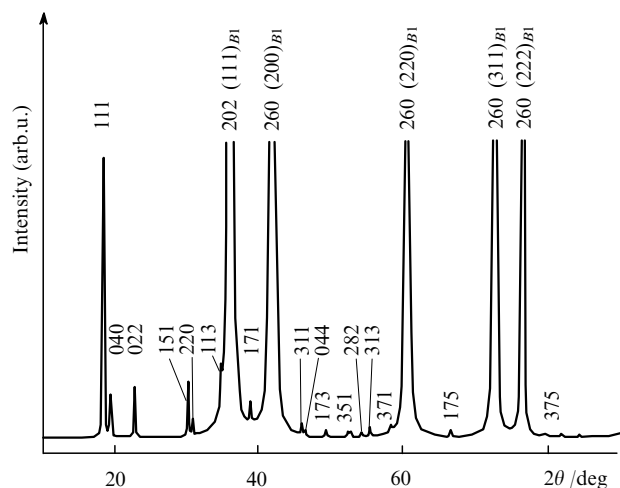


Figure 26. X-Ray diffraction pattern of the completely ordered ($\eta = 1.00$) orthorhombic Ti_3C_2 phase (space group $C222_1$, $a = 0.6109$, $b = 1.2328$ and $c = 0.864$ nm) formed in titanium carbide of composition $\text{TiC}_{0.667}$ ($a_{B1} = 0.432$ nm). Calculated for $\text{CuK}\alpha_{1,2}$ radiation.

The X-ray diffraction pattern of the ordered orthorhombic phase Ti_3C_2 (space group $C222_1$) formed in the carbide of composition $\text{TiC}_{0.667}$ is shown in Fig. 26. A characteristic feature of the orthorhombic superstructure Ti_3C_2 is the presence of three superstructure reflections in the range $19^\circ < 2\theta < 31^\circ$.

A hexagonal ordered phase Ti_6C_5 with the packing defects characteristic of the 4H polytype was found in the Ti–C thin films.¹³⁰ The translation vectors of the unit cell are as follows: $\mathbf{a} = \{2\bar{1}\bar{1}\}_{B1}$, $\mathbf{b} = \{\bar{1}2\bar{1}\}_{B1}$ and $\mathbf{c} = \{111\}_{B1}$. The films were prepared by electron beam sputtering of sintered carbide $\text{TiC}_{0.9}$, by magnetron sputtering of titanium and carbon and by laser beam sputtering of titanium and graphite or carbide $\text{TiC}_{0.9}$. The ordered phase Ti_6C_5 corresponds to disordered carbide $\text{TiC}_{0.83}$ with a lattice constant, a_{B1} , of 0.4326 nm; however, the lattice parameters of the hexagonal ordered phase¹³⁰ correspond to disordered carbide TiC_y with the basis cubic lattice constant $a_{B1} = 0.4319$ nm characteristic of carbide $\text{TiC}_{0.68-0.70}$ (see Fig. 6). The underestimated a_{B1} value can be due to oxygen impurity.

Ordering of nonstoichiometric carbides MC_y can cause the formation of monoclinic and trigonal superstructures M_6C_5 with $C2/m$ (or $C2$) and $P3_1$ symmetry, respectively. The unit cell of monoclinic superstructure M_6C_5 (space group $C2/m$) is shown in Fig. 27 while its translation vectors and the atomic and vacancy coordinates are listed in Table 9. Translation of all superstructure

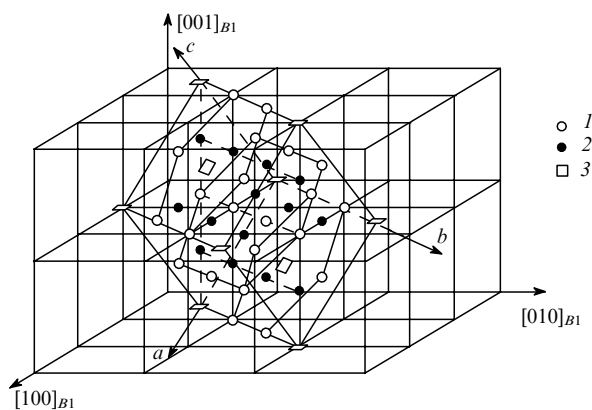


Figure 27. Monoclinic (space group $C2/m$) unit cell of the M_6C_5 superstructure in the crystal lattice with the $B1$ -type structure. Interstitial atom (1), metal atom (2) and vacancy (3).^{70, 126, 134}

Table 9. Characteristics of monoclinic [space group $C2/m$ ($C2_h^3$)] M_6C_5 superstructure: $\mathbf{a}_m = \frac{1}{2}\langle 1\bar{1}2 \rangle_{B1}$, $\mathbf{b}_m = \frac{3}{2}\langle 110 \rangle_{B1}$, $\mathbf{c}_m = \frac{1}{2}\langle 112 \rangle_{B1}$.^{70, 126, 134}

Atom	Position	Atomic coordinates in ideal ordered structure		
		x/a_m	y/b_m	z/c_m
C1 (vacancy)	2 (<i>a</i>)	0	0	0
C2	2 (<i>d</i>)	0	1/2	1/2
C3	4 (<i>g</i>)	0	1/3	0
C4	4 (<i>h</i>)	0	1/6	1/2
M1	4 (<i>i</i>)	1/4	0	3/4
M2	8 (<i>j</i>)	1/4	2/3	3/4

sites of the reciprocal lattice of the monoclinic ordered phase M_6C_5 (space group $C2/m$) showed that the first Brillouin zone of the disordered fcc lattice contains five inequivalent superstructure vectors belonging to three stars, $\{\mathbf{k}_9\}$, $\{\mathbf{k}_4\}$ and $\{\mathbf{k}_3\}$. These superstructure vectors are included in the MC_y (space group $Fm\bar{3}m$) $\rightleftharpoons$ M_6C_5 (space group $C2/m$) phase transition channel involving the formation of the monoclinic ordered phase M_6C_5 .

The non-metal sublattice of the monoclinic superstructure M_6C_5 (space group $C2/m$) is divided into four inequivalent sublattices differing in site occupation probabilities by carbon atoms. Because of this, the non-metal sublattice is characterised by alternation of two types of non-metal atomic planes along the $[1\bar{1}1]_{B1}$ direction. In the first type of atomic planes one third of all sites belongs to the first sublattice while the other sites belong to the third sublattice, each site of the first sublattice being surrounded by six sites of the third sublattice. In the second type of planes one third of all sites belongs to the second sublattice while the other sites belong to the fourth sublattice; each site of the second sublattice is surrounded by six sites of the fourth sublattice.

The trigonal unit cell (space group $P3_1$) of superstructure M_6C_5 is shown in Fig. 28. Its translation vectors and the atomic and vacancy coordinates in ideal trigonal superstructure M_6C_5 are listed in Table 10. The disorder–order phase transition channel involving the formation of the trigonal superstructure M_6C_5 includes thirteen arms of three stars, $\{\mathbf{k}_9\}$, $\{\mathbf{k}_4\}$ and $\{\mathbf{k}_3\}$.

The unit cell of monoclinic superstructure M_6C_5 (space group $C2$) is presented in Fig. 29. The translation vectors of this unit cell and the atomic and vacancy coordinates in ideal monoclinic

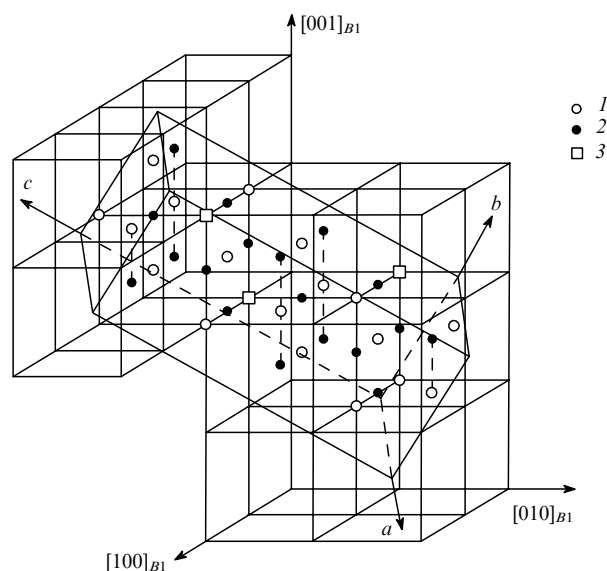
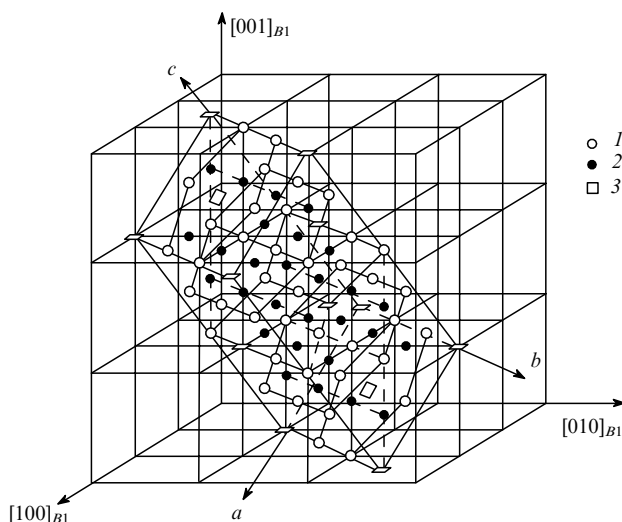


Figure 28. Trigonal (space group $P3_1$) unit cell of the M_6C_5 superstructure in the crystal lattice with the $B1$ -type structure. Interstitial atom (1), metal atom (2) and vacancy (3).^{70, 126, 134}

Table 10. Characteristics of trigonal [space group $P3_1 (C_3^2)$] M_6C_5 superstructure: $\mathbf{a}_{tr} = \frac{1}{2}\langle 2\bar{1}\bar{1} \rangle_{B1}$, $\mathbf{b}_{tr} = \frac{1}{2}\langle \bar{1}12 \rangle_{B1}$, $\mathbf{c}_{tr} = 2\langle \bar{1}\bar{1}1 \rangle_{B1}$.^{70, 126, 134}

Atom	Position	Atomic coordinates in ideal ordered structure		
		x/a_{tr}	y/b_{tr}	z/c_{tr}
C1 (vacancy)	3 (a)	1/9	8/9	1/6
C2	3 (a)	4/9	5/9	1/6
C3	3 (a)	7/9	2/9	1/6
C4	3 (a)	1/9	5/9	1/3
C5	3 (a)	4/9	2/9	1/3
C6	3 (a)	7/9	8/9	1/3
M1	3 (a)	1/9	5/9	1/12
M2	3 (a)	4/9	2/9	1/12
M3	3 (a)	7/9	8/9	1/12
M4	3 (a)	1/9	2/9	1/4
M5	3 (a)	4/9	8/9	1/4
M6	3 (a)	7/9	5/9	1/4

**Figure 29.** Monoclinic (space group $C2$) unit cell of the M_6C_5 superstructure in the crystal lattice with the $B1$ -type structure. Interstitial atom (1), metal atom (2) and vacancy (3).^{70, 126, 134}

superstructure M_6C_5 are given in Table 11. The transition channel involving the formation of this ordered phase M_6C_5 includes nine superstructure vectors of the reciprocal lattice belonging to four stars, $\{\mathbf{k}_9\}$, $\{\mathbf{k}_4\}$, $\{\mathbf{k}_3\}$ and $\{\mathbf{k}_0\}$. The non-metal sublattice of this superstructure is divided into five inequivalent sublattices and is characterised by alternation of two types of non-metal atomic planes along the $[1\bar{1}1]_{B1}$ direction. The first type of atomic plane contains an equal number of sites of the first, third and fifth sublattices, each site of a given sublattice being surrounded by the sites belonging to the other two sublattices. The second type of atomic plane is formed by the sites belonging to the second and fourth sublattices; here, each site of the fourth sublattice is surrounded by six sites of the second sublattice.

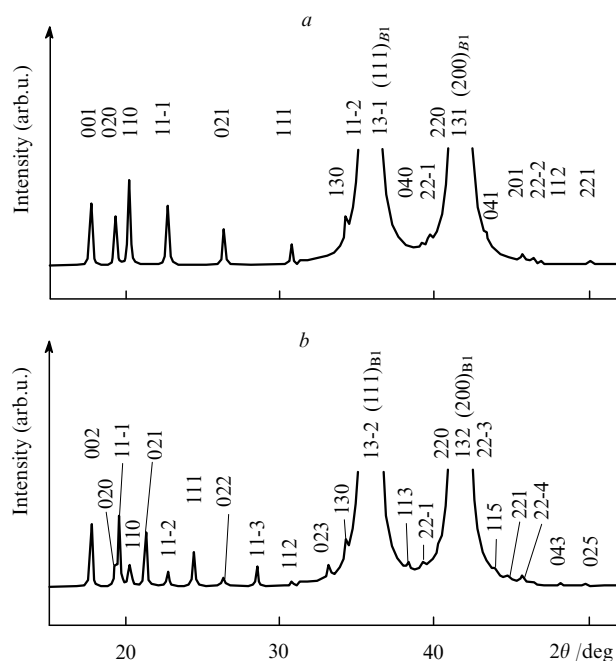
In Fig. 30 we present the X-ray diffraction patterns of the ideal, completely ordered monoclinic phases Ti_6C_5 (space groups $C2/m$ and $C2$) formed in titanium carbide $TiC_{0.83}$ ($a_{B1} = 0.4326$ nm). Positions and intensities of superstructure reflections in the X-ray diffraction pattern of the ideal, completely ordered trigonal phase Ti_6C_5 (space group $P3_1$, $a = b = 0.5299$, $c = 1.4987$ nm) match those of the monoclinic phase Ti_6C_5 (space group $C2/m$), since the transition channels involving the formation of both phases include the same superstructure vectors. For the real monoclinic and trigonal ordered phases Ti_6C_5 , the intensities of superstructure reflections should be different due to

Table 11. Characteristics of monoclinic [space group $C2 (C_2^3)$] M_6C_5 superstructure: $\mathbf{a}_m = \frac{1}{2}\langle 1\bar{1}\bar{2} \rangle_{B1}$, $\mathbf{b}_m = \frac{3}{2}\langle 110 \rangle_{B1}$, $\mathbf{c}_m = \langle 112 \rangle_{B1}$.^{70, 126, 134}

Atom	Position	Atomic coordinates in ideal ordered structure		
		x/a_m	y/b_m	z/c_m
C1 (vacancy)	2 (a)	0	0	0
C2 (vacancy)	2 (b)	0	1/3	1/2
C3	2 (a)	0	1/3	0
C4	2 (a)	0	2/3	0
C5	2 (b)	0	0	1/2
C6	2 (b)	0	2/3	1/2
C7	4 (c)	0	1/6	1/4
C8	4 (c)	0	1/2	1/4
C9	4 (c)	0	5/6	1/4
M1	4 (c)	1/4	1/6	1/8
M2	4 (c)	1/4	1/2	1/8
M3	4 (c)	1/4	5/6	1/8
M4	4 (c)	1/4	0	3/8
M5	4 (c)	1/4	1/3	3/8
M6	4 (c)	1/4	2/3	3/8

the difference between the directions and magnitudes of static atomic displacements. Analysis of the X-ray diffraction pattern taking into account these displacements allows unambiguous symmetry determination (monoclinic or trigonal) of the ordered phase Ti_6C_5 .

The intensities of superstructure reflections of the Ti_6C_5 phases are very low: for instance, the intensity of the first superstructure reflection is 230–240 and 30–32 times lower than those of the $(111)_{B1}$ and $(222)_{B1}$ reflections, respectively. Comparison of the X-ray diffraction patterns of completely ordered phases Ti_2C

**Figure 30.** X-Ray diffraction patterns of completely ordered ($\eta = 1.00$), ideal monoclinic Ti_6C_5 phases (space group $C2/m$ and $C2$) formed in titanium carbide of composition $TiC_{0.83}$ ($a_{B1} = 0.4326$ nm). Calculated for $CuK_{\alpha 1,2}$ radiation.

Characteristics of the monoclinic Ti_6C_5 phase:

space group $C2/m$, $a = c = 0.5299$ nm, $b = 0.9177$ nm, $\beta = 109.47^\circ$ (a);
space group $C2$, $a = 0.5299$ nm, $b = 0.9177$ nm, $c = 1.0597$ nm,
 $\beta = 109.47^\circ$ (b).

and Ti_6C_5 shows that the intensity of the first superstructure reflection of the Ti_2C phase is nearly an order of magnitude higher than that of the Ti_6C_5 phase.

For all completely ordered phases M_6C_5 the relative stoichiometric concentration of interstitial atoms (y_{st}) equals 5/6. Consideration of the non-metal sublattices of these superstructures reveals that the $[\bar{1}\bar{1}\bar{1}]_{B1}$ direction is characterised by alternation of the $(\bar{1}\bar{1}\bar{1})_{B1}$ atomic planes with completely occupied (by interstitial atoms) sites and the defect $(\bar{1}\bar{1}\bar{1})_{B1}$ planes in which one third of sites is vacant (see Figs 27–29). Each vacancy is surrounded by six interstitial atoms that form a regular hexagon. Peculiarities of completely ordered carbide structures M_6C_5 have been studied in detail.¹³⁴

Completely ordered monoclinic and trigonal carbide structures M_6C_5 with $C2/m$ (or $C2$) and $P3_1$ symmetry, respectively, are characterised by the identical environment of the metal atoms by the sites of the non-metal sublattice that form the first and second coordination spheres. Indeed, there are only two types of site for the metal atoms in these structures, *viz.*, M_1^1 (metal atom with one vacancy in the first and one vacancy in the second coordination sphere) and M_1^2 (metal atom with one vacancy in the first and two vacancies in the second coordination sphere). In ideal, completely ordered structures M_6C_5 (space groups $C2/m$, $P3_1$ and $C2$) two thirds of all metal atoms occupy the sites of the type M_1^1 while the other metal atoms occupy the sites of the type M_1^2 .

V. Phase diagrams of the Ti–C system constructed with allowance for the ordering of TiC_y

The results of experimental,^{14, 17, 70, 126, 127} theoretical^{1–3, 12, 22, 135–137} and numerous structural studies of nonstoichiometric carbides MC_y with the $B1$ -type basis structure including titanium carbide TiC_y , revealed the possibility of formation of superstructures of the types M_2C , M_3C_2 and M_6C_5 . Particular types of superstructures formed during the ordering of a given carbide MC_y and the corresponding concentration ranges are determined by the positions of the upper and lower boundaries of the homogeneity region of the disordered carbide and by the equilibrium conditions at these boundaries.

The most efficient method for calculating the low-temperature phase equilibria associated with the ordering of nonstoichiometric compounds is the above-mentioned OPF approach. Calculations of the phase diagram of an ordering system by this method require only knowledge of the $F_0(T)$, $F_1(T)$ and $F_2(T)$ parameters of the free energy $F(y, 0, T)$ of disordered nonstoichiometric carbide MC_y . These parameters for TiC_y are listed in Section II.2.

According to the results of thermodynamic calculations^{8, 60, 65} and crystal structure analysis,⁴ the M_2X_3 , M_4X_3 , M_6X_5 and M_8X_7 superstructures can be formed by the first-order phase transition mechanism, whereas the M_2X superstructure can be formed by the second-order phase transition mechanism. Transition between two ordered phases occurs as a first-order phase transition.

1. Calculated phase diagrams of the Ti–C system

Let us consider the phase diagram of the Ti–C system obtained from the OPF calculations with allowance for the ordering of nonstoichiometric titanium carbide TiC_y .^{1, 20}

There is only one compound capable of ordering in the Ti–C system, cubic carbide TiC_y . At the lower boundary of the homogeneity region, titanium carbide is in equilibrium with metallic α -Ti (at $T < 1150$ K) or β -Ti (at $T > 1150$ K). According to calculations,¹⁸ at $1000 < T < 1900$ K the carbide that exists near the lower boundary of the homogeneity region of the disordered phase TiC_y has composition $\text{TiC}_{0.32}$ – $\text{TiC}_{0.37}$. The exact position of the lower boundary of the homogeneity region has not experimentally been determined so far; different estimates gave $\text{TiC}_{0.48}$ (see Ref. 8) or $\text{TiC}_{0.47}$ (see Ref. 41) at 1900 K. According to calculations,⁴⁴ at 1900 K near the lower boundary of the homogeneity region the carbide has a $\text{TiC}_{0.52}$ composition. Calculations^{8, 41, 44} revealed that as the temperature is lowered,

the lower boundary of the homogeneity region of disordered TiC_y is shifted towards the region with higher y at a rate that is somewhat higher than that predicted by calculations.¹⁸

The low-temperature portion of the phase diagram of the Ti–C system, corresponding to the ordering of carbide TiC_y , was calculated by the OPF method.^{18, 20}

The broad homogeneity region of TiC_y allows the formation of phases of the types Ti_2C , Ti_3C_2 and Ti_6C_5 (Fig. 31) during the ordering under thermodynamic equilibrium conditions. According to calculations, an ordered phase Ti_2C is formed by the second-order phase transition mechanism with the disorder–order transition temperature $T_{\text{trans}} = 920$ – 950 K. The homogeneity region of the Ti_2C phase is fairly broad ($\text{TiC}_{0.42}$ – $\text{TiC}_{0.56}$ at 700 K and $\text{TiC}_{0.40}$ – $\text{TiC}_{0.54}$ at 800 K) and is confined from the left and from the right by two-phase regions, (α -Ti + Ti_2C) and (Ti_2C + Ti_3C_2), respectively. The ordered Ti_3C_2 and Ti_6C_5 phases have homogeneity regions of comparable width ($\text{TiC}_{0.59}$ – $\text{TiC}_{0.71}$ for Ti_3C_2 and $\text{TiC}_{0.74}$ – $\text{TiC}_{0.87}$ for Ti_6C_5 at 700 K) and are formed by the first-order phase transition mechanism. All order–order phase transformations in titanium carbide also occur as first-order phase transitions. The calculated values of T_{trans} , ΔS_{trans} and the heat of phase transition, ΔH_{trans} , for all possible order–order and disorder–order first-order phase transformations of titanium carbide are listed in Table 12. By and large, the ordering in carbide TiC_y occurs at $T < 1000$ K.

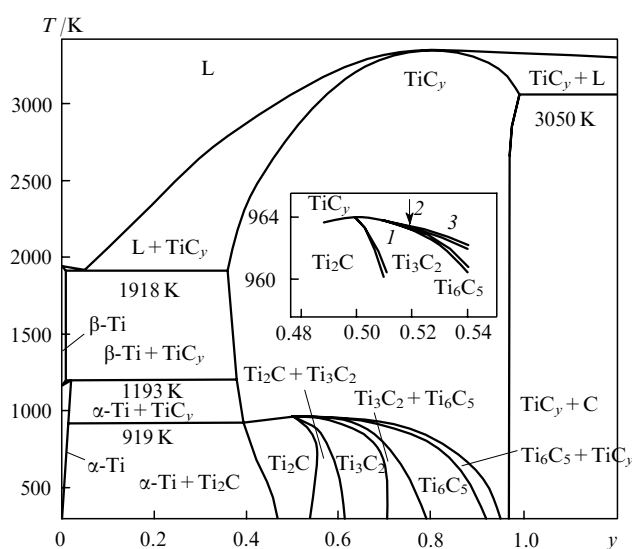


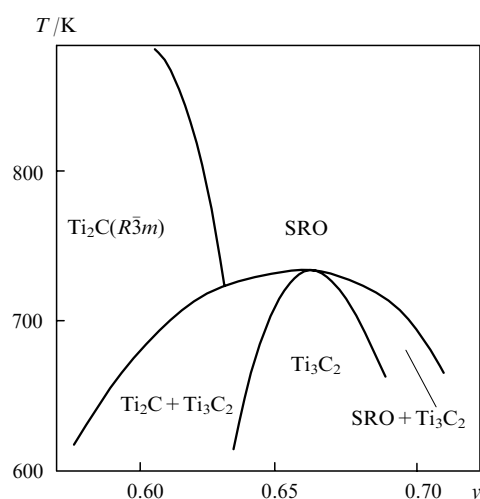
Figure 31. Equilibrium phase diagram of the Ti–C system constructed with allowance for atomic ordering of nonstoichiometric cubic titanium carbide TiC_y (see Ref. 1). A portion of the ordering region corresponding to peritectoid transformation $\text{Ti}_3\text{C}_2 + \text{TiC}_y \rightarrow \text{Ti}_6\text{C}_5$ ($T = 963$ K) is shown in the inset (magnified); the coordinates, $y = \text{C/Ti}$, of points 1, 2 and 3 are 0.5236, 0.524 and 0.5255, respectively.

The calculated phase diagram of the Ti–C system (see Fig. 31) is in agreement with the results of experimental studies (see Section IV). Different authors reported the formation of an ordered phase Ti_2C with cubic or trigonal symmetry (space group $Fd\bar{3}m$ or $R\bar{3}m$, respectively) in carbide TiC_y in the region $0.5 \leq y \leq 0.65$ at $T < 1100$ K. The X-ray diffraction patterns of annealed titanium carbide of composition $\text{TiC}_{0.60}$ – $\text{TiC}_{0.70}$ exhibited superstructure reflections characteristic of the ordered phase Ti_3C_2 . Recently,¹³⁰ an ordered phase Ti_6C_5 with hexagonal symmetry was found in thin Ti–C films.

The existence of a trigonal ordered phase Ti_2C and an orthorhombic ordered phase Ti_3C_2 was also confirmed by the Monte Carlo calculations of the phase diagram of the Ti–C system for the composition range $\text{TiC}_{0.57}$ – $\text{TiC}_{0.70}$ (Fig. 32).^{10, 12} Landesman *et al.*¹³⁸ showed that short-range order and disorder–

Table 12. Thermodynamic characteristics of the disorder–order and order–order phase transformations in nonstoichiometric titanium carbide TiC_y (see Ref. 1).

y	$\text{Ti}_2\text{C} - \text{Ti}_3\text{C}_2$			$\text{Ti}_3\text{C}_2 - \text{Ti}_6\text{C}_5$			$\text{Ti}_6\text{C}_5 - \text{TiC}_y$		
	T_{trans} /K	ΔS_{trans} /J mol ⁻¹ K ⁻¹	ΔH_{trans} /kJ mol ⁻¹	T_{trans} /K	ΔS_{trans} /J mol ⁻¹ K ⁻¹	ΔH_{trans} /kJ mol ⁻¹	T_{trans} /K	ΔS_{trans} /J mol ⁻¹ K ⁻¹	ΔH_{trans} /kJ mol ⁻¹
0.52	948	0.09	0.08	—	—	—	—	—	—
0.53	926	0.15	0.14	961	0.003	0.003	962	0.02	0.02
0.54	893	0.25	0.22	959	0.013	0.013	961	0.03	0.03
0.55	853	0.28	0.24	956	0.03	0.03	960	0.04	0.04
0.56	795	0.32	0.25	951	0.05	0.05	959	0.06	0.05
0.58	460	0.29	0.13	940	0.12	0.12	955	0.10	0.09
0.60	—	—	—	924	0.19	0.18	949	0.15	0.14
0.62	—	—	—	902	0.29	0.26	942	0.22	0.21
0.63	—	—	—	891	0.35	0.31	938	0.26	0.24
0.64	—	—	—	877	0.41	0.36	934	0.30	0.28
0.65	—	—	—	860	0.48	0.42	929	0.35	0.32
0.66	—	—	—	841	0.56	0.47	924	0.40	0.37
0.68	—	—	—	794	0.74	0.59	912	0.50	0.46
0.70	—	—	—	733	0.91	0.66	898	0.62	0.56
0.72	—	—	—	639	0.99	0.63	882	0.75	0.67
0.73	—	—	—	566	1.00	0.57	874	0.82	0.72
0.74	—	—	—	472	0.90	0.42	864	0.90	0.78
0.75	—	—	—	320	0.69	0.22	854	0.97	0.83
0.76	—	—	—	—	—	—	843	1.05	0.88
0.78	—	—	—	—	—	—	818	1.20	0.98
0.80	—	—	—	—	—	—	789	1.34	1.06
0.82	—	—	—	—	—	—	755	1.46	1.10
0.83	—	—	—	—	—	—	728	1.49	1.08
0.84	—	—	—	—	—	—	713	1.49	1.07
0.85	—	—	—	—	—	—	689	1.48	1.02
0.86	—	—	—	—	—	—	662	1.43	0.95
0.88	—	—	—	—	—	—	601	1.27	0.76
0.90	—	—	—	—	—	—	528	1.05	0.55
0.92	—	—	—	—	—	—	444	0.82	0.36
0.94	—	—	—	—	—	—	348	0.58	0.20
0.95	—	—	—	—	—	—	294	0.46	0.14

**Figure 32.** Portion of the phase diagram of the Ti–C system obtained from Monte Carlo calculations with allowance for the ordering of nonstoichiometric titanium carbide TiC_y in the composition range $\text{TiC}_{0.57} - \text{TiC}_{0.70}$ (see Refs 10, 12).

SRO denotes a phase with the B1-type structure and short-range order.

order transitions in nonstoichiometric carbides and nitrides can be described by using the Ising Hamiltonian for the non-metal fcc sublattice. In this case the Hamiltonian is defined as the sum of the effective energies, V_n , of the pairwise interactions between the sites

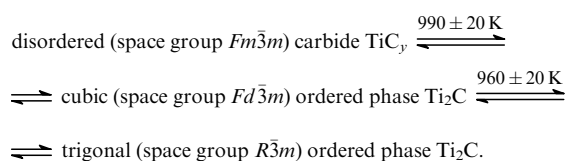
in the non-metal sublattice that are the n th neighbours. The energies V_n of the pairwise interactions in the non-metal sublattice of the carbides $\text{TiC}_{0.76}$ and $\text{TiC}_{0.65}$ were calculated^{10, 12} not only for the nearest (V_1) and next-nearest (V_2) neighbours, but also for more distant sites in the third (V_3) and fourth (V_4) coordination spheres. The energies of the pairwise interactions were calculated from the experimental data on high-temperature diffuse neutron scattering¹³⁹ using three methods, namely, the mean field approximation, the inverse Monte Carlo method and the cluster variation method. The best agreement with the experiment was achieved when the phase diagram was calculated by the Monte Carlo method. The formation of an ordered orthorhombic phase Ti_3C_2 , was reported to occur as a first-order phase transition.^{12, 139} This conclusion is consistent with the results of OPF calculations of the ordering in TiC_y .^{18, 20}

Some distinctions in the mutual positions of the ordered phases Ti_2C and Ti_3C_2 in the phase diagrams of the Ti–C system obtained from the OPF (see Fig. 31) and Monte Carlo calculations (see Fig. 32) are due to the fact that the OPF method treats the free energy of a compound as a function of its composition and long-range order parameters, whereas in the second method the energies of the interatomic interactions are determined by the short-range order parameters.

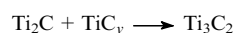
2. Experimental phase diagram of the Ti–C system constructed with allowance for low-temperature (at $T < 1000$ K) equilibria

The phase diagram of the Ti–C system at $T < 1000$ K was constructed based on the experimental results on the ordering of carbide TiC_y .²¹ Using the data on the structure and electrical

resistance of annealed and quenched samples of TiC_y , it was shown that cubic ordered phase Ti_2C (space group $Fd\bar{3}m$) has a homogeneity region extending from $\text{TiC}_{0.49-0.51}$ to $\text{TiC}_{0.54-0.55}$, while the trigonal superstructure Ti_2C (space group $R\bar{3}m$) is formed in the composition range $\text{TiC}_{0.55-0.59}$. The $\text{TiC}_{0.59-0.63}$ range corresponds to a two-phase region [Ti_2C (space group $R\bar{3}m$) + Ti_3C_2 (space group $C222_1$)]. The existence region of the orthorhombic ordered phase Ti_3C_2 (space group $C222_1$) is fairly narrow and does not exceed $\text{TiC}_{0.63-0.67}$. The lowest annealing temperature was 770 K. Since no ordered phase Ti_6C_5 was detected after annealing the $\text{TiC}_{0.83}$ and $\text{TiC}_{0.85}$ samples at such a low temperature, the transition temperature of this phase was assumed to be lower than 770 K. The portion of the equilibrium phase diagram of the Ti–C system corresponding to the ordering of nonstoichiometric titanium carbide TiC_y is presented in Fig. 33. A consecutive transition was suggested²¹ in the range $0.54 \leq y \leq 0.57$



The ordered orthorhombic phase Ti_3C_2 is formed following a peritectoid reaction



at 990 ± 10 K in the composition range $0.61 \leq y < 0.63$. The ordered phases Ti_2C with cubic and trigonal symmetry can be observed over a broad composition range of nonstoichiometric titanium carbide, from $\text{TiC}_{0.40}$ to $\text{TiC}_{0.63}$. However, only in the $\text{TiC}_{0.49-0.50-0.58-0.59}$ range is the homogeneity region of the ordered phase Ti_2C (see Fig. 33). The composition range in which the formation of an ordered phase Ti_6C_5 is possible is shown tentatively since this phase was not found experimentally. The hysteresis in the temperature dependences of the electrical resistance²¹ suggested that the $\text{TiC}_y \rightleftharpoons \text{Ti}_2\text{C}$ and $\text{TiC}_y \rightleftharpoons \text{Ti}_3\text{C}_2$ transformations are first-order phase transitions with $T_{\text{trans}} = 980-1000$ K. This value is in good agreement with the value $T_{\text{trans}} \approx 1000$ K found for titanium carbide $\text{TiC}_{0.55}$ from electrical resistance measurements.¹⁴⁰

Thus, experiments revealed that ordering of TiC_y in the ranges $0.52 \leq y \leq 0.55$, $0.56 \leq y \leq 0.58$ and $0.62 \leq y < 0.68$ at $T < 1000$ K leads respectively to the formation of the cubic

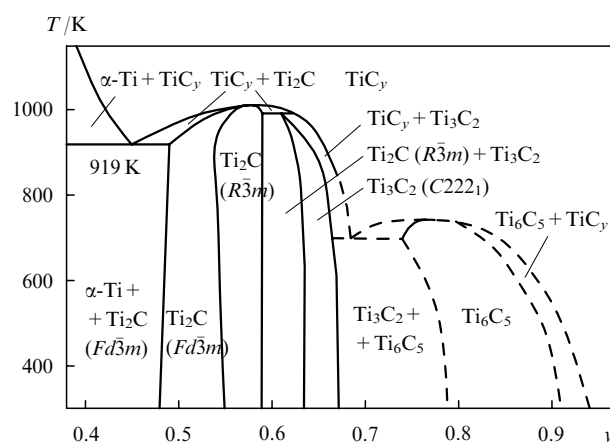


Figure 33. Low-temperature portion of the equilibrium phase diagram of the Ti–C system.²¹

Formation of the ordered orthorhombic Ti_3C_2 phase occurs at 990 ± 10 K as the peritectoid transformation $\text{Ti}_2\text{C} + \text{TiC}_y \rightarrow \text{Ti}_3\text{C}_2$; the region of phase equilibria involving ordered Ti_6C_5 phase is tentatively shown by the dashed line.

(space group $Fd\bar{3}m$) and trigonal (space group $R\bar{3}m$) ordered phase Ti_2C and orthorhombic ordered phase Ti_3C_2 (space group $C222_1$). This is consistent with the phase diagram of the Ti–C system (see Fig. 31) obtained from OPF calculations¹⁸ (note that for Ti_2C -type superstructures the OPF method leads to a common region of existence, from $\text{TiC}_{0.46}$ to $\text{TiC}_{0.58}$, without separation into the cubic and trigonal phases).

As mentioned above (see Section III), recent studies of the Ti–C system revealed the existence of molecular cluster-like compounds Ti_8C_{12} and $\text{Ti}_{13}\text{C}_{22}$ in addition to nonstoichiometric cubic titanium carbide TiC_y . The phase diagram of the Ti–C system constructed with allowance for the ordering of nonstoichiometric carbide TiC_y and for the existence of molecular cluster-like compounds Ti_8C_{12} and $\text{Ti}_{13}\text{C}_{22}$ (TiC_2) is shown in Fig. 34.

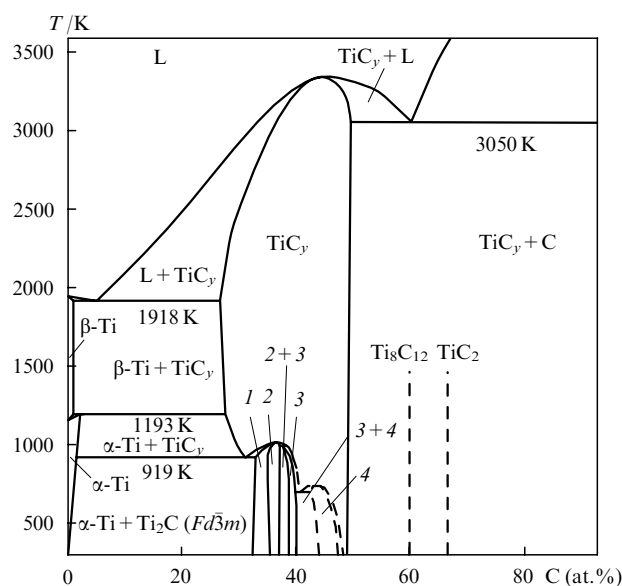


Figure 34. Phase diagram of the Ti–C system constructed with allowance for the existence of molecular cluster-like compounds Ti_8C_{12} and $\text{Ti}_{13}\text{C}_{22}$ (TiC_2) and for the atomic ordering of nonstoichiometric cubic titanium carbide TiC_y .

Ti_2C (space group $Fd\bar{3}m$) (1), Ti_2C (space group $R\bar{3}m$) (2), Ti_3C_2 (space group $C222_1$) (3) and Ti_6C_5 (Ti_2C , Ti_3C_2 and Ti_6C_5 are the ordered phases of titanium carbide TiC_y) (4).

VI. Conclusion

For more than a century it was thought that there is only one compound in the Ti–C system, namely, cubic titanium carbide TiC_y with a broad homogeneity region. However, the studies of this system carried out in 1990s revealed the formation of (i) ordered phases of nonstoichiometric titanium carbide with different composition and symmetry and (ii) molecular cluster-like compounds.

Among the new phases of titanium carbide, the ordered phase Ti_2C , which can have a cubic or trigonal symmetry, has been studied in most detail. This phase is readily formed as a result of annealing the TiC_y samples at 1300–1500 K followed by gradual lowering of the temperature down to 600–700 K over a period of several hours. It can also be found even in the TiC_y samples ($y = 0.5-0.58$) synthesised by solid-phase vacuum sintering of titanium and carbon at 2000–2200 K and cooled down to 300 K during further self-cooling of the furnace. Using a special regime of long-term annealing, one can obtain the Ti_2C phase with the maximum extent of long-range order.

Ordered phases of the Ti_3C_2 and Ti_6C_5 types are much more hard to obtain. Similar to the Ti_2C phase, they can be of different symmetry while their chemical composition remains unchanged.

Bulk samples of these phases can be obtained only after long-term (several hundreds of hours) annealing at $T < 1000$ K. The results of experimental and theoretical studies suggest that these phases are in thermodynamic equilibrium at temperatures below 900–1000 K. A hexagonal Ti_6C_5 phase was found in thin films synthesised by electron beam and laser sputtering of titanium carbide.

Molecular cluster-like compounds Ti_8C_{12} (Ti_2C_3) and $\text{Ti}_{13}\text{C}_{22}$ ($\sim \text{TiC}_2$) were obtained by laser-assisted plasmachemical synthesis. The most convenient procedure for preparation of these compounds in the crystalline form is to stabilise them in thin films deposited on a substrate (molecular clusters with a characteristic atomic ratio, $\text{C}:\text{Ti} = 1.5$ or 2).¹⁴¹ This allows one to obtain thin films of a compound Ti_2C_3 or TiC_2 with the crystal structure similar to that of the substrate. Indeed, the synthesis of titanium oxide, fullerene and amorphous carbon nanocrystals with a different structure on the solid surfaces of different chemical nature (graphite, polymers, oxides) was reported.¹⁴² Chemical modification of the substrate surface or heat treatment of the film cast provide additional possibilities of forming a particular type of the crystal structure of the film.

The main methods of experimental detection of new compounds and phases include X-ray, electron or neutron diffraction. We believe that the model X-ray diffraction patterns of most of the phases of the Ti–C system, first reported in this review will essentially facilitate identification of new phases and interpretation of the results obtained.

Thus, analysis of studies on the Ti–C system carried out in 1985–2000 showed that not only titanium carbide TiC_x , but also other chemical compounds and phases are formed in this system. They were discovered using novel, advanced methods of synthesis, thorough studies of phase equilibria at temperatures below 1300 K and highly sensitive mass spectrometric and diffraction methods of analysis of products of the chemical interaction. One can expect (and some experimental proofs have already been reported) that binary systems comprising carbon and other transition metals can appear to be no less interesting than the Ti–C system.

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Redox reactions of actinides in carbonate and alkaline solutions

V P Shilov, A B Yusov

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Abstract. Data on redox reactions involving uranium, neptunium, plutonium and americium ions in carbonate and alkaline solutions are generalised. The results of kinetic studies of these reactions are analysed and their mechanisms are discussed. The bibliography includes 169 references.

I. Introduction

Progress in the chemistry of actinides has long been associated predominantly with the necessity of solving technological problems. Early chemical investigations were concerned primarily with the reactions of actinides in acidic media, whereas the reactions in alkaline media were little studied. However, these scarce data are of most interest. Thus, the use of carbonate and alkaline solutions made it possible to stabilise valence states of actinides, which are either unstable or difficult to prepare in acidic media. For instance, Am(IV) was stabilised and Cf(V) and Cm(VI) were first obtained in carbonate media. The most prominent example is the discovery of heptavalent neptunium, plutonium and americium, which gave impetus to the outburst of studies of alkaline solutions of actinides in the late 1960s and in the early 1970s. In recent years, interest in redox reactions of actinides in alkaline media was rekindled. The reason is that there is an acute need to solve a number of problems associated with storage and processing of alkaline waste of radiochemical industry, which were accumulated in large amounts at plants both in Russia and abroad. Extensive studies in this field gave new interesting results, which are not only of applied but also of scientific importance.

In the last decade, the properties of actinides in carbonate and alkaline media were surveyed in reviews. For example, the compositions and structures of carbonate complexes in solutions and in the solid state were covered in detail in the review;¹ however, no consideration was given to redox reactions. The report² was devoted to the chemistry of actinides in alkaline media, including redox reactions. Unfortunately, this report is not easily accessible to Russian researchers. Besides, the results of more recent investigations were published in the literature.

The aim of the present review is to systematise and analyse the available data on redox reactions of uranium, neptunium, plutonium, americium and curium in bicarbonate, carbonate and alkaline solutions.[†] We do not consider the data on photochemical and radiochemical reactions, which were generalised in the publications^{3,4} in sufficient detail. Studies of electrochemical reactions involving actinide ions are also beyond the scope of our review.

II. Redox potentials

To predict the possibility of a particular redox reaction occurring, the data on redox potentials (hereinafter referred to as potentials) of actinide pairs in carbonate and alkaline media are required. The measured and estimated (calculated) formal potentials (*i.e.*, potentials at equal concentrations of the oxidised and reduced forms) are given in Table 1.

III. Reactions in carbonate solutions

It can be seen from Table 1 that tri- and tetravalent uranium, neptunium and plutonium can be oxidised by molecular oxygen, whereas trivalent neptunium and plutonium can also be oxidised by water (in the pH range of 9–12, the potentials of the O₂/H₂O and H₂O/H₂ pairs vary from 0.70 to 0.52 V and from –0.53 to –0.71 V, respectively).³⁸ Besides, U(V), Pu(V) and Am(IV) are unstable in disproportionation reactions, Np(VI) must oxidise Np(IV), whereas Am(VI) can oxidise Am(III) and Am(IV).

1. Disproportionation and reproporation reactions

a. Disproportionation of actinides(V)

The kinetics of disproportionation of U(V) in carbonate solutions was examined by cyclic chronopotentiometry.³⁹ It was found that U(V), which was generated on the electrode surface through reduction of U(VI), rapidly disappeared in solution. This process is best described by a model on the basis of the second-order reaction

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[†] It should be noted that the reaction mechanisms were not considered in most of original studies and it is impossible to make justified conclusions about these mechanisms based on the available data. In this connection, we write the reaction equations in the formal form, *i.e.*, denote actinide ions as Np(VI), Pu(IV), *etc.* In addition, many reactions proceed in rather broad ranges of pH or alkali concentrations due to which the valence state of the actinide ion may vary.

Table 1. Formal potentials of actinide pairs.

Solution	Potential of the pair /V (relative to the normal hydrogen electrode)				Ref.	Solution	Potential of the pair /V (relative to the normal hydrogen electrode)				Ref.
	VII/VI	VI/V	V/IV	IV/III			VII/VI	VI/V	V/IV	IV/III	
Uranium						Plutonium					
0.1 M NaHCO ₃		−0.98 ^a	—	—	5	1 M (NaHCO ₃ +	—	—	0.3–0.35 ^d	—	
1 M NaHCO ₃		−0.63 ^b	—	—	5	+ Na ₂ CO ₃)					
0.05 M Na ₂ CO ₃		−0.671	—	—	6	(pH 11.0)					
0.75 M Na ₂ CO ₃ +		−0.527	—	—	7	0.1 M K ₂ CO ₃	—	0.30	—	—	13
+ 0.6 M NaClO ₄						1 M K ₂ CO ₃	—	0.32	0.6	−0.495	8, 13
0.1–3 M Na ₂ CO ₃		−0.71	—	—	5	1 M NaOH	0.849	0.23	—	—	20, 25
1 M K ₂ CO ₃		−0.6	0	−2.08	8		—	0.21	—	−0.95	26
1 M NaOH		−0.65	—	−2.6	9, 10	4 M NaOH	—	—	0.44	—	25
Neptunium								—	0.26–0.29	—	27
0.05 M Na ₂ CO ₃	—	0.445	—	—	6	4.6 M NaOH	0.715	—	—	—	20
1 M Na ₂ CO ₃	—	0.44	—	—	11	7.9 M NaOH	—	0.21	—	—	28
2 M Na ₂ CO ₃	—	0.47 ^{b, c}	—	−1.4 ^d	12	10.1 M NaOH	0.540	0.20	—	—	20, 28
(pH 13)						2.5 M LiOH	—	0.2518	—	—	22
2 M Na ₂ CO ₃	—	0.27 ^b	—	—	12	4 M LiOH	—	0.2556	—	—	22
(pH 13–14)						Americium					
0.2 M K ₂ CO ₃	—	0.43	—	—	13	1 M Na ₂ CO ₃	—	0.9	—	0.924	29, 30
0.8 M K ₂ CO ₃	—	0.44	—	—	13	2 M Na ₂ CO ₃	—	—	—	0.887	30
1 M K ₂ CO ₃	—	0.44	0.1	−1.32	8	2 M (NaHCO ₃ +	—	—	—	0.92	31
				−1.3 ^b	12	+ Na ₂ CO ₃)					
3 M K ₂ CO ₃	—	0.44	—	—	13	(pH 9.7)					
1 M NaOH	0.582	0.18	—	—	14, 15	2 M (NaHCO ₃ +	—	0.975	—	0.89	30, 32,
	0.587	0.12	0.13	−1.8	16, 17,	+ Na ₂ CO ₃)					33
					18, 19	(pH 10)		0.93	—	—	32
4 M NaOH	0.462	—	—	—	20	1 M K ₂ CO ₃	—	0.90	0.5	0.86	8, 13
10.4 M NaOH	0.225	—	—	—	20	2.82 M (KHCO ₃ +	—	—	0.99	—	34
1 M LiOH	0.604	—	—	—	21	+ K ₂ CO ₃)					
2.5 M LiOH	—	0.1527	—	—	22	(pH 8.87)					
4 M LiOH	—	0.1498	—	—	22	2.82 M (KHCO ₃ +	—	—	0.81	—	34
Plutonium						+ K ₂ CO ₃)					
0.05 M Na ₂ CO ₃	—	0.334	—	—	6	(pH 11.2)					
1 M Na ₂ CO ₃	—	0.33	—	—	23	1 M NaOH	1.05	0.65	—	—	35, 36
2 M Na ₂ CO ₃	—	0.35 ^c	—	—	24			0.68	0.25–0.50	<0.25	37
2 M Na ₂ CO ₃ +	—	0.33 ^c	—	—	24	Curium					
+ 1 M NaOH						1 M K ₂ CO ₃	—	—	0.5	1.6	8
2 M Na ₂ CO ₃ +	—	0.31 ^c	—	—	24	1 M NaOH	—	—	—	0.7	10
+ 2 M NaOH											

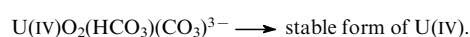
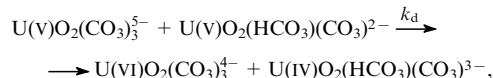
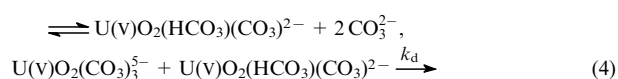
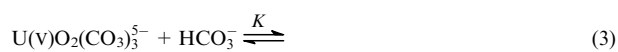
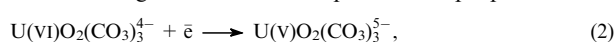
^a Determined by polarography. ^b Determined by cyclic voltammetry scan. ^c The diffusion potential between a 2 M Na₂CO₃ solution and a saturated calomel electrode was ignored. ^d Estimated by us based on the data of the study;²⁴ under these conditions, an equilibrium mixture of Pu(VI), Pu(V) and Pu(IV) was formed.

$$-\frac{d[U(V)]}{dt} = 2k_d[U(V)]^2, \quad (1)$$

where k_d is the rate constant of disproportionation.

The rate constants for disproportionation of U(V) in a 1 M NaHCO₃ solution (pH 8.57, $T = 25^\circ\text{C}$) remains unchanged as the concentration of U(VI) is varied in the range from 1 to 10 mmol litre^{−1}. An increase in pH[‡] leads to a decrease in the constant k_d both at a constant CO₃^{2−} content (17 mmol litre^{−1}) and at a constant HCO₃[−] content (0.68 mol litre^{−1}). In the pH range of 8.57–9.23, the constant k_d varies from ~15–20 to 2–3 litre mol^{−1} s^{−1}.

The following mechanism of the process was proposed:³⁹



The experimental $\log k_d - \log[HCO_3^-]$ plot yields a straight line with a slope of 0.84 ± 0.06 . Consequently, the reaction order with respect to the bicarbonate ion is close to unity. The slope of the plot of k_d vs. the concentration of free carbonate ions (on the logarithmic coordinates) is equal to -1.87 ± 0.1 , i.e., is close to -2 .

It should be emphasised that the reaction (2) proceeds on the electrode surface, whereas the reactions (3) and (4) take place in solution. In 0.25–1 M NaHCO₃ solutions, the solvated electron can lose the ‘reducing’ properties. Thus, it was found that Np(V) was oxidised to Np(VI) upon γ irradiation of its aerated or argon-

[‡] In bicarbonate–carbonate solutions, pH is generally controlled by changing the ratio between [CO₃^{2−}] and [HCO₃[−]].

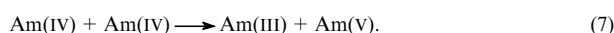
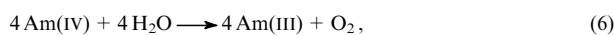
saturated bicarbonate solutions. This oxidation did not take place in a solution of Na_2CO_3 , whereas irradiation of Np(VI) led to its reduction.⁴⁰

Disproportionation of Pu(V) was not examined. It was only noted that Pu(V) , which was generated upon electrochemical reduction of Pu(VI) in a bicarbonate solution, underwent disproportionation with a high rate and exclusively Pu(IV) was accumulated in the solution.²³ An increase in pH slows down disproportionation of Pu(V) [like disproportionation of U(V)]. At pH 11.0, the process is completed in 6–8 h. The hexa-, penta- and tetravalent plutonium ions were found in the equilibrium mixture, *i.e.*, the following reaction took place



b. Disproportionation of Am(IV)

Americium(IV), which was prepared in bicarbonate-carbonate solutions by electrolytic oxidation of Am(III) , was reduced with water (the first-order reaction with respect to americium) and underwent disproportionation (second-order reaction).^{32, 33}



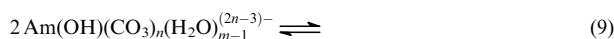
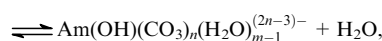
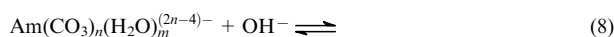
In a 1.3 M $\text{NaHCO}_3 + \text{Na}_2\text{CO}_3$ solution (pH 10), the activation energy of the second-order reaction in the temperature range of 30–65 °C is $100.8 \pm 4.0 \text{ kJ mol}^{-1}$.

In a 1.5 M $\text{NaHCO}_3 + \text{Na}_2\text{CO}_3$ solution, the rate constant for disproportionation of Am(IV) was measured at different pH by spectrophotometry.⁴¹ Americium(IV) was prepared by irradiating a solution of Am(III) containing the BrO^- ions with UV light. After termination of irradiation, Am(IV) was transformed spontaneously into Am(III) and Am(V) according to the reactions (6) and (7) in a time varying from a few minutes to 3–4 days (depending on pH). The conversion of Am(IV) into Am(III) was 50%–65%.

Taking into account the final proportion of Am(III) , it can be concluded that the second-order reaction (7) prevailed. The rate constant of this reaction increased from 6.6×10^{-2} to $262 \text{ litre mol}^{-1} \text{ s}^{-1}$ as pH was increased from 10.39 to 12.13.

In a 1.5 M $\text{KHCO}_3 + \text{K}_2\text{CO}_3$ solution, $2k_d$ increased from 6.6×10^{-2} to $450 \text{ litre mol}^{-1} \text{ s}^{-1}$ as pH was increased from 8.40 to 11.70.

Judging from the slopes of the plots of $2k_d$ vs. pH (on the logarithmic coordinates), the disproportionation reaction of Am(IV) in $\text{KHCO}_3 + \text{K}_2\text{CO}_3$ and $\text{NaHCO}_3 + \text{Na}_2\text{CO}_3$ solutions is second order with respect to the OH^- ions. This is attributable to the fact that the first step involves hydrolysis of americium carbonate complexes:



If the concentration of K_2CO_3 in a $\text{KHCO}_3 + \text{K}_2\text{CO}_3$ solution is higher than 3 mol litre^{-1} , disproportionation of Am(IV) proceeds much more slowly and this reaction is very slow at a concentration of $4.0\text{--}5.88 \text{ mol litre}^{-1}$. Apparently, this is associated with an increase in the number of the carbonate groups in the coordination sphere of Am(IV) resulting in a decrease in the potential of the Am(IV)/Am(III) pair and an increase in the potential of the Am(V)/Am(IV) pair. As a consequence, the equilibrium of the reaction (9) is sharply shifted to the left and Am(IV) becomes stable.

c. Reproportionation of $\text{Np(IV)} + \text{Np(VI)}$

The reaction



was examined in 1.7–4.0 M K_2CO_3 solutions by spectrophotometry ($\lambda = 490 \text{ nm}$).⁴² The concentrations of Np(VI) and Np(IV) are lowered according to the equation

$$-\frac{d[\text{Np(vi)}]}{dt} = -\frac{d[\text{Np(vi)}]}{dt} = k'[\text{Np(vi)}][\text{Np(IV)}]. \quad (11)$$

The apparent rate constant of the reaction k' remains virtually unchanged upon a twofold change in the concentrations of Np(VI) and Np(IV) and decreases by a factor of 4 as the K_2CO_3 content is increased from 1.71 to 4 mol litre^{-1} . The authors of the cited study⁴² attributed this fact to an increase in the number of the carbonate groups in the complex Np(IV) ion [like in the Am(IV) ion, see above], which hinders charge transfer.

In the temperature range of 52–76.5 °C, the activation energy of the reaction (10) in K_2CO_3 solutions is $103 \pm 2 \text{ kJ mol}^{-1}$, which is virtually equal to this value (104 kJ mol^{-1}) for the reproportionation reaction $\text{Np(IV)} + \text{Np(VI)}$ in solutions of HClO_4 and HNO_3 .

In the presence of sulfate ions, the reaction (10) slows down. The addition of SO_4^{2-} ($0.21 \text{ mol litre}^{-1}$) to a 2.08 M K_2CO_3 solution led to a decrease in k' from 1470 to $390 \text{ litre mol}^{-1} \text{ min}^{-1}$. Hence, the sulfate ion has a more substantial effect on the reaction rate than the carbonate ion. This fact remains to be explained.

2. Reactions analogous to disproportionation and reproportionation

a. Reactions of Am(III) with Am(VI)

Judging from the potentials of the Am(VI)/Am(V) and Am(IV)/Am(III) pairs in carbonate-bicarbonate solutions (see Table 1), Am(VI) can oxidise Am(III)



Actually, Am(IV) and Am(V) are accumulated in solution when equimolar carbonate solutions containing tri- and hexavalent americium ($6.2 \times 10^{-4} \text{ M}$) are mixed in different proportions.³⁰ If the difference between the formal potentials is 60 mV ($[\text{CO}_3^{2-}] = 1 \text{ mol litre}^{-1}$), the rate constant

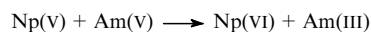
$$K = \frac{[\text{Am(IV)}][\text{Am(V)}]}{[\text{Am(III)}][\text{Am(VI)}]}$$

must be equal to 10 (the experimental value is 11.2 ± 1.5).

Hence, four valence forms, *viz.*, Am(III) , Am(IV) , Am(V) and Am(VI) , can coexist in solutions with pH 9.5–10.5.

b. Reactions of Np(V) with Am(V)

The reaction



was studied by spectrophotometry from the intensity of light absorption of Am(III) ($\lambda = 508 \text{ nm}$) and Np(VI) (470 nm) in 0.45–1.71 M Na_2CO_3 solutions.⁴³ The Am(III) concentration was increased half as rapidly as the Np(VI) concentration. Hence, the following equation was proposed for this reaction:



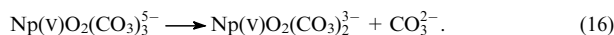
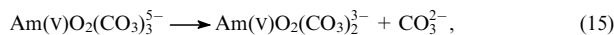
and a change in the concentrations of the reacting compounds is described by the equation

$$-\frac{d[\text{Am(v)}]}{dt} = -\frac{1}{2} \frac{d[\text{Np(v)}]}{dt} = k'[\text{Am(v)}][\text{Np(v)}]. \quad (14)$$

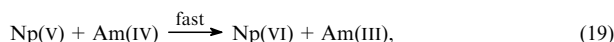
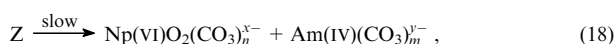
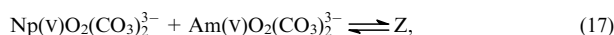
The validity of the Eqn (14) is confirmed by the fact that the constant k' ($T = 64 \text{ °C}$) is independent of the initial concentrations of Np(V) ($0.65\text{--}1.9 \text{ mmol litre}^{-1}$) and Am(V) ($0.65\text{--}1.3 \text{ mmol litre}^{-1}$). The reaction rate (the order with respect to the CO_3^{2-} ions $n = -1.53$) decreases monotonically as the Na_2CO_3 content is increased. In the temperature range of

50.5–69.7 °C, the activation energy is $60 \pm 4 \text{ kJ mol}^{-1}$ regardless of the Na_2CO_3 concentration.

Most likely, the process starts with dissociation of the Am(V) and Np(V) carbonate complexes [like in the case of disproportionation of U(V)]. Hence, we believe that at a constant ionic strength of solution (μ), the reaction order with respect to CO_3^{2-} would be more close to -2 . In this medium, pentavalent actinides can exist as tricarbonates complexes.¹ In this case, it can be assumed that the following reactions proceed:



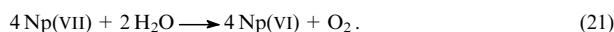
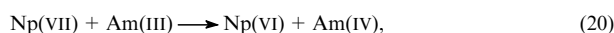
Next, the following charge transfer processes take place



where Z is an activated complex.

c. Reactions of Am(III) with Np(VII)

In a 2.82 M $\text{KHCO}_3 + \text{K}_2\text{CO}_3$ solution, the potential of the Am(IV)/Am(III) pair varies from 0.99 to 0.81 V as pH is increased from 8.9 to 11.2.³⁴ In carbonate and bicarbonate media, the potentials of the Np(VII)/Np(VI) pair vary in the ranges which are apparently comparable with the range mentioned above or are even broader. Actually, the potential of this pair in a 1 M NaOH solution is 0.582 or 0.587 V (see Table 1) and increases by 0.118 V as pH is decreased by unity ($\mu = 1$),¹⁶ i.e., this potential at pH 11 and pH 10 must be no lower than 0.9 V and no higher than 1 V, respectively. In carbonate solutions, these values may vary due to the formation of the Np(VI) and Np(VII) complexes with the carbonate ions, but these changes are insignificant. Hence, Np(VII) can serve as an oxidiser of Am(III) in bicarbonate and carbonate media. However, Np(VII) is reduced with water under the same conditions. The yield of Am(IV) depends on the ratio between the reaction rates



After the addition of an aliquot of an alkaline solution of neptunium(VII) to a 1.5 M KHCO_3 solution of americium(III), the latter is oxidised already in the course of stirring (10–30 s).⁴⁴ The intensity of the absorption band of Am(III) carbonate complexes with a maximum at 507 nm decreases (in some cases, the band even disappears). The light absorption resulting from superposition of broad bands belonging to Am(IV) and Np(VI) is observed at wavelengths shorter than 450 nm. When the dry salt $\text{K}_4\text{Fe(CN)}_6 \cdot 3\text{H}_2\text{O}$ was placed in a cell, light absorption at 350–400 nm was decreased and the band with a maximum at $\sim 507 \text{ nm}$ simultaneously regained its initial intensity. This unambiguously indicates that Np(VII) oxidises Am(III) to Am(IV) . The rate constant for the bimolecular reaction (20) is larger than $5 \times 10^3 \text{ litre mol}^{-1} \text{ s}^{-1}$.⁴⁴ This value is many orders of magnitude larger than the rate constant of the reaction (21) for which the conversion of Np(VII) at pH 9.08 reaches 50% in 1.2 min.⁴⁵ In the presence of a two- or threefold excess of Np(VII) , Am(III) is also oxidised only to the tetravalent state.

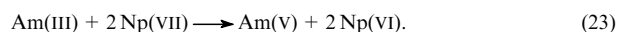
The same phenomena are observed in $\text{KHCO}_3 + \text{K}_2\text{CO}_3$ or $\text{NaHCO}_3 + \text{Na}_2\text{CO}_3$ mixtures at $\text{pH} \leq 10.9$. At higher pH (including 1.5 M K_2CO_3 or Na_2CO_3 solutions without additives of bicarbonate), the addition of a stoichiometric amount of Np(VII) leads to complete oxidation of Am(III) to Am(IV) , which then disappears due to disproportionation [see the reaction (7)]. This is evidenced by the appearance of Am(III) in an amount half as large as the initial value. The reaction of Am(III) with Np(VII)

taken in a threefold excess afforded Am(VI) , which is characterised by light absorption at 450–600 nm. Hence, Np(VII) oxidises not only Am(III) but also Am(V)



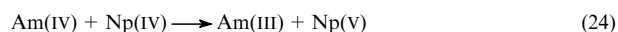
The addition of $\text{K}_4\text{Fe(CN)}_6 \cdot 3\text{H}_2\text{O}$ crystals to this solution led to a decrease in absorption at 450–600 nm but the absorption of Am(III) was not observed, i.e., Am(VI) was reduced to Am(V) .

The addition of a solution of Np(VII) in 0.01 M NaOH to a solution of Am(III) in 6 M K_2CO_3 resulted in oxidation of approximately one-half of the initial amount of Am(III) . However, the absorption bands of Am(IV) and Am(VI) were not observed. The concentration of Am(III) was not increased upon the addition of $\text{K}_4\text{Fe(CN)}_6 \cdot 3\text{H}_2\text{O}$. Hence, Am(III) is partially oxidised to Am(V) in this medium

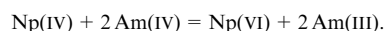


d. Reactions of Am(IV) with Np(IV) or Pu(IV)

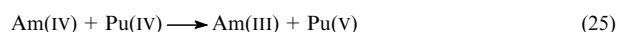
In a 0.5 M $\text{NaHCO}_3 + 1 \text{ M Na}_2\text{CO}_3$ solution, americium(IV) oxidises neptunium(IV), which is taken in an equimolar amount, to neptunium(VI) in 1–2 min.⁴⁶ The process starts with the reaction



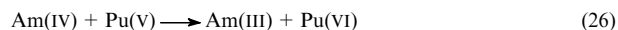
followed by the more rapid reaction (19), because only Am(III) , Np(VI) and Np(IV) are present in the solution after the disappearance of Am(IV) , i.e., the process is described by the equation



Compared to the reaction (24), oxidation of Pu(IV) with americium(IV)



proceeds more slowly.⁴⁷ The subsequent reaction



must proceed faster.

3. Oxidation reactions

a. Oxidation with molecular oxygen

Oxidation of uranium(V) in a 1 M Na_2CO_3 solution and oxidation of uranium(IV) in a 1 M NaHCO_3 solution with atmospheric oxygen were examined in the study.⁵ In both cases, U(VI) was accumulated in the reaction products. The kinetic parameters of the reactions were not reported. The kinetics of U(IV) oxidation in carbonate-bicarbonate solutions was investigated.⁴⁸ When air was passed with a rate of 130 ml min^{-1} through a 1 M $\text{NaHCO}_3 + 0.25 \text{ M Na}_2\text{CO}_3$ solution (40 ml) containing uranium ($1.3 \times 10^{-2} \text{ mol litre}^{-1}$), U(VI) was formed with a rate of $1.3 \times 10^{-5} \text{ mol litre}^{-1} \text{ min}^{-1}$. A threefold decrease in the concentration of $\text{HCO}_3^- + \text{CO}_3^{2-}$ led to an increase in the rate of oxidation by $\sim 30\%$; the addition of copper ammoniate caused acceleration of oxidation.

Plutonium(III), which was prepared by electrolysis of Pu(IV) in a 1 M K_2CO_3 solution, underwent oxidation with atmospheric oxygen within a few minutes after termination of electrolysis. The supply of atmospheric oxygen was increased on stirring of the solution and oxidation was accelerated.²⁴

Dissolution of NpO_2 crystals in an aerated 1 M NaHCO_3 solution was examined.⁴⁹ The rate of dissolution of NpO_2 in this solution (210 ppm per day) proved to be much higher than that in water (2.5 ppm per day) or in a saturated NaCl solution (25 ppm per day). Neptunium(V) was detected in bicarbonate solutions, which indicates that NpO_2 is oxidised under the action of O_2 and HCO_3^- .

b. Oxidation with hydrogen peroxide

Hydrogen peroxide was also used for uranium oxidation (a suspension of a UO_2 powder in 0.5 M NaHCO_3 or NH_4HCO_3

solutions, $T = 20\text{ }^{\circ}\text{C}$).⁵⁰ To accelerate dissolution of UO_2 , $\text{Fe}(\text{CN})_6^{4-}$ and $\text{Fe}(\text{CN})_6^{3-}$ were added to the system. The proportion of uranium oxidised during the same period was approximately halved when pH was increased from 7.5 to 9, whereas a subsequent increase in pH has no effect on the oxidation rate.

c. Oxidation with water

Neptunium(III), which was prepared by an electrochemical method in a carbonate solution,¹² was spontaneously oxidised with water, which hindered the measurement of its absorption spectrum.

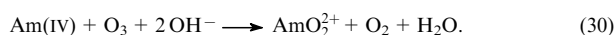
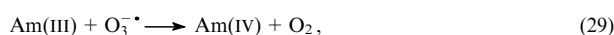
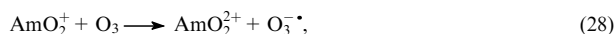
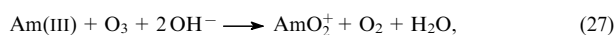
d. Oxidation with ozone

In the study,⁵¹ solutions of Am(VI) and Am(V) were prepared with the use of ozone. When oxygen containing 5% O_3 was passed through a 0.1 M NaHCO_3 solution containing a suspension of $\text{Am}(\text{OH})_3$ during 1 h, Am(VI) was formed quantitatively at any temperature in the range from 0 to $90\text{ }^{\circ}\text{C}$.

In a 2 M Na_2CO_3 solution, Am(III) is oxidised with ozone to Am(VI) at room and lower temperatures. In heated solutions, accumulation of Am(V) takes place.

Americium(V) involved in double carbonate with sodium was readily oxidised to Am(VI) with ozone in NaHCO_3 solutions at room temperature. However, ozone oxidised $\text{Am}(\text{OH})_3$ in 0.03–0.1 M KHCO_3 solutions to form Am(V), which precipitated as the salt KAmO_2CO_3 .

The kinetics of ozonation was not studied in detail. Nevertheless, some conclusions can be made about the mechanisms of the reactions that take place. Experiments on oxidation of Pu(III) with ozone in aqueous 0.25–1 M HClO_4 solutions enriched with the ^{18}O isotope demonstrated that water and ozone each supply one oxygen atom to form the PuO_2^{2+} ion.⁵² Oxidation of U(IV) with ozone is also accompanied by the transfer of the oxygen atom from ozone (apparently, as an inner-sphere process).⁵³ Oxidation of Am(III) with ozone may be schematically described by the following equations (without considering the complex formation with the carbonate ions):



In carbonate solutions, Am(III) exists as the complex AmCO_3^+ , $\text{Am}(\text{CO}_3)_2^-$ or $\text{Am}(\text{CO}_3)_3^{3-}$ ions depending on the composition of these solutions.⁵⁴ Based on the two last-mentioned complex ions, the crystalline compounds $\text{NaAm}(\text{CO}_3)_2 \cdot 4\text{H}_2\text{O}$ and $\text{Na}_3\text{Am}(\text{CO}_3)_3 \cdot 3\text{H}_2\text{O}$ containing water molecules in the coordination sphere of Am(III) were obtained.⁵⁵ Oxidation with ozone is accompanied by the replacement of the water molecule in the coordination sphere of Am(III) followed by elimination of the oxygen molecule [see the reaction (27)]. This mechanism was confirmed by our experiments on oxidation of Am(III) with ozone in a 5 M K_2CO_3 solution. Apparently, an increase in the concentration of the carbonate ions leads to an increase in the number of the CO_3^{2-} groups in the coordination sphere of Am(III) due to the displacement of the water molecules as a result of which the insertion of the ozone molecule is hindered and oxidation occurs as an outer-sphere process to form Am(IV).

e. Oxidation with $\text{S}_2\text{O}_8^{2-}$ ions

Neptunium(V). The kinetics of Np(V) oxidation with the persulfate ions was studied by spectrophotometry from the change in absorption of Np(VI) at 470 nm.⁵⁶ A decrease in the concentration of Np(V) is described by the following equation

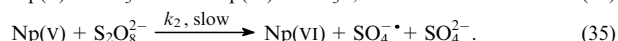
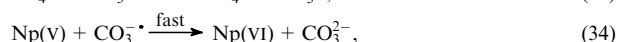
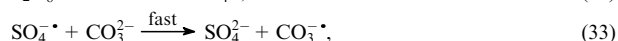
$$-\frac{d[\text{Np(V)}]}{dt} = 2\{k_1 + k_2[\text{Np(V)}]\}[\text{S}_2\text{O}_8^{2-}]. \quad (31)$$

It was found that two competitive reactions take place, viz., the first-order (rate constant k_1) and second-order (rate constant k_2) processes (the zero and first orders with respect to neptunium, respectively).

Variation in the $\text{S}_2\text{O}_8^{2-}$ concentration from 50 to 500 mmol litre⁻¹ ($[\text{Np(V)}] = 16\text{ mmol litre}^{-1}$ at $50\text{ }^{\circ}\text{C}$) has no effect on the rate constants k_1 and k_2 for Np(V) oxidation in a 0.94 M Na_2CO_3 solution. As the Na_2CO_3 concentration is increased from 0.84 to 1.92 mol litre⁻¹ ($T = 50.4\text{ }^{\circ}\text{C}$), k_1 decreases from 4.7×10^{-5} to $2.3 \times 10^{-5}\text{ min}^{-1}$, whereas the constant k_2 ($k_2 = 0.15\text{ litre mol}^{-1}\text{ min}^{-1}$) remains unchanged.

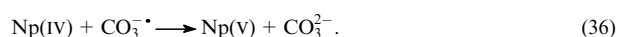
In a 0.93 M K_2CO_3 solution, the constants k_1 and k_2 remain unchanged as $[\text{Np(V)}]_0$ is increased from 1.07 to 2.13 mmol litre⁻¹ and $[\text{S}_2\text{O}_8^{2-}]_0$ is increased from 30 to 150 mmol litre⁻¹, but an increase in the K_2CO_3 concentration from 0.93 to 4.50 mol litre⁻¹ ($T = 51.0\text{ }^{\circ}\text{C}$) is accompanied by a decrease in k_1 and an increase in k_2 .

The activation energies of the first- and second-order reactions (E_1 and E_2 , respectively) are 138 and 71 kJ mol⁻¹, respectively. The energy E_1 is virtually equal to the activation energy of thermal decomposition of $\text{S}_2\text{O}_8^{2-}$ (140 kJ mol⁻¹).⁵⁷ Hence, it can be assumed that the direct reaction of $\text{S}_2\text{O}_8^{2-}$ with Np(V) in carbonate solutions occurs simultaneously with thermal decomposition of $\text{S}_2\text{O}_8^{2-}$ followed by the reaction of the $\text{SO}_4^{\cdot-}$ radical ions with Np(V).



Neptunium(IV). Oxidation of Np(IV) with persulfate ions was studied in 0.86–3.30 M K_2CO_3 solutions by spectrophotometry from a change in absorption of Np(VI) ($\lambda = 490\text{ nm}$) and Np(IV) ($\lambda = 800\text{ nm}$).⁵⁸ Typical kinetic curves for a decrease in the amount of Np(IV) and accumulation of Np(VI) assume an S shape. The concentration of Np(V) (calculated) passes through a maximum, which is reached within 10–15 min after the beginning of the reaction.

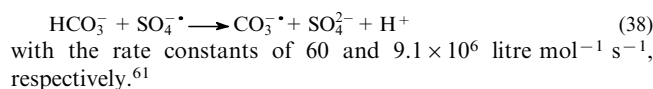
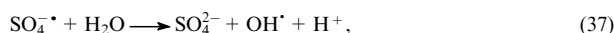
At constant temperature and concentration of K_2CO_3 , the initial oxidation rate (V_0) of neptunium(IV) is independent of its initial concentration. The rate V_0 is comparable with the rate of thermal decomposition of the $\text{S}_2\text{O}_8^{2-}$ ions and is directly proportional to their concentration. Consequently, the process starts with the reactions (32) and (33) followed by the reaction



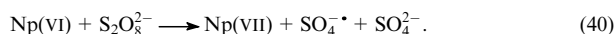
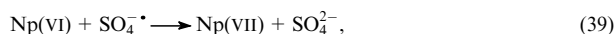
The rate constant for this reaction was estimated at $6.9 \times 10^3\text{ litre mol}^{-1}\text{ s}^{-1}$.⁵⁹ As Np(V) is accumulated, the contribution of the reactions (34) and (35) becomes more and more noticeable. Neptunium(VI) reacts with neptunium(IV) according to the reaction (10).

Neptunium(VI). In bicarbonate solutions containing Np(VI) (1.5 mmol litre⁻¹) and $\text{S}_2\text{O}_8^{2-}$ (50 mmol litre⁻¹), Np(VI) was only partially oxidised at $60\text{ }^{\circ}\text{C}$ in the presence of alkali metal (potassium, sodium or lithium) or ammonium cations.⁶⁰ Accumulation of Np(VII) as MNP_4O_4 took place within first 30 min after mixing of the reagents, whereas subsequent storage of these reagents for 120 min led to only a slight increase in the Np(VII) content. As the concentration of MHCO_3 was increased from 16 to 46 mmol litre⁻¹, the yield of Np(VII) was increased from 17% to 44% in a KHCO_3 medium (pH 7.30–7.70) and from 18% to 29% in a NaHCO_3 medium (pH 7.30). A further increase in the MHCO_3 concentration led to a decrease in the yield of Np(VII). In aqueous solutions containing KHCO_3 (93 mmol litre⁻¹) or NaHCO_3 (46 mmol litre⁻¹), the formation of Np(VII) was not observed. In solutions of LiHCO_3 and NH_4HCO_3 , the maximum yields of Np(VII) were lower.

The following scheme of the process can be proposed. Thermal decomposition of $\text{S}_2\text{O}_8^{2-}$ affords the $\text{SO}_4^{\cdot -}$ radical ions [see the reaction (32)]. Then, the following reactions proceed:



At a bicarbonate concentration of 10–100 mmol litre⁻¹, the $\text{SO}_4^{\cdot -}$ radical anions are predominantly consumed in the reaction (38). However, it is known that the $\text{CO}_3^{\cdot -}$ radical anion cannot oxidise Np(VI) in a carbonate medium.⁶² Hence, either the $\text{SO}_4^{\cdot -}$ radical anion or the $\text{S}_2\text{O}_8^{2-}$ ion must serve as an oxidiser of Np(VI)

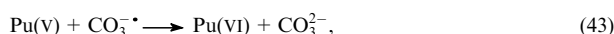
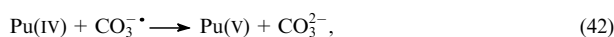


Neptunium(VII) is involved in two competitive processes. In one process, neptunium(VII) partially precipitates as the solid compound MNP_2O_4 (see Ref. 63) and is stabilised. In another process, the remaining Np(VII) is involved in a carbonate complex and reduced with water.⁴⁵

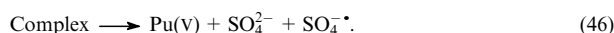
Plutonium(IV). The kinetics of Pu(IV) oxidation with the $\text{S}_2\text{O}_8^{2-}$ ions in 1.07–1.57 M Na_2CO_3 solutions was studied by spectrophotometry from a change in light absorption of Pu(IV) and Pu(VI).⁶⁴ The initial oxidation rates of Pu(IV) to Pu(VI) linearly increased as the concentration of Pu(IV) was increased from 2 to 8 mmol litre⁻¹ according to the empirical dependence

$$V_0 = a + b[\text{Pu(IV)}]. \quad (41)$$

It was assumed that two competitive processes of Pu(IV) oxidation occurred. The rate V_0 nonlinearly increased as the concentration of the $\text{S}_2\text{O}_8^{2-}$ ions was increased. Based on analysis of the experimental data, the following sequence of Pu(IV) oxidation with the $\text{S}_2\text{O}_8^{2-}$ ions was proposed. First, the reactions (32) and (33) proceed followed by the reactions



Simultaneously, Pu(IV) reacts with the $\text{S}_2\text{O}_8^{2-}$ ions that remain undecomposed



It was assumed⁶⁴ that Pu(IV) is oxidised directly with the $\text{SO}_4^{\cdot -}$ radicals. However, this reaction plays virtually no part in this medium. A change in the concentration of $\text{CO}_3^{\cdot -}$ has a substantial effect on the mechanism of the radical pathway of Pu(IV) oxidation and is only slightly reflected in intramolecular oxidation.

In the temperature range of 70–81.5 °C, the activation energies of radical and intramolecular oxidation are 134 ± 8 and $96 \pm 8 \text{ kJ mol}^{-1}$, respectively.

Americium(III) and americium(V). Upon heating in a 0.1 M NaHCO_3 solution, americium(III) is oxidised under the action of $\text{Na}_2\text{S}_2\text{O}_8$ to Am(VI).⁵¹ In a 2 M Na_2CO_3 solution in the presence of $\text{Na}_2\text{S}_2\text{O}_8$ (0.01 mol litre⁻¹), americium(VI) is formed only at 90 °C.⁵¹ In a 0.1 M $\text{KHCO}_3 + \text{K}_2\text{CO}_3$ solution, americium(III) is oxidised under the action of the $\text{S}_2\text{O}_8^{2-}$ ions to americium(V), which precipitates as the KAmO_2CO_3 complex.

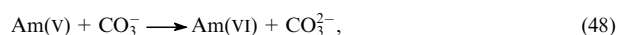
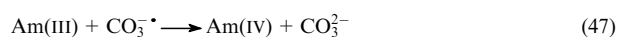
The kinetics of Am(III) oxidation with the persulfate ions was examined in solutions of K_2CO_3 (see Refs 65 and 66), $(\text{NH}_4)_2\text{CO}_3$ and Na_2CO_3 (see Ref. 66).⁸ The course of the reaction was followed from a change in light absorption of Am(III)

($\lambda = 508 \text{ nm}$) and Am(VI) ($\lambda = 688 \text{ nm}$ ⁶⁵ or 550 nm ⁶⁶). The concentration of Am(III) was decreased with a constant rate and this change slowed down only toward the end of the process. Accumulation of Am(VI) started when only 10%–20% of Am(III) remained in the solution. Until then Am(VI), apparently, disappeared due to the involvement in the reaction (12) although the data on this process at high temperature are lacking. The higher was the CO_3^{2-} concentration and the lower was the $\text{S}_2\text{O}_8^{2-}$ concentration, the longer was the induction period. After completion of the induction period, Am(VI) was accumulated in solution almost linearly.

The rate of Am(III) oxidation is independent of the concentrations of americium (in the range of 0.25–1.58 mmol litre⁻¹) and K_2CO_3 and is directly proportional to the concentration of $\text{S}_2\text{O}_8^{2-}$ (12.5–200 mmol litre⁻¹).^{65, 66} At the same time, the rate of Am(V) oxidation, *i.e.*, the rate of Am(VI) accumulation, increases as the concentration of Am(V) is increased only to 0.6 mmol litre⁻¹ and then remains constant. The formation of Am(VI) is accelerated as the concentration of $\text{S}_2\text{O}_8^{2-}$ is increased, whereas an increase in the K_2CO_3 content slows down the Am(VI) formation.

The activation energy of Am(III) oxidation is equal to that of Am(V) oxidation. These values are $143 \pm 8 \text{ kJ mol}^{-1}$ in a 1.9 M K_2CO_3 solution ($T = 58\text{--}83^\circ\text{C}$),⁶⁵ $143 \pm 8 \text{ kJ mol}^{-1}$ in a 1.5 M Na_2CO_3 solution and $159 \pm 8 \text{ kJ mol}^{-1}$ in a 1.9 M $(\text{NH}_4)_2\text{CO}_3$ solution.⁶⁶

The following sequence of Am(III) and Am(V) oxidation can be proposed. Thermal decomposition of $\text{S}_2\text{O}_8^{2-}$ [see the reactions (32) and (33)] affords the $\text{SO}_4^{\cdot -}$ and $\text{CO}_3^{\cdot -}$ radical anions followed by the reactions



and the reaction (12). The rate constant of the reaction (47) is $2.5 \times 10^7 \text{ litre mol}^{-1} \text{ s}^{-1}$.⁶⁷

To our knowledge, americium(IV) does not react with $\text{CO}_3^{\cdot -}$ and, hence, Am(V) may be formed only upon disproportionation of Am(IV).

The plot of the rate constant for An(V) oxidation ($\text{An} = \text{U}$, Np or Pu) with the $\text{CO}_3^{\cdot -}$ radical anions *vs.* the potential of the An(VI)/An(V) pair yields a straight line on the logarithmic coordinates, which is characteristic of the Marcus outer-sphere electron transfer.⁶ It is reasonable to suggest that oxidation of Am(V) will be described by an analogous plot. Extrapolation of the straight line to the potential of 0.92 V [*i.e.*, to Am(V)] gave $\log k \approx 6$ ($\text{litre mol}^{-1} \text{ s}^{-1}$). This value is smaller than $\log k$ for the reaction (47) although the Am(VI)/Am(V) and Am(VI)/Am(III) pairs have similar potentials (see Table 1) and oxidation of both ions occurs without the structural rearrangements. Apparently, the lower rate of Am(V) oxidation as compared to the rate of Am(III) oxidation is responsible for the occurrence of the induction period observed upon accumulation of Am(VI). Taking into account that

$$k_{\text{Am(III)}}[\text{Am(III)}] \approx k_{\text{Am(V)}}[\text{Am(V)}],$$

for oxidation of Am(III) and Am(V) with persulfate ions we have

$$k_{\text{Am(V)}} \approx 0.1 k_{\text{Am(III)}}.$$

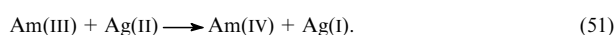
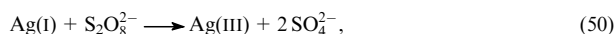
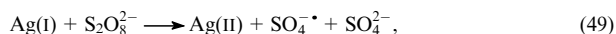
The results obtained with the use of this ratio agree with the results of extrapolation. Our data on radiolysis and photolysis of Am(III) and Am(V) also indicate that these ions differ in their ability to be oxidised in carbonate solutions. Apparently, the $\text{CO}_3^{\cdot -}$ radical anions interact with Am(III) and Am(V) through different mechanisms. Oxidation of Am(V), like oxidation of U(V), Np(V) and Pu(V), proceeds through the outer-sphere charge transfer. By contrast, oxidation of Am(III) can be accompanied by hydrogen abstraction from the water molecule. It should be noted that oxidation of Am(III) with the $\text{OH}^{\cdot}$ radical in HClO_4 solutions proceeds through hydrogen abstraction from the water molecule involved in the hydration shell about the Am(III) ion.⁶⁸

§ Semiquantitative data on the kinetics of this process published in earlier studies were surveyed in the review.⁶⁵

A comparison of the calculated rates of formation of the $\text{SO}_4^{\cdot -}$ radical ions and oxidation of Am(III) shows that $\sim 40\%$ of the radical oxidisers goes into the latter reaction. The fact that Am(III) oxidation is somewhat accelerated in solutions containing more than 2 mol litre^{-1} of K_2CO_3 is indicative of the less significant role of side reactions rather than of the direct interaction of Am(III) with $\text{S}_2\text{O}_8^{2-}$ as has been suggested in the study.⁶⁶

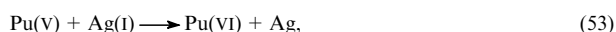
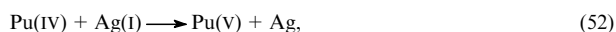
f. Oxidation with silver compounds

Americium(IV), which is unstable in acidic media, was stabilised in carbonate solutions. Americium(III) was subjected to the action of a mixture of AgNO_3 and $\text{K}_2\text{S}_2\text{O}_8$. In this case, several oxidisers appeared in the solution⁶⁹



In addition, the reactions (33) and (47) took place.

Solid AgO also oxidises Am(III) to Am(IV).⁶⁹ Silver oxide was used also for oxidation of Pu(IV) in a 45% K_2CO_3 solution.^{10, 70} In the temperature range of $75\text{--}90^\circ\text{C}$, complete oxidation of plutonium occurred during 45 min. Apparently, the following reactions proceeded:



along with the reaction (5).

g. Oxidation with ClO^- ions

It is known that macroamounts of Pu(IV) in a 45% K_2CO_3 solution are oxidised to Pu(VI) with the hypochlorite ions.⁷⁰ When heated to an above-room temperature, the reaction was completed in 5–10 min. The data on this process are scarce, which does not allow one to make conclusions about the reaction mechanism.

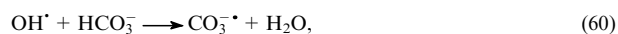
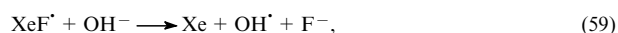
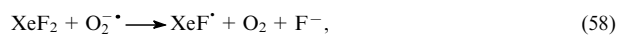
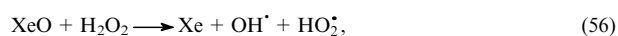
h. Oxidation with xenon compounds

The reactions of the americium ions with xenon compounds in bicarbonate and carbonate media were examined in the studies.^{71–73} Xenon compounds were chosen as oxidisers in view of the fact that the potentials of the Xe(VIII)/Xe(VI) and Xe(II)/Xe(0) pairs are higher than the potentials of the Am(IV)/Am(III) and Am(VI)/Am(V) pairs. The calculated potential of the XeF_2/Xe pair in an acidic medium is 2.3 V .⁷⁴ In an alkaline medium, the potential of this pair was not determined but it was found that xenon difluoride partially oxidises Pu(VI) to Pu(VII) in $0.2\text{--}1.2 \text{ M}$ NaOH solutions.⁷⁵ In a 1 M NaOH solution, the potential of the latter pair is 0.85 V . Hence, XeF_2 must oxidise Am(III).

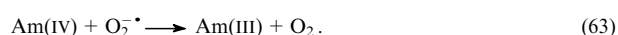
The addition of a XeF_2 solution, which was cooled to 0°C , to a 1.5 M KHCO_3 solution of Am(III) led to oxidation of the latter to Am(IV) in the course of stirring, which was established by spectrophotometry. The stoichiometric coefficient $n = \Delta[\text{Am(IV)}]/\Delta[\text{XeF}_2]$ is 0.23 .^{71, 72} It should be noted that this is yet another known procedure for the chemical preparation of Am(IV) in carbonate solutions (photo- and electrochemical methods are not considered). Upon the addition of dry $\text{K}_4\text{Fe(CN)}_6 \cdot 3 \text{H}_2\text{O}$ to the resulting solution, americium reverted to Am(III). In the presence of a tenfold excess of XeF_2 , americium(III) was completely oxidised to Am(IV). Other valence states were not found. In a $\text{KHCO}_3 + \text{K}_2\text{CO}_3$ solution, the coefficient n decreased as the K_2CO_3 content was increased. In a 1.5 M K_2CO_3 solution, $n < 0.01$. In this medium, Am(III) was oxidised by at most 5% . In more concentrated K_2CO_3 solutions, americium(III) was not oxidised.

In aqueous solutions, not only does XeF_2 react with reducing agents but it also undergoes hydrolysis. The scheme of hydrolysis was proposed in the studies^{76, 77} and was thereafter substantiated.⁷⁸ Taking into account this scheme and the reactions of

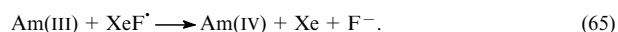
Am(III) and Am(IV), the following sequence of processes occurring in the course of Am(III) oxidation can be suggested. The reactions



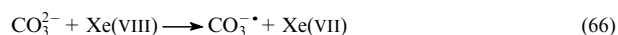
are followed by the reaction (47) and then by the reactions



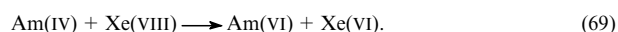
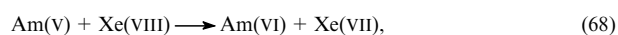
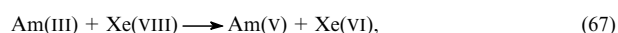
The direct reactions of Am(III) with xenon compounds are also not ruled out.



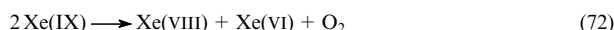
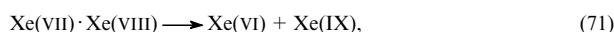
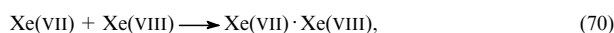
Oxidation of Am(III) under the action of Na_4XeO_6 in carbonate solutions was examined in the studies.^{71, 73} In an alkaline medium, the potential of the Xe(VIII)/Xe(VI) pair is close to 0.9 V .⁷⁹ This potential increases as pH is decreased and its values in a carbonate medium is higher than 1 V . Hence, the perxenate ion can oxidise americium(III) in bicarbonate and carbonate solutions. When $\text{Na}_4\text{XeO}_6 \cdot n \text{H}_2\text{O}$ was added to a 0.75 M $\text{KHCO}_3 + \text{K}_2\text{CO}_3$ solution (pH 10) containing Am(III) ($2 \times 10^{-4} \text{ mol litre}^{-1}$) until the concentration of the former reached $1 \times 10^{-4} \text{ mol litre}^{-1}$, the mixture turned yellow already in 1 min. Analysis of the solution for different valence states of americium [by spectrophotometry and by reduction with $\text{K}_4\text{Fe(CN)}_6 \cdot 3 \text{H}_2\text{O}$] revealed the presence of Am(IV), Am(V) and Am(VI). [Recall that XeF_2 oxidises Am(III) only to Am(IV)]. The $-\Delta[\text{Am(III)}]/\Delta[\text{Xe(VIII)}]$ ratio varied from 0.3 to 0.7. In the presence of a 30-fold excess of perxenate ions, americium was quantitatively oxidised to the hexavalent state. The same situation was observed in a 1.5 M KHCO_3 or K_2CO_3 solution. In a 5.9 M K_2CO_3 solution, perxenate ions decomposed and did not oxidise Am(III). As regards the mechanism of the reaction of Na_4XeO_6 with Am(III), the following conclusions can be made. If the process



took place, the subsequent reaction (47) would afford only Am(IV), which does not react with the $\text{CO}_3^{\cdot -}$ radical anions. For instance, this situation was observed upon photochemical oxidation of Am(III) in the presence of $\text{S}_2\text{O}_8^{2-}$, N_2O , BrO^- or BrO_3^- at pH $8.5\text{--}10.5$.^{41, 80–82} The appearance of Am(V) and Am(VI) in solutions, where disproportionation of Am(IV) proceeds very slowly, indicates that Xe(VIII) serves as an oxidiser of americium to the pentavalent state

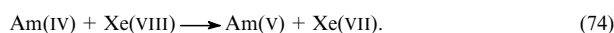
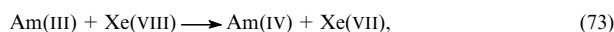


Two-electron reactions can proceed, for example, through the transfer of the oxygen atom. Americium(IV) involved in the reaction (69) is generated in the reaction (12). Like Xe(VIII), xenon(VII) can apparently oxidise Am(III), Am(IV) and Am(V). In addition, it was suggested that Xe(VII) is involved in the following processes:⁸³



The rate constant of the reaction (72) is $2 \times 10^7 \text{ litre mol}^{-1} \text{ s}^{-1}$.

The reactions of Am(III) and Am(IV) with the perxenate ions can also proceed by a one-electron mechanism:

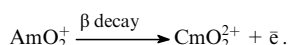


The ability of Na_4XeO_6 to oxidise Am(IV) was proved as follows. Trivalent americium ($0.13 \text{ mmol litre}^{-1}$) in a $1.5 \text{ M KHCO}_3 + \text{K}_2\text{CO}_3$ solution was quantitatively oxidised to Am(IV) under the action of XeO_3 with the use of the photochemical method.⁷¹ The addition of perxenate ions to the solution led to the rapid formation of Am(V) and Am(VI). The stoichiometric coefficient $-\Delta[\text{Am(IV)}]/\Delta[\text{Xe(VIII)}]$ was 0.2.

The potential of the XeO_3/Xe pair was estimated⁸⁴ at 2.10 and 1.24 V in acidic and alkaline solutions, respectively. Hence, XeO_3 could oxidise Am(III) in carbonate solutions. However, we experimentally established⁷¹ that this reaction proceeded only under UV or γ irradiation.

i. β Decay as an oxidative process

Attempts to prepare curium(VI) by chemical methods failed due to the high oxidation potential of the Cm(IV)/Cm(III) pair and, presumably, low stability of curium(V). At the same time, there is reason to believe that Cm(VI) in carbonate solutions must be rather stable. Hence, another procedure for the preparation of Cm(VI) was chosen. This procedure makes use of β decay of the ^{242}Am isotope (half-life is 16.07 h). The compound $\text{K}_3\text{AmO}_2(\text{CO}_3)_2$, which was synthesised in the study,⁸⁵ contains americium with the following isotopic composition: 92% ^{241}Am , 1.4% ^{242}Am and 6.6% ^{243}Am . Before the synthesis, the starting americium specimen was purified from ^{242}Cm that was accumulated. The resulting compound was kept over a period from 18 to 40 h and then dissolved in a 0.1 M NaHCO_3 solution upon ozone bubbling to oxidise Am(V) to Am(VI). Under these conditions, curium(III) was not oxidised. It was expected that the daughter curium-242 isotope, which was generated *via* β decay of the ^{242}Am isotope in the course of storage of $\text{K}_3\text{AmO}_2(\text{CO}_3)_2$, would exist as the 'hot' ion, which has the parent composition but whose charge is larger by unity, *i.e.*,



The estimation, which was carried out taking into consideration all nuclear-physics processes attendant on β decay of the ^{242}Am isotope, demonstrated that up to 60%–70% of the daughter ^{242}Cm isotope must be stabilised as the CmO_2^{2+} ions. The latter can be found after dissolution of $\text{K}_3\text{AmO}_2(\text{CO}_3)_2$. With the aim of establishing the valence state of ^{242}Cm , $\text{K}_4\text{UO}_2(\text{CO}_3)_3$ was precipitated from the resulting solution. The precipitate captured 96%–99% of AmO_2^+ and AmO_2^{2+} ions and only 3%–5% of Cm(III) ions. When the solution was in contact with freshly precipitated LaF_3 , 97%–99% of the Cm(III) ions and no more than 3% of the Am(VI) ions were sorbed. Under the same conditions, 92%–95% of the NpO_2^+ ions (analogues of CmO_2^+) were sorbed. Experiments demonstrated that curium-242 was concentrated either with penta- and hexavalent actinides [in the $\text{K}_4\text{UO}_2(\text{CO}_3)_3$ precipitate] or only with hexavalent actinides (in a solution over the LaF_3 precipitate). Hence it follows that ^{242}Cm differs in chemical properties from curium(III), *i.e.*, ^{242}Cm was obtained in the hexavalent state.

This procedure was used also for the preparation of californium(V).⁸⁶ In carbonate solutions, the ^{249}Cf isotope, which is generated upon β decay of tetravalent berkelium-249, exists as Cf(V) sorbed on the $\text{Na}_4\text{UO}_2(\text{CO}_3)_3$ precipitate.

4. Reduction reactions

a. Reduction with water

Neptunium(VII). The gradual transformation of Np(VII) into Np(VI) in carbonate solutions was studied by spectrophotometry from a change in the intensity of absorption at $\lambda = 460 \text{ nm}$.⁴⁵ For a $0.5 \text{ M KHCO}_3 + \text{K}_2\text{CO}_3$ solution with $\mu = 1$, the change in the Np(VII) concentration is described by the equation

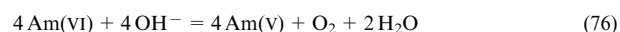
$$-\frac{d[\text{Np(VII)}]}{dt} = k[\text{Np(VII)}]. \quad (75)$$

At 25°C , the constant k decreases from 56.4×10^{-2} to $0.79 \times 10^{-2} \text{ min}^{-1}$ as pH is increased from 9.08 to 11.03. The plot of $\log k$ vs. pH yields a straight line with a slope of -0.98 , *i.e.*, this reaction is first order with respect to the hydrogen ions (or reciprocal first order with respect to the OH^- ions). In the temperature range of 25 – 35°C , the activation energy of reduction of Np(VII) to Np(VI) was estimated⁴⁵ at 33 kJ mol^{-1} (pH 10.0).

Instability of Np(VII) in carbonate solutions results from the high oxidation potential of the Np(VII)/Np(VI) pair ($\geq 1 \text{ V}$; see Section III.2.c). Under these conditions, the potential of oxygen liberation from water is 0.64 V .

It is commonly assumed that the first step of H_2O decomposition under the action of strong oxidisers involves hydrogen abstraction to form the $\text{OH}^\bullet$ radical. However, the oxidation potential of the $\text{OH}^\bullet/\text{OH}^-$ pair at pH 10 is 2.1 V . Due to the large difference in the potentials of the above pairs, reduction of Np(VII) with water cannot proceed through the formation of the $\text{OH}^\bullet$ radical. However, another reaction, *viz.*, oxidation of water to H_2O_2 is also thermodynamically possible. The standard potential of the $\text{H}_2\text{O}_2/\text{H}_2\text{O}$ pair is 1.77 V . In carbonate solutions, this potential is lowered to 1.1 – 1.2 V . For the reaction to follow this pathway, two Np(VII) ions must be simultaneously involved in this reaction. However, this reaction is first order with respect to neptunium. To resolve this contradiction, it was suggested^{87,88} that the thermally excited Np(VII) ion and the nonexcited Np(VII) ion form a dimer through two OH groups. This dimer subsequently decomposes into two Np(VI) ions and the H_2O_2 water molecule. Hydrogen peroxide reduces two more Np(VII) ions.

Americium(VI) and americium(IV). The overall equation for reduction of Am(VI) with water in a $1.3 \text{ M Na}_2\text{CO}_3$ solution (pH 11.25) has the form



(taking into account the high pH of the medium, the hydroxy ions rather than water molecules formally serve as a reducing agent).

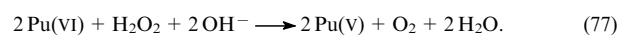
At 25°C , the rate constant for the first-order reaction was estimated at $(0.14 \pm 0.01) \times 10^{-4} \text{ s}^{-1}$. In the temperature range of 25 – 75°C , the activation energy is $63.8 \pm 4 \text{ kJ mol}^{-1}$ (see Refs 32 and 33).

In a $1.3 \text{ M NaHCO}_3 + \text{Na}_2\text{CO}_3$ solution (pH 10), the rate constant (at 30°C) for reduction of Am(IV) with water [see the reaction (6)] is $(0.6 \pm 0.3) \times 10^{-4} \text{ s}^{-1}$. In the temperature range of 30 – 65°C , the activation energy is $96.6 \pm 12.0 \text{ kJ mol}^{-1}$ (see Ref. 33).

Probably, the mechanisms of Am(VI) and Am(IV) reduction with water are analogous to the mechanism of Np(VII) reduction.

b. Reduction with hydrogen peroxide

Plutonium(VI). The reaction of Pu(VI) with H_2O_2 was studied in 0.005 – 0.1 M NaHCO_3 solutions by stopped-flow spectrophotometry.⁸⁹ The results of this study indicate that the following reaction takes place

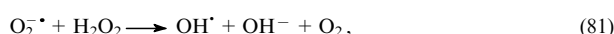
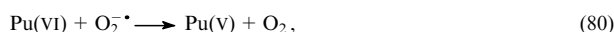


It was established experimentally that Pu(VI) forms a complex with H_2O_2 . Thus, a 0.05 M NaHCO_3 solution containing Pu(VI) ($0.6 \text{ mmol litre}^{-1}$) was injected into a 0.05 M NaHCO_3 solution containing H_2O_2 ($3 \text{ mmol litre}^{-1}$). The rate constant for the formation of the Pu(VI) complex with H_2O_2 (k) was estimated at

$(6.9 \pm 0.8) \times 10^3$ litre mol⁻¹ s⁻¹. Doubling of the initial H₂O₂ concentration led to an increase in the constant k to $(7.2 \pm 0.7) \times 10^3$ litre mol⁻¹ s⁻¹. The rate of disappearance of the complex cannot be described by the first-order equation. Reduction began with the reactions⁸⁹



According to the scheme proposed in the study,⁸⁹ the subsequent step involves the reaction of Pu(VI) with HO₂[•] followed by other reactions. However, rather high pH was not taken into account. Since the reaction (57) is efficient at pH 8.5, it is apparently followed by the processes



and then by the reactions (60) and (43).

When Pu(VI) and H₂O₂ were taken at the initial concentrations of 0.11 and 11.2 mmol litre⁻¹, respectively, the apparent rate constant of the first-order reaction [see Eqn (79)] increased from 1.12 to 24.2 s⁻¹ as the concentration of HCO₃⁻ was decreased from 0.05 to 0.005 mol litre⁻¹. An increase in the concentration of H₂O₂ in a 0.005 M NaHCO₃ solution from 11 to 22 mmol litre⁻¹ led to an increase in the first-order rate constant from 24 to 34 s⁻¹.

c. Reduction with Fe(CN)₆⁴⁻ ions

Neptunium(VI). Reduction of Np(VI) with the Fe(CN)₆⁴⁻ ions was studied in aqueous solutions of Na₂CO₃ ([Na₂CO₃] ≤ 0.05 mmol litre⁻¹) by the stopped-flow method.⁹⁰ For the process in a 0.05 M Na₂CO₃ solution,

$$\frac{\Delta[\text{Np(VI)}]}{\Delta[\text{Fe(CN)}_6^{4-}]} = 1.01 \pm 0.01,$$

which corresponds to the reaction



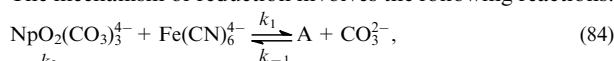
The kinetics of the reaction is described by the empirical equation

$$-\frac{d[\text{Np(VI)}]}{dt} = k'[\text{Np(VI)}][\text{Fe(CN)}_6^{4-}], \quad (83)$$

where $k' = (a + b[\text{CO}_3^{2-}])^{-1}$.

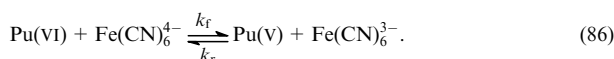
In a 0.004 M Na₂CO₃ solution (μ was maintained at 0.2 by adding NaCl) $k' = 2.8 \times 10^3$ litre mol⁻¹ s⁻¹ (at 25 °C). At a constant concentration of Na₂CO₃ (0.004 mol litre⁻¹), the change in the ionic strength from 0.1 to 1 had no effect on k' but the same increase in μ in a 0.05 M Na₂CO₃ solution led to doubling of k' .

The mechanism of reduction involves the following reactions:



where A is an intermediate formed upon the replacement of one CO₃²⁻ group in NpO₂(CO₃)₃⁴⁻ by the Fe(CN)₆⁴⁻ ion.

Plutonium(VI). The reaction of Pu(VI) with the Fe(CN)₆⁴⁻ ions proceeds⁹¹ analogously to the reaction of Np(VI) with these ions considered above



In a 0.05 M Na₂CO₃ solution (25 °C), $k_f = 1214 \pm 20$ and $k_r = (3.64 \pm 0.20) \times 10^4$ litre mol⁻¹ s⁻¹ for the forward (f) and reverse (r) reactions, respectively. The empirical dependence of the

rate constant for the forward reaction on the concentration of the carbonate ions takes the form

$$\ln k_f = \ln a + n \ln [\text{CO}_3^{2-}]. \quad (87)$$

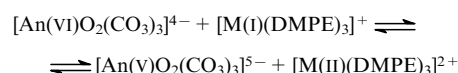
At 25 °C, $\ln a = 4.74 \pm 0.11$ and $n = 0.80 \pm 0.03$ for $\mu = 0.2$ (NaCl), $[\text{Pu(VI)}] = 0.2$ mmol litre⁻¹, $[\text{Fe(CN)}_6^{4-}] = 0.4$ mmol litre⁻¹. The rate constant k_f is virtually independent of the CO₃²⁻ concentration.

The reactions (82) and (86) have much in common. However, it is not improbable⁹¹ that these reactions proceed through different mechanisms. In particular, the characteristics of the reaction (82) are inconsistent with the mechanism of the outer-sphere electron transfer, which seemed to be most probable.

Americium(IV) and americium(VI). The reactions of Am(IV) and Am(VI) with the Fe(CN)₆⁴⁻ ions were not studied in detail. Nevertheless, it is known that these reactions in bicarbonate-carbonate media afford Am(III) and Am(V), respectively. Americium(V) is resistant to the hexacyanoferrate(II) ions. As mentioned above, the ratio between Am(IV) and Am(VI) in the initial mixture can be precisely established with the use of reduction with the Fe(CN)₆⁴⁻ ions followed by the determination of the reaction products by spectrophotometry.

d. Reduction with the [Tc(DMPE)₃]SO₃CF₃ and [Re(DMPE)₃]SO₃CF₃ compounds

The [M(DMPE)₃]SO₃CF₃ compounds [M = Tc, Re, DMPE is 1,2-bis(dimethylphosphino)ethane] serve as outer-sphere reducing agents. These compounds were used in studies of the reactions with Np(VI) and Pu(VI) in carbonate solutions.⁹² The equilibrium constants of the reactions



($T = 25$ °C, $\mu = 0.3$, $[\text{CO}_3^{2-}] = 0.05$ mol litre⁻¹) were calculated. The rate constants and the activation energies of these reactions were determined. The rate constants of the self-exchange reactions for the Np(VI)/Np(V) and Pu(VI)/Pu(V) pairs, which were calculated according to the Marcus equation, are 0.69 and 3.0 litre mol⁻¹ s⁻¹, respectively, when Tc(DMPE)₃⁺ was used as a reducing agent and are 0.64 and 8.9 litre mol⁻¹ s⁻¹, respectively, when Re(DMPE)₃⁺ was used as a reducing agent.

IV. Reactions in alkaline media

1. Disproportionation and reproporation reactions

a. Disproportionation of Np(VI) and Am(VI)

The necessary condition for self-oxidation–self-reduction reactions of hexavalent actinides is the similarity of the formal potentials E_f for the VII/VI and VI/V pairs. In the case of neptunium and americium, the potentials of these pairs in 1 M NaOH solutions differ by ~0.4 V. An increase in the alkali concentration leads to a sharp decrease in the potentials $E_f^{\text{VII/VI}}$, whereas $E_f^{\text{VI/V}}$ are changed only slightly. Hence, penta-, hexa- and heptavalent neptunium or americium can coexist in 10 M and more concentrated NaOH solutions.

Upon rapid 10–20-fold dilution with a 17 M NaOH solution, a colourless 5×10^{-3} M neptunium(VI) solution turned green, which is characteristic of Np(VII).⁹³ The visible regions of the absorption spectra of these solutions, which were measured after the removal of a suspension of air bubbles, were similar to the absorption spectrum of Np(VII). The difference was observed only in the short-wavelength region [due to the presence of Np(VI) in the solution]. The equilibrium



was established at room temperature in less than 1 min. The position of the equilibrium depends substantially on the NaOH concentration. The determined equilibrium constants

$$K = \frac{[\text{Np(VII)}][\text{Np(V)}]}{[\text{Np(VI)}]^2}$$

in solutions with different compositions are given in Table 2.

Disproportionation of Np(VI) was studied also in hot NaOH solutions.⁹⁴ Under these conditions, the solubilities of neptunates are much higher as compared to those in the cold. In addition, the viscosity of alkaline solutions decreases as the temperature is increased due to which the formation of a suspension of air bubbles ceases. The determined equilibrium constants are well reproducible.

Table 2. Equilibrium concentrations of Np(VII) and equilibrium constants K for disproportionation reactions of Np(VI) in alkaline solutions ($T = 21-23^\circ\text{C}$).⁹³

[NaOH] /mol litre ⁻¹	10 ⁴ [Np(VI)] ₀ /mol litre ⁻¹	10 ⁴ [Np(V)] /mol litre ⁻¹	10 ⁵ [Np(VII)] _p /mol litre ⁻¹	10 ² K
8.7	9.52	—	1.2	0.017
10.7	9.52	—	3.5	0.16
11.8	2.38	—	1.4	0.44
12.4	5.00	—	3.8	0.8
13.6	2.38	—	2.8	2.4
14.8	4.55	—	7.8	6.8
15.3	2.38	—	4.3	8.0
17.2	2.38	—	5.1	13.2
13.6	2.38	0.33	1.8	2.2
13.6	2.38	0.84	1.5	3.4
13.6	2.38	2.50	0.45	2.5

Interestingly, the equilibrium constants are virtually independent of the temperature under the conditions studied. Consequently, the activation energies of Np(VI) disproportionation and Np(VII) reduction with pentavalent neptunium must be equal within the experimental error.

When studying disproportionation of actinides in aqueous solutions of KOH and CsOH and in aqueous-methanolic solutions of KOH, Tananaev⁹⁵ found that the nature of alkali is of little importance, whereas a decrease in the water content is favourable for disproportionation. For example, disproportionation in a solution containing 60 vol.% of methanol proceeds to a noticeable extent even at $[\text{KOH}] = 4 \text{ mol litre}^{-1}$.

Disproportionation of Am(VI) was examined in the study.⁹⁶ A 18 M NaOH solution (2.5–3.0 ml) cooled to 0°C and a cooled weakly acidic 0.03 M americium(VI) solution (0.2 ml) were mixed in a quartz cell and the absorption spectrum of the mixture was recorded. This spectrum had a band with a maximum at 740–750 nm, which is characteristic of Am(VII). Since there were no other oxidisers in the solution, the formation of Am(VII) was attributed to self-oxidation–self-reduction of Am(VI)

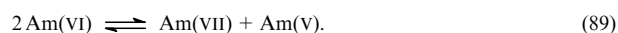


Table 3. Equilibrium constants for disproportionation reaction of Am(VI) in NaOH solutions at $0-3^\circ\text{C}$.

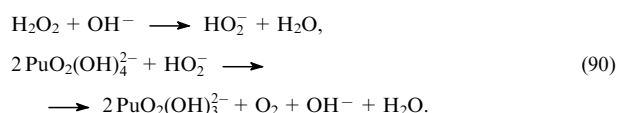
[NaOH] /mol litre ⁻¹	10 ³ [Am(VI)] ₀ /mol litre ⁻¹	Equilibrium concentration /mol litre ⁻¹			K
		Am(VII)	Am(V)	Am(VI)	
8.5	1.74	not found	—	—	—
12.4	1.61	0.20	0.20	1.21	2.7×10^{-2}
14.2	2.04	0.34	0.34	1.36	6.2×10^{-2}
15.4	2.30	0.80	0.80	0.70	1.3
16.6	1.37	0.45	0.45	0.47	0.9
17.2	1.39	0.61	0.61	0.17	13

The estimated equilibrium constants of this reaction are given in Table 3.

Americium(VI) is somewhat more prone to disproportionation than neptunium(VI). In both cases, the NaOH concentration has a similar effect on the equilibrium of the reaction.

b. Disproportionation of Pu(V)

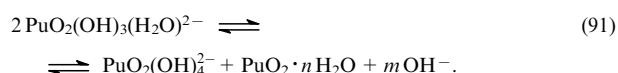
Comparison of the potentials of the Pu(V)/Pu(IV) and Pu(VI)/Pu(V) pairs shows that Pu(V) must undergo disproportionation in a wide range of alkali concentrations. The kinetics of this process was studied by spectrophotometry.⁹⁷ In experiments, Pu(V) was prepared predominantly by reducing Pu(VI) with H_2O_2 in an alkaline medium



Then the accumulation of Pu(VI) in the solution was tracked. When precipitating, plutonium(IV) captured a portion of Pu(V). Taking into account the balance of all valence states of plutonium in the solution and in the precipitate [without considering reduction of Pu(VI) with α -radiolysis products of water], it was concluded that the following reaction proceeds in the solution:



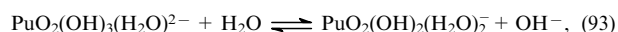
In alkaline media, Pu(V) exists as the $\text{PuO}_2(\text{OH})_3(\text{H}_2\text{O})^{2-}$ and $\text{PuO}_2(\text{OH})_4^{3-}$ ions, freshly precipitated Pu(IV) exists as $\text{Pu}(\text{OH})_4$ (more precisely, as $\text{PuO}_2 \cdot n\text{H}_2\text{O}$) and Pu(VI) occurs as $\text{PuO}_2(\text{OH})_4^{2-}$ (see Ref. 2). Hence, the reaction (5) can be described as follows:



The constant $2k$ was estimated from the initial rate of disproportionation of Pu(V)

$$V_0 = -\frac{d[\text{Pu(V)}]}{dt} = 2k[\text{Pu(V)}]^2. \quad (92)$$

It was found that the rate constant sharply increased as the NaOH concentration was decreased from 7.6 to $0.5 \text{ mol litre}^{-1}$. On the logarithmic coordinates, the plot of $2k$ vs. the activity of the OH^- ions yields a straight line with a slope of -2.8 . However, taking into account that the activity coefficient of Pu(V) decreases on going from a 0.5 M NaOH solution to a 7.6 M solution, it can be assumed that the reaction order with respect to the OH^- ions is close to -2 . Consequently, the fast step preceding the formation of an activated complex, proceeds with the replacement of the OH group in the Pu(V)-containing $\text{PuO}_2(\text{OH})_3(\text{H}_2\text{O})^{2-}$ ion by the H_2O molecule



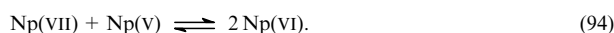
i.e., as expected, lower-charged species are involved in the reaction.

The constant $2k$ increases as the temperature is increased. Thus, an increase in the temperature of a 3.3 M NaOH solution from 10 to 30°C leads to an increase in $2k$ from 0.51×10^{-2} to $6.15 \times 10^{-2} \text{ litre mol}^{-1} \text{ s}^{-1}$. The activation energy is approximately 88 kJ mol^{-1} .

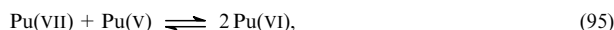
The results of experiments with Np(V) in $0.5-1 \text{ M LiOH}$, NaOH, KOH and CsOH solutions at $25-80^\circ\text{C}$ demonstrated that Np(V) remained unchanged in the conditions under study.

c. Reproportionation Np(VII) + Np(V) and Pu(VII) + Pu(V)

As mentioned above, the potential of the Np(VII)/Np(VI) pair sharply increases at the alkali concentration of $\leq 10 \text{ mol litre}^{-1}$ and the reaction (88) goes in the reverse direction



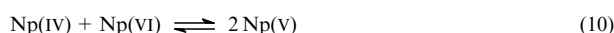
An analogous reaction proceeded also with plutonium



because the potential of the Pu(VII)/Pu(VI) pair is substantially higher than the potential of the Pu(VI)/Pu(V) pair in a wide range of alkali concentrations. The kinetics of the reaction (94) in a LiOH solution was studied by pulse radiolysis.⁹⁸ It was established that the rate constant of the reaction is independent of the alkali concentration in the range of 0.033–2.0 mol litre⁻¹ and its average value in a LiOH solution is $(2.3 \pm 0.9) \times 10^7$ litre mol⁻¹ s⁻¹. In NaOH solutions, the rate constants of the reaction are smaller. Apparently, the reaction (95) also proceeds with a high rate.

d. Reproportionation Np(VI) + Np(IV) and Pu(VI) + Pu(IV)

The reaction



in deaerated 0.025–4.0 M LiOH solutions was examined in the study.¹⁸ The reaction was completed in the course of stirring of a suspension of Np(IV) hydroxide in a LiOH solution with a Np(VI) solution in the same alkali. The formal potential of the Np(V)/Np(IV) pair was estimated from the equilibrium constants.

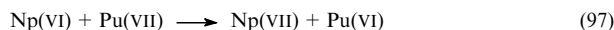
The addition of an equimolar amount of Pu(VI) to a 4 M NaOH solution containing Pu(IV) hydroxide led to the rapid formation of Pu(V),²⁵ i.e., the following reaction proceeded:



2. Reactions analogous to disproportionation and reproportionation

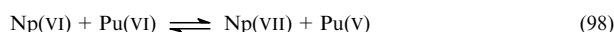
a. Reactions of Np(VI) with Pu(VII) and Pu(VI)

The reaction



proceeds rapidly at room temperature.⁹⁹ This reaction is irreversible at any concentrations of alkali because Pu(VII) is a stronger oxidiser than Np(VII) and the potentials of the Pu(VII)/Pu(VI) and Np(VII)/Np(VI) pairs change in parallel with the OH⁻ concentration.

In alkaline solutions, Np(VI) can be oxidised not only with heptavalent but also with hexavalent plutonium.²⁸ The reaction



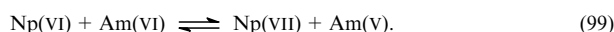
is reversible and proceeds with a high rate, which indicates that the ions of penta-, hexa- and heptavalent actinides in concentrated alkaline solutions have similar structures. According to the recent EXAFS study,¹⁰⁰ neptunium(VII) in alkaline solutions is involved in the $\text{NpO}_4(\text{OH})_2^{3-}$ ion. Hence, neptunium(VII), like Np(V) and Np(VI), is in a tetragonal–bipyramidal environment formed by oxygen atoms due to which the electron transfer is not accompanied by a substantial structural rearrangement of the ions involved in the reaction. The position of the equilibrium depends on the alkali concentration. In a 7.8 M NaOH solution (at 24 °C), the equilibrium constant

$$K = \frac{[\text{Np(VII)}][\text{Pu(V)}]}{[\text{Np(VI)}][\text{Pu(VI)}]}$$

is 1.8×10^{-2} ; its value increases to 14×10^{-2} as the NaOH concentration is increased to 10.1 mol litre⁻¹.

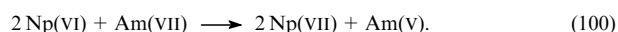
b. Reactions of Np(VI) with Am(VI) and Am(VII)

Neptunium(VII) is rapidly formed upon the addition of a bicarbonate or weakly acidic Am(VI) solution to a 1 M NaOH solution containing Np(VI) (see Ref. 36)



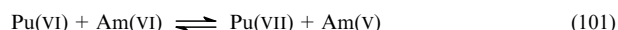
The position of the reaction equilibrium depends on the concentration of the OH⁻ ions. Oxidation of Np(VI) starts at $[\text{OH}^-] \approx 0.016$ mol litre⁻¹. The yield of Np(VII) increases as the alkali concentration is increased and it reaches 100% in 3–4 M NaOH solutions. Americium(V) does not react with Np(VI) in alkaline solutions.

The addition of a cooled freshly prepared (by ozonation) Am(VII) solution in 3–4 M NaOH to an alkaline solution of Np(VI) rapidly affords Np(VII)^{101, 102}

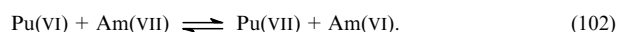


c. Reactions of Pu(VI) with Am(VI) and Am(VII)

The equilibrium of the reaction



is established immediately after mixing the reagents,³⁶ but is noticeably shifted to the right only at an alkali concentration higher than 7.5 mol litre⁻¹. Plutonium(VII) is virtually immediately formed upon the addition of freshly prepared (by ozonation) Am(VII) to a 1 M NaOH solution containing Pu(VI)^{101, 102}



3. Oxidation reactions

a. Oxidation with molecular oxygen

Neptunium(V) and plutonium(V). Oxygen bubbling through 0.5–2 M LiOH or NaOH solutions containing neptunium(V) for 24 h did not yield Np(VI). As the alkali concentration and the reaction time were increased, Np(V) was slowly transformed into Np(VI) under the action of both pure O₂ and atmospheric oxygen.¹⁰³ In an aerated 8 M NaOH solution containing Np(V) (1 mmol litre⁻¹), ~10% of Np(V) was oxidised during 3 months. In the same solution containing F⁻ (0.1 mol litre⁻¹), ~50% of Np(V) was oxidised during one month. A change in the temperature of the solution from 0 to 50 °C exerts only a slight effect on the kinetics of Np(V) oxidation.

Plutonium(V) is also oxidised with atmospheric oxygen in 4 M and 8 M NaOH solutions. In the latter case, the rate constant of the reaction (1.4×10^{-3} h⁻¹) is smaller than the rate constant of Np(V) oxidation (4.7×10^{-3} h⁻¹), whereas plutonium(V) in a 4 M NaOH solution is oxidised faster than Np(V). This is, apparently, associated with a change in the reaction mechanism. Most likely, oxygen reacts with Pu(IV) that is generated through disproportionation of Pu(V).

Neptunium(IV) and plutonium(IV). A freshly precipitated suspension of neptunium(IV) hydroxide [we will denote this compound and plutonium(IV) hydroxide as $\text{NpO}_2 \cdot n\text{H}_2\text{O}$ and $\text{PuO}_2 \cdot n\text{H}_2\text{O}$, respectively] is slowly oxidised with oxygen.¹⁰⁴ At 23 °C, a suspension of $\text{NpO}_2 \cdot n\text{H}_2\text{O}$ (7 mmol litre⁻¹) in 2–14 M NaOH solutions is completely oxidised during ~1–2 days. In addition to neptunium(V), Np(VI) is formed in substantial amounts. As the alkali concentration is increased, the reaction slightly slows down and the proportion of Np(VI) is decreased.

It is believed that oxygen is adsorbed on the surface of Np(IV) hydroxide species followed by successive or synchronous electron transfer. The intermediate that formed in the course of O₂ reduction (hydrogen peroxide) is not accumulated in solution.

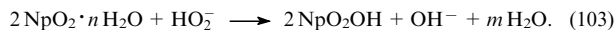
A suspension of $\text{PuO}_2 \cdot n\text{H}_2\text{O}$ in 0.5–4 M NaOH solutions does not react with oxygen. Prolonged air bubbling through a 5 M NaOH solution containing this suspension affords different ionic forms of plutonium whose concentration is 10% higher than that obtained upon argon bubbling.¹⁰⁴

b. Oxidation with hydrogen peroxide

Neptunium(IV). The addition of H₂O₂ (100 mmol litre⁻¹) to a 0.5 M NaOH solution containing a $\text{NpO}_2 \cdot n\text{H}_2\text{O}$ suspension (10 mmol litre⁻¹) at 20 °C gave rise to a dissolved Np(V) peroxide complex. Oxidation of Np(IV) was completed in less than 10 min. Then Np(V) gradually precipitated.¹⁰⁵

In NaOH 1–16 M solutions, the formation of Np(V) starts once the reagents have been mixed but the reaction rate decreases as the NaOH concentration is increased. The Np(V) peroxide complex is stable over a long period and the solid phase does not appear for at least 3 h.¹⁰⁵

The formation of Np(V) slows down as the H₂O₂ concentration is decreased. At [H₂O₂] = 5 mmol litre⁻¹, 9% of Np(IV) remains in the precipitate after completion of the reaction. Taking into account that hydrogen peroxide in an alkaline medium exists as the HO₂⁻ ion, it may be written



Decomposition of H₂O₂ proceeds as a competitive reaction.

The formation of Np(V) (and precipitation) is accelerated as the temperature is increased from 20 to 60 °C.

Plutonium(IV). When a 1 M NaOH solution containing a freshly precipitated PuO₂ · nH₂O suspension (1 mmol litre⁻¹) and H₂O₂ (10 mmol litre⁻¹) was kept at 20 °C for 7 h, the concentration of plutonium in the ionic form remained the same as that in a check experiment performed in the absence of H₂O₂. In more concentrated alkaline solutions, the higher is the NaOH concentration, the higher is the rate of Pu(IV) oxidation. Thus in a 12 M NaOH solution containing PuO₂ · nH₂O (10 mmol litre⁻¹) and H₂O₂ (50 mmol litre⁻¹), the Pu(V) peroxide complex was detected in an amount of 0.4 mmol litre⁻¹ already after 8 min.¹⁰⁵

Slow oxidation of Pu(IV) with hydrogen peroxide in a 1 M NaOH solution takes place upon the addition of a trivalent iron salt (to the concentration of 0.1 mol litre⁻¹). The addition of Co(II) and Cu(II) salts has a weaker effect on oxidation of Pu(IV) with hydrogen peroxide. No effect of Ni(II) was observed.¹⁰⁵

Americium(III). Oxidation of Am(OH)₃ to Am(IV) under the action of hydrogen peroxide was first presented in the paper.¹⁰⁶ These data are confirmed by the results of a more detailed study.¹⁰⁷ An acidic solution of Am(III) containing H₂O₂ was neutralised with ammonia. The precipitate that formed [presumably, Am(III) hydroperoxide] was treated with a concentrated ammonia or KOH solution to obtain Am(IV) hydroxide. The process was accelerated upon heating to 90 °C. At this temperature, Am(IV) hydroxide was obtained in quantitative yield according to several procedures:

- by treatment of Am(OH)₃ with a H₂O₂ and KOH solution;
- by treatment of Am(III) hydroperoxide with a H₂O₂ and KOH solution;
- by treatment of Am(III) hydroperoxide with a KOH solution.

c. Oxidation with ozone

Neptunium(VI) and neptunium(V). Neptunium(VII) was first prepared by oxidation of a suspension of sodium or potassium neptunates with ozone in 0.5–3.5 M alkaline solutions.^{108,109} The kinetics of the reaction of ozone with Np(VI) depends on the state of the latter. In the case of ozonation of neptunate suspensions in NaOH (or KOH) solutions, the rate of Np(VII) formation depends on the mode of ozone supply and the properties of the solid phase. Thus, the rate of Np(VI) oxidation is decreased upon prolonged storage of the precipitates. In the study,¹⁴ it was suggested that a suspension of Np(V) hydroxide in NaOH solutions be used in these reactions. In the course of ozonation, Np(V) is oxidised to soluble Np(VI), which is transformed into the heptavalent state. The maximum concentration of Np(VII) obtained in NaOH (or KOH) solutions is 6–8 g litre⁻¹. The Np(VII) content of 30 g litre⁻¹ was achieved upon ozonation of neptunates in 2–3 M LiOH solutions¹¹⁰ due to high solubility of lithium neptunates.¹¹¹

The kinetics of Np(VII) formation in alkaline solutions containing Np(VI) ions is determined by the rate of ozone supply and intensity of stirring, *i.e.*, by diffusion factors.^{109,112,113} At low concentrations of the reagents, the reaction of Np(VI) with O₃ is kinetically controlled. The accumulation of Np(VII) obeys the equation¹¹²

$$\frac{d[\text{Np(VII)}]}{dt} = k[\text{Np(VI)}][\text{OH}^-]^{0.5}[\text{O}_3]^{0.5}. \quad (104)$$

In the temperature range of 0–20 °C, the activation energy is close to 20 kJ mol⁻¹.¹¹²

An analogous dependence of the rate of Np(VII) accumulation on the ozone concentration was found in the study.¹¹³ In a solution with a constant LiOH concentration, the rate of oxidation (*V*) of Np(VI) (10 mmol litre⁻¹) at a constant rate of ozone supply remains unchanged, *i.e.*,

$$V = \frac{d[\text{Np(VII)}]}{dt} = \text{const.} \quad (105)$$

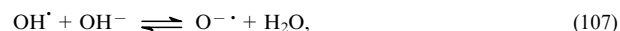
The plot of *V* vs. the LiOH concentration yields a curve with a maximum at [OH⁻] ≈ 1.5–2 mol litre⁻¹. It was proposed that the OH[•] radical¹¹² or the O^{-•} radical ion¹¹³ serve as a direct oxidiser of Np(VI). However, in our opinion, the O₃^{-•} radical ion¹¹⁴ serves as an oxidiser. Thus as the LiOH concentration is lowered beyond 1 mol litre⁻¹, the rate of Np(VI) oxidation decreases due to acceleration of O₃^{-•} decomposition giving rise to O₂^{-•}.

Neptunium(VI) is oxidised with ozone even at pH 9–10 although the reaction rate is noticeably lower.¹¹⁵ Moreover, heptavalent neptunium is partially generated upon ozonation of a NpO₂OH suspension in water.¹¹⁶

The completeness of Np(VI) oxidation with ozone in alkaline solutions depends on its concentration. For example, Np(VI) was oxidised by 80% at its concentration of (2–4) × 10⁻⁵ mol litre⁻¹,¹¹² whereas 98%–100% of Np(VI) was oxidised at the concentration of 3 × 10⁻³ mol litre⁻¹.¹¹³

Neptunium(IV). When a mixture of O₂ and O₃ (0.7 vol.%) is passed through 0.5–1 M NaOH solutions containing a suspension of NpO₂ · nH₂O (1 mmol litre⁻¹), neptunium(IV) is oxidised to Np(V) and Np(VI) already within minutes after the onset of the process and the suspension is dissolved. Further ozonation affords Np(VII). Accumulation of Np(VII) is accelerated as the alkali concentration is increased. In a 14 M NaOH solution, neptunium is quantitatively transformed into the heptavalent state already within 8 min after the onset of oxidation.¹⁰⁴

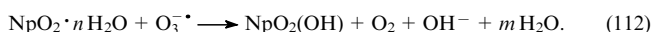
Ozone can directly oxidise tetra-, penta- and hexavalent neptunium. However, in a strongly alkaline medium, ozone initially reacts with the OH⁻ ions to form the ozonide ions. In this case, the reactions may be described by the scheme¹¹⁷



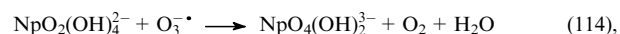
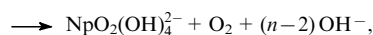
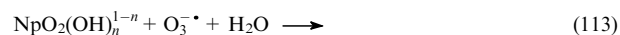
or the scheme¹¹⁸



The ozonide ions oxidise all valence forms of neptunium to the heptavalent state. The process starts with the reaction



Neptunium(V) is oxidised both in the solid phase and after the formation of the soluble NpO₂(OH)_{*n*}¹⁻ⁿ complex (*n* = 2–3). In this case, the following reactions proceed



the rate constants are (2.1 ± 0.3) × 10⁶ and (2.1 ± 0.2) × 10⁵ litre mol⁻¹ s⁻¹, respectively.¹¹⁴

Accumulation of Np(VII) occurs after the disappearance of Np(IV) and Np(V).

Plutonium(VI). Like Np(VII), heptavalent plutonium was first prepared by ozonation.^{108,119} Presently, this procedure is commonly used for the preparation of pure Pu(VII) solutions with different concentrations.

The reaction of Pu(VI) with O₃ in alkaline media proceeds analogously to the reaction of Np(VI).¹¹³ In homogeneous solutions, the reaction rate is determined by the diffusion factors. In the mode of steady ozone supply, the rate of this reaction is described by the zero-order equation

$$V = \frac{d[\text{Pu(VII)}]}{dt} = \text{const.} \quad (115)$$

The completeness of oxidation of Pu(VI) (7.5 mmol litre⁻¹) in alkaline solutions ([NaOH] < 1 mol litre⁻¹) depends on instability of Pu(VII) whose reduction with water is accelerated as the concentration of the OH⁻ ions is decreased.¹²⁰

Plutonium(IV). Oxidation of Pu(IV) with ozone was examined in the study.¹⁰⁴ A suspension of PuO₂·*n*H₂O (0.3–0.5 mmol litre⁻¹) in a 0.5–8 M NaOH solution was oxidised with a mixture of O₂ and O₃ (0.7 vol.%). The resulting Pu(VII) and Pu(VI) rapidly reacted with Pu(IV). Hence, accumulation of Pu(VII) becomes possible after the complete disappearance of Pu(IV). In a 1 M NaOH solution, Pu(VII) is formed most rapidly (84 min), whereas the time of this reaction increases to 300 min (and more) in an 8 M NaOH solution.

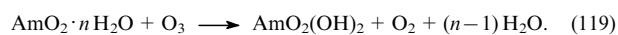
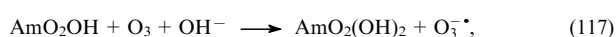
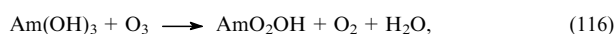
The oxidation process involves the reactions (106)–(108) and reactions analogous to (112)–(114).

Americium(VI). When a gas mixture containing O₃ (20–50 mg litre⁻¹) was passed through a cooled (0 °C) solution of americium(VI) in 3–4 M NaOH during 30–60 min, the colour and absorption spectrum of the solution were changed.^{101,102} After the addition of the resulting freshly ozonated alkaline solution of americium to an excess of Pu(VI) in 1 M NaOH, plutonium immediately took on the colour characteristic of Pu(VII). The absorption spectrum of the resulting solution agrees satisfactorily with the absorption spectrum of pure Pu(VII).

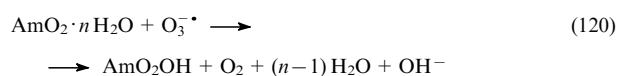
It is known³⁷ that Am(VI) does not oxidise Pu(VI) in solutions containing NaOH at a concentration lower than 3 mol litre⁻¹. Hence, the formation of Pu(VII) in the experiments described above indicates that americium(VI) is transformed into Am(VII) upon ozonation of its alkaline solutions. Heptavalent americium reacts with Pu(VI) according to Eqn (102). The yield of Am(VII) upon ozonation can be estimated from the amount of Pu(VII) formed. In different experiments, its value varied from 40% to 60%. The same results were obtained in the study of the stoichiometry of the reaction (100).

Americium(III). Oxidation of Am(III) was examined in a wide pH range.¹²¹ Ozone oxidises Am(OH)₃ to Am(VI) both in neutral and alkaline (1 M NaOH) media. In a 1 M NaOH solution, oxidation proceeds slowly. Therefore, it is necessary to lower the temperature to 0 °C for the enhancement of solubility of O₃. In a 0.1 M NaOH solution (at 25 °C), Am(OH)₃ is oxidised with a moderate rate to form Am(VI), which gives a soluble yellow complex. The absorption spectrum of this complex is identical to the spectrum of the solution, which was prepared by adding alkali to an acidic solution of AmO₂²⁺. In water, Am(III) is oxidised by passing ozone for 1–2 h (*T* = 90 °C). In the course of ozonation, pH of the solution must be no lower than 5.

Apparently, the mechanism of Am(III) oxidation in solutions with pH lower than 12 is analogous to the mechanism of oxidation in carbonate solutions. This mechanism involves the inner-sphere transfer of the oxygen atom from O₃ as the first step. The general scheme of oxidation is as follows:

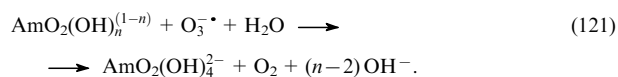


In alkaline solutions (pH > 12), the reactions (106)–(108), (118) and (119) and also the reaction

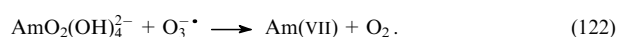


are the major processes.

Americium(V) is oxidised in both the solid phase and in the dissolved form existing as the AmO₂(OH)_{*n*}^{1-*n*} complex (*n* = 2–3)



At 0 °C, Am(VII) is formed in 3–4 M NaOH solutions



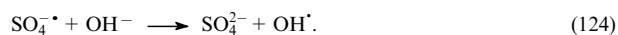
d. Oxidation with S₂O₈²⁻ ions

Neptunium(VI). The kinetics of Np(VI) oxidation was examined in 0.1–0.7 M NaOH solutions at *T* > 50 °C.¹²² The initial reaction rate did not depend on the Np(VI) concentration (up to 0.3 mmol litre⁻¹) and increased in directly proportion to the S₂O₈²⁻ concentration (the latter was increased from 25 to 300 mmol litre⁻¹)

$$\frac{d[\text{Np(VII)}]}{dt} = -\frac{d[\text{Np(VI)}]}{dt} = k[\text{S}_2\text{O}_8^{2-}]. \quad (123)$$

In a 0.2 M NaOH solution heated to 60 °C, the rate constant of the reaction is 2 × 10⁻⁴ min⁻¹. At [OH⁻] = 0.7 mol litre⁻¹ and μ = 1, the activation energy is 140 kJ mol⁻¹, which is consistent with the activation energy of thermal decomposition of the persulfate ions.⁵⁷

The first step of Np(VI) oxidation with the persulfate ions in 0.2–0.7 M NaOH solutions involves decomposition of the S₂O₈²⁻ ions [reaction (32)] followed by the reaction



The fast reactions (124), (107) and (108) afford the O₃^{·-} radical ions, which oxidise Np(VI) to Np(VII) according to the reaction (114).

Calculations demonstrated that the rate of Np(VII) accumulation in a NaOH solution is three times lower than the rate of formation of the SO₄^{·-} radical ions. Consequently, decomposition of O₃^{·-} is of considerable importance in this process, as in the case of Np(VI) oxidation with ozone at [OH⁻] < 1 mol litre⁻¹. The rate of Np(VII) accumulation decreases as the alkali concentration is increased to 0.9 mol litre⁻¹. The plot of Np(VII) accumulation in a 1 M NaOH solution (μ = 2) goes through a maximum. In 3–4 M NaOH solutions, neptunium(VII) is not formed at all.

Apparently, decomposition of S₂O₈²⁻ in alkaline solutions proceeds not only through thermal decomposition [reaction (32)] but also under the action of the OH⁻ ions, reducers being formed in the latter case. This pathway becomes dominant in 3–4 M NaOH solutions. On a further increase in the alkali concentration to 5–6 mol litre⁻¹, the formation of Np(VII) resumes. Under these conditions, the mechanism of decomposition of persulfate ions is, evidently, changed once again. An increase in the ionic strength of solution has virtually no effect on the rate of Np(VI) oxidation in a 0.2 M NaOH solution but the reaction rate is decreased in a 0.7 M NaOH solution.

Hydroxides of some *d* elements serve as catalysts of the Np(VII) formation. In a 4 M NaOH solution, the S₂O₈²⁻ ions oxidise N(VI) even at 20 °C in the presence of Fe(III), Ag(I), Cu(II), Ni(II) or Co(II) salts in concentrations of 5 × 10⁻⁵, 1 × 10⁻⁵, 5 × 10⁻⁶, 1 × 10⁻⁷ or 2 × 10⁻⁸ mol litre⁻¹, respectively. In alkaline solutions containing Ni(II) or Co(II) com-

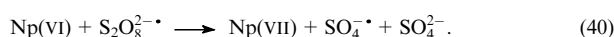
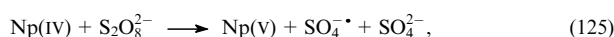
pounds, Np(VII) is completely reduced during 15–20 h. After storage for one day, silver(I) salts retain catalytic activity.

In a 0.5 M NaOH solution, the catalytic activity of the *d*-metal ions is less pronounced.

In the temperature range of 30–50 °C, the activation energies of Np(VI) oxidation in the presence of the Ag(I) and Co(II) ions are 67 and 42 kJ mol⁻¹, respectively.

Neptunium(IV). In deaerated 0.5–14 M NaOH solutions containing a suspension of hydrated Np(IV) oxide (7 mmol litre⁻¹), Np(V), Np(VI) and Np(VII) are successively accumulated under the action of S₂O₈²⁻.¹²³ All steps of oxidation are accelerated as the concentrations of NaOH and S₂O₈²⁻ are increased and the temperature is raised. In a 4 M NaOH solution containing S₂O₈²⁻ (20 mmol litre⁻¹), the transformation of neptunium(IV) into the dissolved Np(VI) form proceeds by 95% at 21 °C during 11–12 min. After the next 5–7 min, Np(VII) is generated. In a 4 M NaOH solution, the activation energy of Np(VI) oxidation with persulfate ions is 68 kJ mol⁻¹. In the presence of insufficient persulfate, Np(V) and Np(VI) were found in the solution (*T* = 36 °C) after completion of the reaction.

The oxidation process involves the following reactions [Np(V) and Np(VI) react both in the solid and liquid phases after the formation of soluble complexes]:

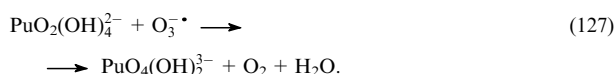


Then, the reactions (124), (107), (108) and (112)–(114) proceed.

Plutonium(VI). It was found¹²⁴ that the reaction of Pu(VI) (0.75 mmol litre⁻¹) with the S₂O₈²⁻ ions in KOH solutions afforded Pu(VII), which was accumulated according to the kinetic equation (reaction is zero order with respect to plutonium and first order with respect to S₂O₈²⁻)

$$\frac{d[\text{Pu(VII)}]}{dt} = -\frac{d[\text{Pu(VI)}]}{dt} = k[\text{S}_2\text{O}_8^{2-}]. \quad (126)$$

In a 1 M KOH solution, the activation energy of Pu(VI) oxidation is 146 kJ mol⁻¹, which is similar to the activation energy of thermal decomposition of the persulfate ions. Oxidation proceeds with the participation of the O₃^{·-} radical ions [see the reactions (32), (124), (107) and (108)]



In hot KOH solutions containing the S₂O₈²⁻ ions, oxidation of Pu(VI) is accompanied by reduction of Pu(VII). As the KOH concentration is increased from 0.2 to 1.2 mol litre⁻¹ ([S₂O₈²⁻] = 0.1 mol litre⁻¹, *T* = 80 °C), the rate of Pu(VII) accumulation initially somewhat increases, peaks at the KOH concentration of 0.5 mol litre⁻¹ and then decreases. The yield of Pu(VII) {the [Pu(VII)]/[Pu(VI)]₀ ratio} is linearly increased as the KOH concentration is increased to ~1 mol litre⁻¹ and then is sharply decreased. At a low alkali concentration, the rate of Pu(VII) reduction with water increases and, hence, its yield is decreased under these conditions. An increase in the KOH concentration leads to the enhancement of stability of Pu(VII) and an increase in its yield. In solutions with [KOH] > 1 mol litre⁻¹, oxidation of Pu(VI) ceases. This is attributed to catalytic decomposition of S₂O₈²⁻ to form reducers. One would expect a change in these dependences at other temperatures and concentrations of persulfate ions.

Plutonium(IV). Hexavalent plutonium is accumulated in 0.5–8 M NaOH solutions containing a suspension of freshly precipitated hydrated Pu(IV) oxide and S₂O₈²⁻ (10–50 mmol litre⁻¹). At [NaOH] ≥ 4 mol litre⁻¹, Pu(VII) is also generated.¹²⁵ The rate of dissolution of hydrated Pu(IV) oxide

increases as the concentrations of NaOH and S₂O₈²⁻ are increased and the temperature is raised from 23 to 62 °C. The following solid-phase reactions are of importance in oxidation and dissolution:



Simultaneously with these reactions, Pu(V) goes into the solution where it is also oxidised to Pu(VI) and undergoes disproportionation. Plutonium(VI) reacts with PuO₂·*n*H₂O. In 4–8 M NaOH solutions, Pu(VI) is oxidised



In addition, O₃^{·-} is formed under these conditions and reactions involving this radical proceed.

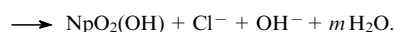
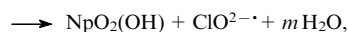
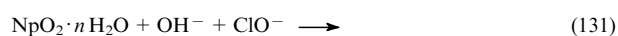
Americium(III). Oxidation of Am(OH)₃ (a pink suspension) with the S₂O₈²⁻ ions in an alkaline medium affords a black or dark-brown precipitate of hydrated Am(IV) oxide.¹⁰⁶ The reaction of Am(OH)₃ (5 mg) with excess K₂S₂O₈ in a 0.1 M NaOH solution on a boiling water bath (2 h) gave rise to an olive-brown precipitate. The examination of products of its dissolution in acid demonstrated¹²¹ that the average oxidation number of americium is 4.53, *i.e.*, the precipitate contains not only Am(IV) but also americium in higher oxidation states.

Pure Am(IV) was prepared by adding Am(III) to a hot 7 M KOH solution saturated with K₂S₂O₈. Then the reaction mixture was kept at 90 °C for 1 h. The precipitate was washed with water to remove an excess of the oxidiser. The average oxidation state of americium in hydrated oxide is 4.0 ± 0.1.¹²¹

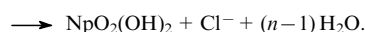
e. Oxidation with ClO⁻ ions

Neptunium(IV). In deaerated 0.5–16 M NaOH solutions containing NpO₂·*n*H₂O, the successive formation of Np(V), Np(VI) and Np(VII) takes place under the action of the ClO⁻ ions.¹²⁶ The time dependence of the Np(VI) concentration in solution passes through a maximum. Initially, a supersaturated solution of Np(VI) is formed from which Np(VI) hydroxide gradually precipitates. Neptunium(VII) is formed in a 2 M NaOH solution (*T* = 25 °C) at [ClO⁻] = 48 mmol litre⁻¹. In more concentrated alkaline solutions, a lower concentration of the hypochlorite ions is sufficient for the formation of Np(VII). The activation energy of the Np(VII) formation is 34 kJ mol⁻¹ (*T* = 25–60 °C). The oxidation reactions of Np(IV), Np(V) and Np(VI) are accelerated as the temperature is raised and the concentrations of alkali and hypochlorite ions are increased.

The oxidation process involves the following steps:



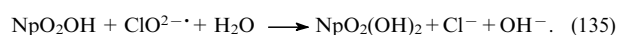
It is not improbable that Np(IV) is oxidised due to the transfer of the oxygen atom taking into account that oxygen is involved in the oxygenated Np(V) and Np(VI) ions



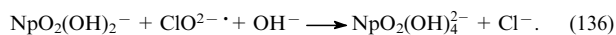
Then the reaction (10) proceeds in the precipitate.

The mechanism of neptunium oxidation can be conclusively established with the use of the ¹⁸O-labelled hypochlorite ions.

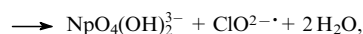
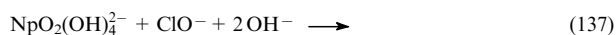
In a precipitate, neptunium(V) reacts with ClO⁻



In solution, the latter reaction proceeds differently

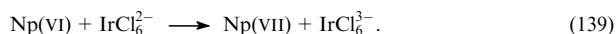


Neptunium(VI) is, in turn, oxidised to Np(VII)



Reproportionation of Np(VII) and Np(V) [reaction (94)] occurs in a dilute alkaline solution, and disproportionation of Np(VI) takes place in 9–16 M NaOH solutions.

Neptunium(VI). In 1–4 M LiOH solutions or 1–8.5 M NaOH solutions, neptunium(VI) is oxidised with K_2IrCl_6 .¹²⁷

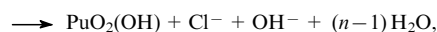
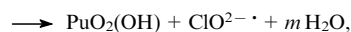
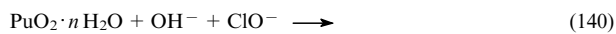


Neptunium(VII) thus prepared slowly disappears because IrCl_6^{3-} is hydrolysed and the resulting Ir(III) hydroxide reduces Np(VII).

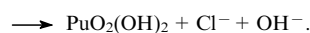
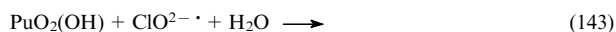
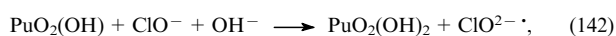
The addition of a NaClO solution to an alkaline solution of neptunium(VI) containing iridium hydroxides leads to the slow formation of Np(VII) because iridium is transformed into higher oxidation states under the action of the ClO^- ions. The ClO^{2-} radical ions that are formed react with Np(VI) [see the reaction (138)].

Plutonium(IV). The hypochlorite ions oxidise a suspension of freshly prepared $\text{PuO}_2 \cdot n\text{H}_2\text{O}$ even at room temperature.¹²⁶ In a precipitate, plutonium is transformed into a hexavalent state. Plutonium(VI) remains partially in solution. Plutonium(VII) appears at the NaOH concentration of about 10 mol litre⁻¹. The rate and completeness of dissolution of Pu(IV) (6.8 mmol litre⁻¹; 60 °C, $[\text{ClO}^-] = 12$ mmol litre⁻¹) are increased as the NaOH concentration is increased. In a 8 M NaOH solution, 92%–94% of plutonium is dissolved. The initial rate of accumulation of plutonium in solution increases as the ClO^- concentration and temperature are increased.

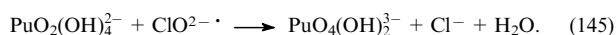
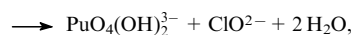
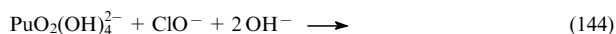
Oxidation of Pu(IV) proceeds analogously to oxidation of Np(IV) and involves the reactions



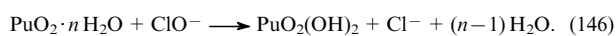
which take place in the solid phase. In 0.4–1.5 M NaOH solutions, plutonium(V) either undergoes disproportionation or is oxidised



Plutonium(V) and Pu(VI) partially go into solution where they are further oxidised



Oxidation of Pu(IV) can also occur through the transfer of the oxygen atom from ClO^-



Americium(III). Precipitation of a pink suspension of Am(III) in an alkaline solution containing ClO^- afforded a dark precipitate.¹²⁸ This process was studied in detail.¹²¹ In a 0.2 M NaOH solution containing ClO^- (0.2 mol litre⁻¹), $\text{Am}(\text{OH})_3$ was transformed into hydrated Am(IV) oxide at 100 °C during 30 min.

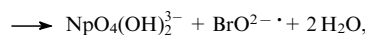
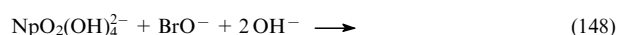
f. Oxidation with BrO^- ions

Neptunium(VI). In alkaline solutions containing Np(VI) (0.2 mmol litre⁻¹), neptunium(VI) is oxidised with the hypobromite ions upon heating to 70 °C.¹²⁹ In 1.74–6.5 M NaOH solutions, the kinetics of the reaction is described by the empirical equation¹³⁰

$$\frac{d[\text{Np(VII)}]}{dt} = -\frac{d[\text{Np(VI)}]}{dt} = k[\text{Np(VI)}][\text{BrO}^-]^{0.6}[\text{OH}^-]^{1.6}, \quad (147)$$

where $k = (6.65 \pm 0.35) \times 10^{-2}$ litre^{2.2} mol^{-2.2} min⁻¹ at 70 °C. In a 6.5 M NaOH solution, the activation energy of the reaction is 87.5 kJ mol⁻¹ ($T = 50.7$ –70 °C).

The rate of Np(VI) oxidation with the BrO^- ions depends on the OH^- concentration in a complicated manner, which reflects both the participation of hydroxyl ions in the formation of an activated complex and the effect of the ionic strength of solution. The fractional order of the reaction with respect to the BrO^- ions results from the fact that the processes



are accompanied by the reactions of Np(VI) with radical products of BrO^- decomposition.

Oxidation of Np(VI) with the hypobromite ions is accelerated upon the addition of *d*-metal salts. In dilute alkali (0.5 mol litre⁻¹), the formation of Np(VII) was observed only in the presence of 2.5×10^{-5} mol litre⁻¹ of Cu(II) or $(1-5) \times 10^{-6}$ mol litre⁻¹ of Ni(II) or Co(II).

Neptunium(IV). In deaerated 0.8–16 M NaOH solutions containing a suspension of $\text{NpO}_2 \cdot n\text{H}_2\text{O}$ (5 mmol litre⁻¹), Np(V), Np(VI) and Np(VII) are formed in the presence of BrO^- .¹³¹ At 25 °C, the rate of Np(VII) accumulation is approximately proportional to the NaOH concentration and the process is accelerated as the BrO^- concentration is increased. In the temperature range of 25–40 °C, the activation energy of this reaction is 32 kJ mol⁻¹. Oxidation is most likely to occur according to the reactions analogous to the reactions (131)–(136) followed by the reactions (10), (148) and (149).

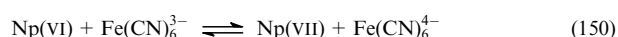
Plutonium(VI). Oxidation of Pu(VI) (0.85 mmol litre⁻¹) with the hypobromite ions was studied in 10.4–12.4 M KOH solutions at 50–90 °C.¹²⁴ The completeness and rate of oxidation are increased as the concentrations of alkali and KBrO are increased (7–100 mmol litre⁻¹). The initial regions of the kinetic plots yield straight lines, which are indicative of oxidation of Pu(VI) with radical products. The activation energy, which we estimated from the results of the study,¹²⁴ is 45–50 kJ mol⁻¹.

The addition of Co(II) and Ni(II) salts to 10^{-5} mol litre⁻¹ leads to substantial acceleration of BrO^- decomposition and Pu(VII) accumulation, which suggests that these processes correlate with each other.

Plutonium(IV). In 0.8–16 M NaOH solutions containing a suspension of $\text{PuO}_2 \cdot n\text{H}_2\text{O}$, Pu(VI) is accumulated both in the precipitate and solution under the action of the hypobromite ions.¹³¹ Plutonium(VII) is formed in 12–16 M NaOH solutions. The rates of all steps increase as the concentrations of alkali and the oxidiser are increased. The activation energy of the Pu(VI) formation in solution is 23 kJ mol⁻¹ and the activation energy of the Pu(VII) formation in a 16 M NaOH solution is ~35 kJ mol⁻¹. Oxidation of plutonium(IV) proceeds analogously to oxidation of neptunium(IV).

g. Oxidation with $\text{Fe}(\text{CN})_6^{3-}$ ions

Neptunium(VI). The reaction



is reversible and its equilibrium depends substantially on the concentration of the hydroxyl ions. In 1–4 M KOH solutions, the equilibrium constant is proportional to $[\text{OH}^-]^4$, whereas this constant in solutions with $\mu = 4$ is proportional to $[\text{OH}^-]^{3.93}$. In a 3.2 M KOH solution, the equilibrium constant (at 23 °C) is 2.0 ± 0.2 . At the concentrations of the reagents of ~ 0.1 mmol litre $^{-1}$, the rate of the reaction (150) is described by the equation¹³²

$$\frac{d[\text{Np(VII)}]}{dt} = -\frac{d[\text{Np(VI)}]}{dt} = k_1[\text{Np(VI)}][\text{Fe(CN)}_6^{3-}].$$

In a 1.5 M KOH solution (at 10 °C), the ionic strength exerts only a slight effect on the rate constant. Thus the constant k_1 changes from 170 to 215 litre mol $^{-1}$ min $^{-1}$ as μ is increased from 1.5 to 3 (KNO₃). The constant k_1 changes almost directly proportional to the concentration of the hydroxyl ions, *viz.*, it increases from 215 to 400 litre mol $^{-1}$ min $^{-1}$ ($\mu = 3$) as the concentration of OH $^-$ is increased from 1.5 to 3 mol litre $^{-1}$. In a 3 M KOH solution, the activation energy of the reaction (150) is 39 kJ mol $^{-1}$ (10–25 °C).

Neptunium(IV). In a 0.5 M NaOH solution containing a $\text{NpO}_2 \cdot n\text{H}_2\text{O}$ suspension (5.1 mmol litre $^{-1}$) and $\text{K}_3\text{Fe(CN)}_6$ (50 mmol litre $^{-1}$), Np(VI) is formed in less than 15 min.¹⁰⁴ In 6–14 M NaOH solutions, neptunium(VI) is further oxidised to Np(VII).

Plutonium(VI). The reaction of Pu(VI) with Fe(CN)_6^{3-} proceeds at a noticeable rate at $[\text{KOH}] > 8$ mol litre $^{-1}$.¹³³ In a 12 M KOH solution containing the ferricyanide ions (2 mmol litre $^{-1}$), Pu(VI) (0.5 mmol litre $^{-1}$) is completely oxidised. The reaction rate is high even in the cold. However, the resulting Pu(VII) solutions appeared to be unstable. Apparently, the cyanide ions that are generated upon hydrolysis of Fe(CN)_6^{3-} and Fe(CN)_6^{4-} serve as a reducing agent.

Plutonium(IV). In a 0.2 M NaOH solution containing a suspension of freshly precipitated $\text{PuO}_2 \cdot n\text{H}_2\text{O}$ (1 mmol litre $^{-1}$), Pu(VI) (0.08 mmol litre $^{-1}$) was accumulated within 10 min after the addition of $\text{K}_3\text{Fe(CN)}_6$ (3.3 mmol litre $^{-1}$). During the same period of time, the concentration of Pu(VI) reached 0.6 and 0.75 mmol litre $^{-1}$ in 1 M and 14 M NaOH solutions, respectively.¹⁰⁴

Americium(III). In alkaline solutions, Am(III) is oxidised with an excess of the ferricyanide ions to Am(V). This reaction affords the soluble $(\text{AmO}_2)_3\text{Fe(CN)}_6$ complex, which gradually decomposes to give a precipitate of $\text{Na}_2\text{AmO}_2(\text{OH})_3 \cdot \text{H}_2\text{O}$. Hydrated Am(IV) oxide is formed at equal concentrations of Am(III) and $\text{K}_3\text{Fe(CN)}_6$.¹³⁴

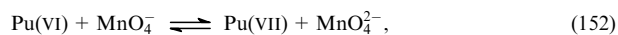
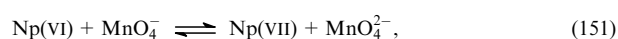
h. Oxidation with CrO_4^{2-} ions

In a 1 M NaOH solution, the potential of the $\text{CrO}_4^{2-}/\text{CrO}_4^{3-}$ pair is estimated at 0.1 V.¹³⁵ Hence, the chromate ions can partially or completely oxidise Np(IV). At room temperature, a suspension of $\text{NpO}_2 \cdot n\text{H}_2\text{O}$ in 0.5–2 M NaOH solutions is slowly oxidised with potassium chromate (the reaction does not proceed to completion during several hours).¹⁰⁴ The resulting Np(V) almost completely remains in the precipitate. The completeness of oxidation is increased as the alkali concentration is increased. In a 14 M NaOH solution, the quantitative transformation of Np(IV) into Np(V) can be achieved already during 1 h. Plutonium(IV) does not react with chromate ions in the range of NaOH concentrations from 0.5 to 14 mol litre $^{-1}$.¹⁰⁴

i. Oxidation with MnO_4^- ions

The standard potential of the $\text{MnO}_4^-/\text{MnO}_4^{2-}$ pair is 0.56 V.¹³⁵ The formal potential increases as the ionic strength of the solution is increased. Hence, the MnO_4^- ion must oxidise Np(IV), Np(V), Np(VI) and Pu(VI), Pu(V), Pu(VI).

Neptunium(VI) and plutonium(VI). The reactions of Np(VI) and Pu(VI) with MnO_4^- are reversible^{99, 136}



their equilibria are rapidly established at 20–25 °C and depend on the alkali concentration. Neptunium(VI) is oxidised in 3–4 M NaOH solutions but the formation of Np(VII) is generally accompanied by the side reaction, *viz.*, gradual reduction of excess MnO_4^- ions with water to MnO_4^{2-} . The potential of the Np(VII)/Np(VI) pair sharply increases as the alkali concentration is decreased, whereas the potential of the $\text{MnO}_4^-/\text{MnO}_4^{2-}$ pair remains virtually unchanged. Because of this, neptunium(VII) rapidly oxidises MnO_4^{2-} to MnO_4^- in solutions with pH 11.

At high concentrations of alkali, the equilibrium of the reaction involving plutonium is shifted to the right. Plutonium(VI) is oxidised with the MnO_4^- ions only in 10–14 M NaOH solutions.¹³⁶ The process is accompanied by the side reaction, *viz.*, reduction of excess MnO_4^- ions with water to MnO_4^{2-} . Dilution of alkali to 2–4 mol litre $^{-1}$ leads to rapid oxidation of the manganate ions with plutonium(VII) to MnO_4^- .

Neptunium(IV). In 0.5–1 M NaOH solutions containing a $\text{NpO}_2 \cdot n\text{H}_2\text{O}$ suspension (5 mmol litre $^{-1}$), neptunium (IV) is oxidised with a fourfold excess of potassium permanganate to Np(VI) during 10 min. Approximately a half amount of Np(VI) remains in the precipitate, whereas the remainder of Np(VI) goes into solution. In 2–14 M NaOH solutions, neptunium passes entirely into solution during the same period of time. At $[\text{NaOH}] > 6$ mol litre $^{-1}$, Np(VII) was also found in the solution.¹⁰⁴

Plutonium(IV). In a 0.5 M NaOH solution containing a freshly precipitated suspension of hydrated Pu(IV) oxide (1 mmol litre $^{-1}$), 10% of dissolved Pu(VI) appears within minutes after the addition of a threefold excess of permanganate ions. The Pu(VI) concentration is not increased with time. An increase in the NaOH concentration is accompanied by an increase in the proportion of dissolved plutonium. In a 14 M NaOH solution, 60% of plutonium is already dissolved.¹⁰⁴

Americium(III). In alkaline solutions, a suspension of Am(OH)_3 is oxidised with the MnO_4^- ions to give hydrated Am(IV) oxide.¹²³

j. Oxidation with FeO_4^{2-} ions

In a 1 M NaOH solution, the potential of the Fe(VI)/Fe(III) pair is 0.8 V.¹³⁵ This value is higher than the potentials of the Np(V)/Np(IV), Np(VI)/Np(V), Np(VII)/Np(VI) and Pu(V)/Pu(IV), Pu(VI)/Pu(V) pairs in alkaline solutions with the same concentrations. The FeO_4^{2-} ion can oxidise Np(IV) and Pu(IV), but the multi-electron transition from Fe(VI) to Fe(III) is accompanied by the structural rearrangement, which is reflected in the rates of the processes.

Neptunium(IV). A suspension (5.1 mmol litre $^{-1}$) of hydrated Np(IV) oxide in a 0.5 M NaOH solution is slowly oxidised to Np(V) and Np(VI) under the action of a 10-fold excess of K_2FeO_4 . An increase in the NaOH concentration is accompanied by acceleration of the process. In a 16 M NaOH solution, neptunium(IV) disappears during several minutes and Np(VII) is formed along with Np(V) and Np(VI).¹⁰⁴

Plutonium(IV). In the presence of potassium ferrate (20 mmol litre $^{-1}$), a freshly precipitated suspension of hydrated Pu(IV) oxide in a 0.5 M NaOH solution is slowly dissolved. At $[\text{PuO}_2 \cdot n\text{H}_2\text{O}] = 1$ mmol litre $^{-1}$, 5.7% of plutonium goes into solution after its storage in the presence of an oxidiser for two days, whereas only 1.5% of plutonium passes into solution in the absence of an oxidiser. In a 14 M NaOH solution, 21% of plutonium goes into solution during the same period of time.¹⁰⁴

k. Oxidation with XeO_6^{4-} ions

Neptunium(VI). In alkaline solutions, neptunium(VI) is oxidised with the XeO_6^{4-} ions only upon heating. In a 1 M KOH solution (at 70 °C), 50% of Np(VI) is oxidised with the XeO_6^{4-} ions already in 15 min ($[\text{Np(VI)}] = 0.2$ mmol litre $^{-1}$, $[\text{XeO}_6^{4-}] = 1$ mmol litre $^{-1}$).¹²⁹ The reaction rate somewhat increases as the alkali

concentration is decreased. The addition of the perxenate ions to weakly acidic or neutral solutions of Np(VI) does not afford heptavalent neptunium.

Plutonium(VI). In 0–12 M NaOH solutions, plutonium(VI) does not react with the perxenate ions.¹¹⁹ This is to some extent associated with a decrease in solubility of Na₄XeO₆ in concentrated NaOH solutions. In hot concentrated KOH solutions, plutonium(VI) is partially oxidised with xenon(VIII), but Pu(VII) is formed in low yield.

l. Oxidation with xenon trioxide

In alkaline solutions, xenon trioxide reacts with Np(VI) more actively than the perxenate ions.¹²⁹ A 1 M KOH solution containing Np(VI) gradually turns green upon the addition of XeO₃ even in the cold. The reaction proceeds during 3 h. Oxidation of a half amount of neptunium(VI) occurs in a matter of minutes and during ~1 min on heating to 50 and 70 °C, respectively. Oxidation of Np(VI) slows down when the alkali concentration is decreased to 0.25 mol litre⁻¹, whereas an increase in this concentration leads to acceleration of oxidation. In 10–11 M NaOH solutions, Np(VI) (0.2 mmol litre⁻¹) is completely oxidised with a tenfold excess of XeO₃ at 20 °C during 35 min.⁷⁴ When Np(VI) and XeO₃ are present in equal concentrations, approximately a half amount of hexavalent neptunium is oxidised during the same period of time.

The reaction of Np(VI) with XeO₃ in alkaline solutions is accompanied by a side process, *viz.*, decomposition of the oxidiser to form perxenate, which can also be involved in oxidation of Np(VI).

m. Oxidation with xenon difluoride

Xenon difluoride oxidises Np(VI) only in solutions containing alkali in a moderate concentration.^{74, 75} When the reactions are carried out with the use of solid XeF₂, Np(VII) is formed in solutions containing NaOH in a concentration from 0.01 to 1.7 mol litre⁻¹. For achieving quantitative oxidation of Np(VI) in 0.2–1.0 M NaOH or KOH solutions, it is necessary to use a 200-fold excess of solid XeF₂.⁷⁵ Aqueous solutions of XeF₂ are more efficient and can oxidise Np(VI) in 5 M KOH solutions. (The reaction proceeds rapidly.⁷⁴)

Xenon difluoride can reduce Np(VII). Thus, the addition of XeF₂ (5–200 mg) to a 1 M NaOH solution (20 ml) containing Np(VII) (0.2 mmol litre⁻¹), which was prepared by ozonation, afforded Np(VI) in 3%–12% yields.

The addition of microconcentrations of Co(II) and Ni(II) salts has no noticeable effect on oxidation of Np(VI) with xenon difluoride in a 0.5 M NaOH solution. In the presence of Cu(II) salts (10⁻⁵ mol litre⁻¹), neptunium(VI) is not oxidised.

When 0.2–1.2 M NaOH solutions of Pu(VI) were treated with a 5–200-fold excess of XeF₂, a colour characteristic of Pu(VII) solutions appeared for only a short period (10 min). Within 3 min after the addition of XeF₂, the yield of Pu(VII) was no higher than 10%.⁷⁵ Oxidation of Pu(VI) was not observed in alkaline solutions at a concentration higher than 2 mol litre⁻¹. Upon the addition of XeF₂ to 0.5–3 M KOH or NaOH solutions containing Pu(VII), which was prepared by ozonation, the mixture rapidly turned colourless and the absorption spectra of the solutions were identical with the absorption spectrum of Pu(VI).

n. Oxidation with silver oxides

Neptunium(VI). Neptunium(VII) was prepared in alkaline solutions with the use of Ag₂O and AgO.⁹³ Oxidation of Np(VI) with silver(I) oxide proceeds at a noticeable rate only in solutions containing alkali in a concentration higher than 8 mol litre⁻¹. At room temperature, the reaction rate was low. It is recommended that the solutions be heated to at least 50 °C. At 60 °C, the process was completed in 15–20 min.

Heating of 9 M and 12 M NaOH solutions containing Np(VI) (0.5 mmol litre⁻¹) and freshly prepared Ag₂O (10 mg ml⁻¹) to 60 °C afforded Np(VII) in 10%–15% and 70%–80% yields,

respectively. The yield of Np(VII) was approximately halved as the amount of Ag₂O was decreased from 10 to 2 mg ml⁻¹. The completeness of Np(VI) oxidation was somewhat improved as the temperature was raised to 90 °C.

Oxide AgO oxidised Np(VI) even in a 0.1 M KOH solution. The reaction rate was high even at room temperature. In solutions heated to 50 °C, the reaction equilibrium was established in 3–5 min. In 2–3 M solutions of alkali, an excess of silver(II) oxide oxidised 92%–93% of the total amount of Np(VI).⁹³

Plutonium(VI). Silver(II) oxide oxidises Pu(VI) only at an alkali concentration higher than 8 mol litre⁻¹.¹³⁶ In an 11 M NaOH solution, the yield of Pu(VII) is close to 100%. In the cold, the reaction rate is low. At 80–90 °C, oxidation of Pu(VI) is completed in less than 15 min.

o. Oxidation with IO₄⁻ ions, copper(III) periodate and sodium bismuthate

Neptunium(VI) is oxidised with the periodate ions only in hot alkaline solutions.¹²⁹ At 85 °C, a half amount of Np(VI) in a 1 M KOH solution containing KIO₄ (0.1 mol litre⁻¹) and Np(VI) (0.2 mmol litre⁻¹) was oxidised during 25 min, whereas the reaction in a 5 M KOH solution was completed in ~10 min.

Plutonium(VI) is not oxidised with the periodate ions both in dilute and concentrated alkaline solutions.¹¹⁹

An excess of copper(III) involved in the complex with the periodate ions rapidly oxidises Np(VI) and Pu(VI) in solutions containing NaOH at concentrations higher than 1 and 11 mol litre⁻¹, respectively.¹³⁷

Heterogeneous oxidation of Np(VI) with sodium bismuthate in dilute alkaline solutions proceeds rather rapidly only at the boiling temperature of the solution.¹²⁹ The absorption spectra of the green solutions, which are obtained after completion of the reaction and separation of the excess oxidiser by centrifugation, are characteristic of Np(VII).

4. Reduction reactions

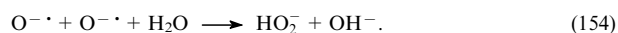
a. Reduction with water

Plutonium(VII). The kinetics of reduction of Pu(VII) (0.16–0.25 mmol litre⁻¹) in 0.044–0.1 M KOH solutions is governed by the equation¹²⁰

$$-\frac{d[\text{Pu(VII)}]}{dt} = k[\text{Pu(VII)}]^{1.2}. \quad (153)$$

The rate constant k decreases as the concentration of the hydroxyl ions is increased. The activation energy of reduction is 60.5 kJ mol⁻¹ ($\mu = 1.0$, $[\text{KOH}] = 0.1 \text{ mol litre}^{-1}$, $T = 25 - 45 \text{ }^{\circ}\text{C}$).

It was suggested¹²⁰ that the OH[•] radical is abstracted from the hydrolysed Pu(VII) anion followed by its transformation into the O^{•-} radical ion [see the reaction(107)] and then into HO₂⁻



The peroxide ion reduces two Pu(VII) ions.

The rate of reduction of Pu(VII) (1.7 mmol litre⁻¹) in 0.3–1.96 M NaOH solutions obeys the equation¹³⁸

$$-\frac{d[\text{Pu(VII)}]}{dt} = k[\text{Pu(VII)}]. \quad (155)$$

The apparent rate constant k is proportional to $[\text{OH}^-]^n$. Here, $n = 1$ and 2 if $[\text{OH}^-] > 1 \text{ mol litre}^{-1}$ and $[\text{OH}^-] = 0.3 - 0.62 \text{ mol litre}^{-1}$, respectively.

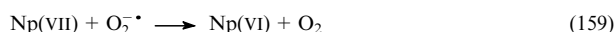
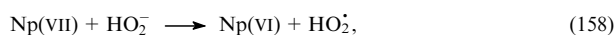
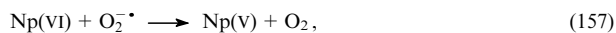
To detect the OH[•] radicals, which can be generated in this reaction, Pu(VII) was added to 0.5 M and 1.0 M NaOH solutions saturated with benzene. In both cases, the final product of the reaction of OH[•] with benzene, *viz.*, phenol, was not detected. Hence, it was concluded¹³⁸ that Pu(VII) involved in the complex PuO₄(OH)₂³⁻ anion eliminates 1/2 O₂ and is transformed into Pu(V), which rapidly reacts with Pu(VII). However, no explanation was given as to how one-half of the oxygen molecule was eliminated.

Based on comparison of the standard potentials of the $\text{OH}^\bullet/\text{OH}^-$ (1.9 V) and Pu(VII)/Pu(VI) pairs in a 1 M NaOH solution, it was concluded that one-electron oxidation of OH^- or H_2O with the Pu(VII) ions is thermodynamically impossible. At the same time, the potential of the $\text{HO}_2^-/\text{OH}^-$ pair in an alkaline medium is 0.867 V.¹³⁵ As in the case of Np(VII) reduction in carbonate solutions, the reaction of Pu(VII) with water proceeds through the formation of a dimer.^{87,88} It was established that in an alkaline medium Pu(VII) exists as the $\text{PuO}_4(\text{OH})_2^{3-}$ anion.¹³³ A decrease in the alkali concentration leads to the appearance of the $\text{PuO}_4(\text{OH})(\text{H}_2\text{O})^{2-}$ species, which are dimerised and then decompose into two Pu(VI) ions and H_2O_2 (or HO_2^-).

In a 0.15 M KOH solution, reduction of Pu(VII) is accelerated in the presence of Fe(III) , Cu(II) , Ni(II) or Co(II) salts.¹²⁰ The effect of trivalent iron becomes noticeable starting with the concentration of 7.7×10^{-7} mol litre⁻¹. The rate of Pu(VII) reduction increases proportionally to an increase in the Fe(III) concentration to at least 3.1×10^{-6} mol litre⁻¹. Analogous results were obtained also for Cu(II) and Ni(II) . The effect of Co(II) in a 0.15 M KOH solution is manifested at its concentration of $\sim 10^{-9}$ mol litre⁻¹. The kinetic curves for Pu(VII) reduction take the shape characteristic of the kinetic curves of autocatalytic reactions. The sensitivity of Pu(VII) to the presence of Co(II) decreases sharply as the OH^- concentration is increased and the curves of Pu(VII) reduction assume the form typical of the kinetic curves of the first-order reactions [as in the case of solutions containing additives of Fe(III) , Cu(II) or Ni(II)]. The catalytic action of d elements is attributed to their capability for being transformed into higher valence forms, which rapidly react with water.

b. Reduction with hydrogen peroxide

Neptunium(VI) and neptunium (VII). The kinetics of the reactions



in alkaline solutions containing Np(VI) or Np(VII) (0.1 mmol litre⁻¹) at pH 9.2–13.7 was studied by pulse radiolysis.¹³⁹ The rate constants for all reactions decrease from 10^4 – 10^5 to 10^2 – 10^3 litre mol⁻¹ s⁻¹ as pH is increased in the above-mentioned range. This is associated with a decrease in the oxidation potentials of the Np(VI)/Np(V) and Np(VII)/Np(VI) pairs.

The kinetics and the mechanism of the reactions of Np(VI) and Np(VII) with H_2O_2 in 1–8.5 M NaOH solutions were examined in the study.¹⁴⁰ It was found that Np(VI) interacts with H_2O_2 to form complexes with 1 : 1 and 1 : 2 compositions. In the latter complex, intramolecular reduction takes place to give the nonequilibrium $\text{Np(V)(O}_2^{\bullet-})$ complex. In the presence of an excess of H_2O_2 , the concentration of this complex tends to an equilibrium value. In the presence of an excess of Np(VI) , the $\text{Np(V)(O}_2^{\bullet-})$ complex reacts directly with Np(VI) . In addition, the complex is decomposed to liberate H_2O_2 , which reduces Np(VI) .

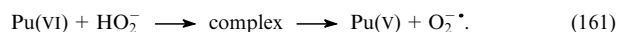
Hydrogen peroxide reduces Np(VII) to Np(VI) (outer-sphere reduction).

Plutonium(VI) and plutonium(VII). In 1–7 M NaOH solutions (at 23 °C), the stoichiometric coefficient for the reaction of Pu(VI) with H_2O_2 varies from 1.6 to 2.0 and approaches 2 as the $[\text{Pu(VI)}]_0/[\text{H}_2\text{O}_2]$ ratio is increased. The stoichiometry changes only slightly as the temperature is lowered to 10 °C.¹⁴¹ It can be assumed that the reaction of Pu(VI) with H_2O_2 proceeds according to Eqn (90). At room temperature, the rate of the process in 2–4 M NaOH solutions obeys the equation

$$-\frac{d[\text{Pu(VI)}]}{dt} = k[\text{Pu(VI)}][\text{H}_2\text{O}_2], \quad (160)$$

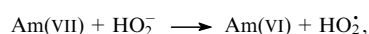
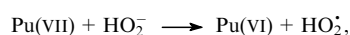
where $k = 5 \times 10^2$ litre mol⁻¹ s⁻¹.

The mechanism of Pu(VI) reduction involves reactions analogous to the reactions (78) and (80), i.e., Pu(VI) forms complexes with hydrogen peroxide. Intramolecular transformations afford Pu(V)



The rate of the reaction of Pu(VI) with H_2O_2 decreases as alkaline solutions of Pu(VI) are aged. For example, the rate constant for the process in a 2 M NaOH solution ($[\text{Pu(VI)}] = 1$ mmol litre⁻¹), which was previously kept for 4 days, decreased to 5 litre mol⁻¹ s⁻¹. Probably, this effect is caused by slow polymerisation of Pu(VI) .

The reactions of Pu(VII) and Am(VII) with H_2O_2 , like those of Np(VII) , proceed through an outer-sphere mechanism. In the study,¹⁴² the rate constants for the reactions

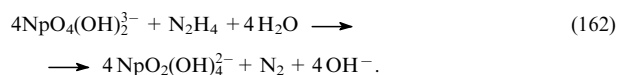


were estimated at $(4-5) \times 10^4$ and $(1-4) \times 10^6$ litre mol⁻¹ s⁻¹, respectively, from the dependence of $\log k$ on the difference between the redox potentials of the An(VII)/An(VI) and $\text{HO}_2^-/\text{OH}^-$ pairs.

Americium(VI). It is impossible to perform complete oxidation of Am(VI) with ozone because of instability of Am(VII) to reduction with water and also due to side reactions involving ozone.¹⁰² It was expected that an increase in the O_3 concentration in the gaseous phase and solution would lead to acceleration of Am(VI) oxidation, whereas reduction of the resulting Am(VII) with water would be of less importance. However, bubbling of a gaseous mixture with a high ozone content through an alkaline solution of Am(VI) resulted in reduction rather than in oxidation of Am(VI) .¹⁴³ This is associated with the fact that a large amount of $\text{O}_3^\bullet$ radicals was formed due to a high concentration of O_3 and these radicals rapidly decomposed. At a concentration lower than 10^{-5} mol litre⁻¹, the rate of their decomposition is described by the first-order rate equation, whereas this decomposition obeys the rate law for a second-order reaction at a concentration higher than 10^{-5} .¹⁴⁴ In the first case, the reaction affords $\text{O}_2^{\bullet-}$, which rapidly reacts with O_3 and, to a small extent, with Am(VI) . In the second case, the reaction yields $\text{HO}_2^\bullet$, which reacts rather slowly with O_3 but efficiently reduces Am(VI) .

c. Reduction with hydrazine N_2H_4

Neptunium(VII). Neptunium(VII) is rapidly reduced with hydrazine. The examination of the reaction stoichiometry demonstrated¹⁴⁵ that 0.25 g-mol of N_2H_4 were consumed per g-mole of Np(VII)



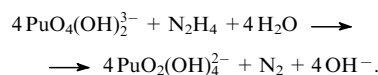
Neptunium(V). In a 2 M NaOH solution, neptunium(V) (0.2 mmol litre⁻¹) does not react with $\text{N}_2\text{H}_4 \cdot 2\text{HCl}$ and other hydrazine derivatives, except for $\text{N}_2\text{H}_4 \cdot \text{HNO}_3$. The latter reduces Np(V) to Np(IV) at a moderate rate.^{146,147} At 20–65 °C, the reaction with $\text{N}_2\text{H}_4 \cdot \text{HNO}_3$ (0.1–0.2 mol litre⁻¹) may take from several hours to several days to give a precipitate consisting of Np(IV) and a portion of captured Np(V) . Precipitation of neptunium slows down as the NaOH concentration is increased. In a 14 M NaOH solution, the precipitate does not form during the time of the experiment.

Apparently, the starting $\text{N}_2\text{H}_4 \cdot \text{HNO}_3$ specimen contains an active compound, which appears after prolonged storage of the reagent at 18–20 °C. For example, HN_3 or $\text{H}_2\text{N}_2\text{O}_2$ can be accumulated in hydrazine. However, these compounds do not reduce Np(V) in an alkaline medium. Hence, the nature of the active compound remains unclear.¹⁴⁷

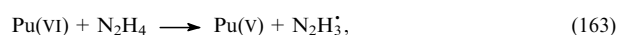
In solutions of LiOH containing hydrazine hydrate, Np(V) is not reduced in the temperature range of 40–80 °C. Under the

same condition, the reaction performed in the presence of PdCl_2 affords a finely dispersed palladium metal on which hydrated Np(IV) oxide precipitates. The processes are accelerated as the PdCl_2 and N_2H_4 concentrations are increased and the temperature is raised, whereas an increase in the alkali concentration from 1 to 5 mol litre⁻¹ slows down these processes.¹⁴⁸

Plutonium(VII). In a 2 M NaOH solution, plutonium(VII) is reduced with hydrazine¹¹⁹



Plutonium(VI). It was found¹⁴⁹ that in 5–8 M NaOH solutions, $\text{N}_2\text{H}_4 \cdot \text{HCl}$ or $\text{N}_2\text{H}_4 \cdot \text{HNO}_3$ taken in a molar ratio of 1 : 3 with respect to Pu(VI) reduce the latter to Pu(V) in the course of stirring, *i.e.*, the following reactions proceed



etc.

Plutonium(V). In 0.5–4 M NaOH solutions, Pu(VI) (0.42 mmol litre⁻¹) is reduced with hydrazine (5 mmol litre⁻¹) to Pu(IV) at 25–55 °C during several minutes.¹⁴⁹ Under these conditions, the reactions (163) and (164) are followed by disproportionation of Pu(V) . Accumulation of Pu(IV) , while slows down, does not cease as the NaOH concentration is increased (higher than 4 mol litre⁻¹). Under these conditions, disproportionation of Pu(V) may be ignored, *i.e.*, the whole of Pu(IV) is formed as the product of Pu(V) reduction

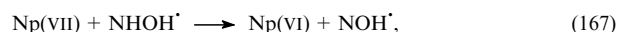
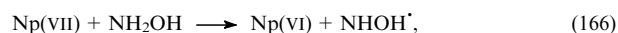


An increase in the N_2H_4 concentration or temperature leads to acceleration of the Pu(IV) formation. Selective spectrophotometric analysis of dissolved precipitates showed that these precipitates always contain Pu(IV) , whereas other valence forms were not detected.

Americium(V). In a 3 M NaOH solution (at 22–23 °C), $\text{N}_2\text{H}_4 \cdot \text{HNO}_3$ (10 mmol litre⁻¹) reduces 50% of pentavalent americium (0.2 mmol litre⁻¹) to Am(III) during ~30 h.¹⁵⁰ The process is accelerated as the concentration of hydrazine is increased or the temperature is raised to 50 °C. An increase in the alkali concentration to 6 mol litre⁻¹ leads to acceleration of the reaction, whereas a further increase in the alkali concentration slows down this process.

d. Reduction with hydroxylamine

Neptunium(VII). In a 1 M NaOH solution ($T \approx 20$ °C), NH_2OH rapidly reduces Np(VII) .¹⁴⁵ The consumption of the reducing agent is 0.75–0.80 mol per mole of Np(VII) . Apparently, after the reactions



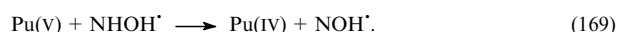
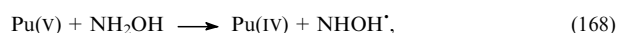
the NHOH^+ and NOH^+ radicals are partially consumed in dimerisation reactions.

Neptunium(V). In 0.5–6 M NaOH solutions, NH_2OH (0.5 mol litre⁻¹) reduces Np(V) (0.4 mmol litre⁻¹) at a temperature higher than 60 °C.¹⁴⁶ Efficient reduction occurs at 80–95 °C. When precipitating, the resulting Np(IV) captures a portion of Np(V) from the solution.

Plutonium(VII). The reaction of NH_2OH (without an excess) with Pu(VII) rapidly affords Pu(VI) . The reaction stoichiometry is expressed as a fraction,¹¹⁹ *i.e.*, the process occurs analogously to the reaction of NH_2OH with Np(VII) .

Plutonium(VI). In 1–14 M NaOH solutions (at 25–60 °C), NH_2OH (5 mmol litre⁻¹) rapidly reduces Pu(VI) (0.5 mmol litre⁻¹) to Pu(V) .¹⁴⁹

Plutonium(V). In NaOH solutions (at an alkali concentration higher than 4 mol litre⁻¹), hydroxylamine reduces Pu(V) (0.5 mmol litre⁻¹) to Pu(IV) at 25 °C (see Ref. 149)



The rate of Pu(IV) precipitation and, consequently, of Pu(V) reduction decreases as the NaOH concentration is increased. However, this dependence is not so sharp as that observed in the case of hydrazine. At room temperature, NH_2OH reduces Pu(V) at a moderate rate even in a 14 M NaOH solution. The rate of this process depends substantially on the NH_2OH concentration and temperature.

Americium(V). In a 3 M NaOH solution (at 22–23 °C), hydroxylamine (0.1 mol litre⁻¹) slowly reduces Am(V) (0.2 mmol litre⁻¹) to Am(III) .¹⁵⁰ The reaction is accelerated as the NH_2OH concentration is increased, whereas an increase in the alkali concentration slows down this process.

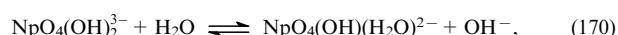
e. Reduction with SO_3^{2-} ions

Neptunium(VII). The kinetics of the reaction of neptunium(VII) with the SO_3^{2-} ions was studied in 0.1–0.5 M NaOH solutions with $\mu = 0.7$ at $T = 20$ –35 °C.¹⁴⁵ Under these conditions, Np(VII) is reduced with an excess of sulfite at a moderate rate. The initial regions of the kinetic curves are satisfactorily described by the first-order reaction equation. However, the rate of reduction increases toward the end of the process. This is associated with the fact that Np(VI) , which is generated in the course of the process, is reduced with sulfite to Np(V) , which reacts with Np(VII) much faster than the sulfite ions. Autocatalytic acceleration of the reaction becomes noticeable when a sufficient amount of Np(VI) is accumulated.

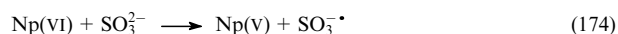
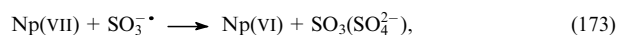
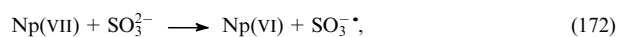
The rate constant for the first-order reaction (k') can be determined from the initial regions of the kinetic curves and then the rate constant k for a bimolecular reaction can be calculated from the $k'/[\text{SO}_3^{2-}]$ ratio. The k value is constant in the range of SO_3^{2-} concentrations from 22 to 135 mmol litre⁻¹, *i.e.*, the reaction order with respect to the sulfite ions is equal to unity. The dependence of k on the OH^- concentration

$$k = \frac{k_1}{[\text{OH}^-]} + \frac{k_2}{[\text{OH}^-]^2}$$

shows that the reaction involves low-charged complex neptunium(VII) anions formed in the processes



In a 0.5 M NaOH solution, the activation energy of Np(VII) reduction is 94 kJ mol⁻¹. The reaction with sulfite proceeds as follows:



and is accompanied by reproporationation [see the reaction (94)].

The process of Np(VII) reduction with sulfite ions is affected by impurities of Cu(II) , Co(II) and Mn(VII) compounds. The catalytic action of copper(II) becomes noticeable at its concentration of 2×10^{-7} mol litre⁻¹.¹⁴⁵ The rate constant for the reaction linearly increases as the CuCl_2 concentration is increased from 5×10^{-7} to $\sim 5 \times 10^{-6}$ mol litre⁻¹

$$k = k^0 + k'[\text{Cu(II)}], \quad (175)$$

where k^0 is the rate constant for the reaction in the absence of a catalyst, $k' = 1.4 \times 10^6$ litre² mol⁻² min⁻¹ at $\mu = 0.7$ and

$T = 25\text{ }^{\circ}\text{C}$. Cobalt(II) and manganese(II) are similar in catalytic activity to copper(II).

In addition to the above-mentioned metal ions, iron(III) also serves as a catalyst of this reaction but the concentration of the latter must be no lower than $10^{-5}\text{ mol litre}^{-1}$. Silver(I) compounds have no effect on the rate of Np(VII) reduction with the SO_3^{2-} ions.

Neptunium(V). At a concentration of 5 mmol litre^{-1} , the sulfite ions have no effect on Np(V).¹⁴⁶ High concentrations of sulfite are required for reduction of Np(V) in $3\text{--}5\text{ M NaOH}$ solutions at $20\text{ }^{\circ}\text{C}$. However, Np(V) ($0.2\text{ mmol litre}^{-1}$) is reduced only by 15% during 24 h even at $[\text{SO}_3^{2-}] = 1\text{ mol litre}^{-1}$.¹⁵¹

Plutonium(VII) and plutonium(V). In $1.2\text{--}2.5\text{ M KOH}$ solutions ($T = 25\text{ }^{\circ}\text{C}$), Pu(VII) is rapidly reduced with the SO_3^{2-} ions.¹⁵² In a 4 M NaOH solution, plutonium(V) does not react with sulfite ions at a concentration of $0.1\text{ mol litre}^{-1}$.¹⁴⁹

Americium(V). The SO_3^{2-} ions slowly reduce Am(V). In a 1.5 M NaOH solution containing Am(V) ($0.23\text{ mmol litre}^{-1}$) and Na_2SO_3 ($0.11\text{ mol litre}^{-1}$), a half amount of Am(V) is reduced at $22\text{--}23\text{ }^{\circ}\text{C}$ during 9 h.¹⁵⁰ The reaction is accelerated as the sulfite concentration is increased.

f. Reduction with $\text{S}_2\text{O}_3^{2-}$ ions

Neptunium(VII) and neptunium(V). The thiosulfate ion acts as a weak reducing agent with respect to Np(VII) and Np(V). In a 2 M NaOH solution containing $\text{Na}_2\text{S}_2\text{O}_3$ ($0.05\text{ mol litre}^{-1}$), a half amount of Np(VII) is reduced at $25\text{ }^{\circ}\text{C}$ in a time longer than 100 min,¹⁴⁵ whereas Np(V) is reduced only by 18% even under the action of $\text{Na}_2\text{S}_2\text{O}_3$ (1 mol litre^{-1}) during 24 h.¹⁵¹ Heating or a decrease in the NaOH concentration to $0.1\text{ mol litre}^{-1}$ leads to a slight acceleration of Np(VII) reduction.¹⁴⁵

Plutonium(VII). The reaction of Pu(VII) with the thiosulfate ions proceeds at a moderate rate. The time of reduction of a half amount of Pu(VII) ($0.5\text{ mmol litre}^{-1}$) in a 2.5 M KOH solution containing $\text{Na}_2\text{S}_2\text{O}_3$ ($2.5\text{ mmol litre}^{-1}$) is 2 min. The reaction rate increases as the concentration of the reducing agent is increased.¹⁵²

g. Reduction with $\text{S}_2\text{O}_4^{2-}$ ions and thiourea dioxide

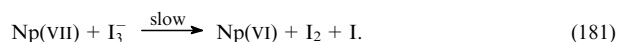
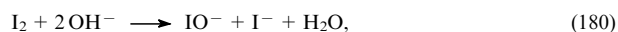
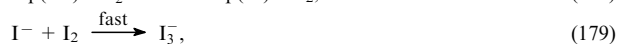
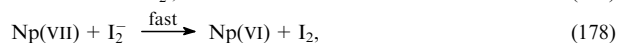
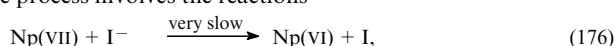
The dithionite ions and thiourea dioxide also reduce Np(V), Pu(V) and Am(V). In a 4 M NaOH solution, dithionite ($0.1\text{ mol litre}^{-1}$) reduces only 30% of neptunium(V) ($0.4\text{ mmol litre}^{-1}$) at $20\text{ }^{\circ}\text{C}$ during one day. In the presence of $(\text{NH}_2)_2\text{CSO}_2$ ($0.1\text{ mol litre}^{-1}$), 20% of Np(V) is reduced at $65\text{ }^{\circ}\text{C}$ for 3 h.¹⁴⁶

In a 4 M NaOH solution containing $\text{S}_2\text{O}_4^{2-}$ (5 mmol litre^{-1}), 90% of plutonium(V) ($0.4\text{ mmol litre}^{-1}$) precipitates at $50\text{ }^{\circ}\text{C}$ for 20 min. In the presence of thiourea dioxide (5 mmol litre^{-1}), the same amount of plutonium precipitates during 2 min.¹⁴⁹ The Pu(IV) and Pu(V) contents in the precipitate are unknown.

In a 1.5 M NaOH solution containing dithionite (5 mmol litre^{-1}), 50% of Am(V) ($0.23\text{ mmol litre}^{-1}$) is reduced at $22\text{--}23\text{ }^{\circ}\text{C}$ for 5 h. In the presence of $(\text{NH}_2)_2\text{CSO}_2$ ($0.1\text{ mol litre}^{-1}$), the same amount of Am(V) is reduced during 0.2 h. Reduction is accelerated as the concentrations of the reagents are increased.¹⁵⁰

h. Reduction with iodide ions

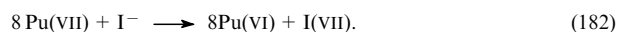
Neptunium(VII). The iodide ions ($90\text{--}160\text{ mmol litre}^{-1}$) reduce Np(VII) at a moderate rate without heating at $[\text{OH}^-] < 0.03\text{ mol litre}^{-1}$.¹⁴⁵ The reaction of Np(VII) directly with I^- proceeds rather slowly. The reaction is accelerated as oxidation products of iodide ions are accumulated in solution. The addition of a mixture of I_2 and KI, i.e., the I_3^- ions, to the reaction mixture exerts an even stronger effect. The presence of Np(VI) has no effect on the reaction. Reduction of Np(VII) is accelerated as the I^- concentration is increased or the alkali concentration is decreased. The process involves the reactions



The possibility of the reaction of Np(VII) with IO^- was not examined.

The addition of microamounts of Co(II), Cu(II) or Mn(II) leads to acceleration of Np(VII) reduction with the I^- ions. The catalytic effect becomes noticeable when these metals are present in concentrations of $(1\text{--}2) \times 10^7\text{ mol litre}^{-1}$.

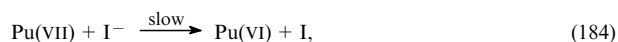
Plutonium(VII). In KOH solutions, plutonium(VII) is reduced with equimolar amounts of KI at a high rate even at room temperature.¹⁵² The reaction proceeds to completion even if the concentration of the reducing agent is 7–8 times lower than the concentration of Pu(VII). Consequently, all intermediate products of oxidation of I^- to IO_4^- (or $\text{H}_3\text{IO}_6^{2-}$) react with Pu(VII) due to the high potential of the Pu(VII)/Pu(VI) pair. The possibility of Pu(VII) reduction with the IO^- and IO_3^- ions was confirmed experimentally. Hence, the reaction of Pu(VII) with insufficient I^- proceeds according to the equation



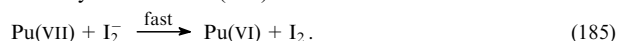
In the presence of an excess of the reducing agent, the character of the reaction depends substantially on the alkali concentration. At $[\text{KOH}] < 2\text{ mol litre}^{-1}$, the rate of Pu(VII) reduction is described by the equation

$$-\frac{d[\text{Pu(VII)}]}{dt} = k[\text{Pu(VII)}][\text{I}^-]. \quad (183)$$

In a 1 M KOH solution (at $25\text{ }^{\circ}\text{C}$), the constant k is $6.5 \times 10^3\text{ litre mol}^{-1}\text{ min}^{-1}$. The constant k decreases by a factor of ~ 50 as the alkali concentration is increased to $3.3\text{ mol litre}^{-1}$. For a 2.5 M KOH solution, the temperature dependence of k in the range of $25\text{--}53\text{ }^{\circ}\text{C}$ corresponds to the apparent activation energy of 25 kJ mol^{-1} . Reduction of Pu(VII) begins with the reaction



followed by the reaction (177)

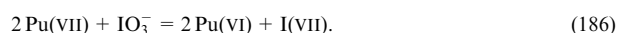


and then the reactions (179) and (180) take place.

The kinetic curves for Pu(VII) reduction with an excess of KI in solutions with $[\text{KOH}] > 2\text{ mol litre}^{-1}$ are distorted, the distortion being stronger at higher alkali concentrations. For 4 M KOH solutions, the curves assume an S shape, which was attributed¹⁵² to the fact that intermediate products of I^- oxidation to I(VII) are involved in Pu(VII) reduction to an increasing extent. In our opinion, under these conditions I_2^- reduces Pu(VI) to Pu(V), which rapidly reacts with Pu(VII).

i. Reduction with iodate ions

Plutonium(VII). In $0.5\text{--}3.5\text{ M KOH}$ solutions (at $15\text{--}35\text{ }^{\circ}\text{C}$), reduction of Pu(VII) with iodate ions proceeds irreversibly according to the stoichiometric equation¹⁵²



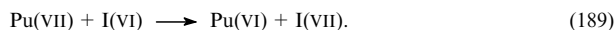
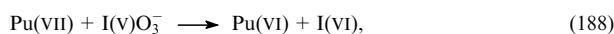
The rate of the process is governed by the equation

$$-\frac{d[\text{Pu(VII)}]}{dt} = k[\text{Pu(VII)}][\text{IO}_3^-]. \quad (187)$$

In a 1 M KOH solution (at $25\text{ }^{\circ}\text{C}$), the rate constant for the reaction (186) is $1.1 \times 10^3\text{ litre mol}^{-1}\text{ min}^{-1}$. As the alkali concentration of increased from 0.17 to $1.7\text{ mol litre}^{-1}$, the constant k decreases in an inverse proportion to $[\text{OH}^-]$ and then remains virtually unchanged up to $[\text{KOH}] = 3.5\text{ mol litre}^{-1}$.

An increase in the temperature leads to a rather small increase in the rate of Pu(VII) reduction. In a 2.5 M KOH solution, the apparent activation energy is 24 kJ mol⁻¹.

The mechanism of Pu(VII) reduction with the iodate ions can be described by the following scheme:



j. Reduction with Fe(CN)₆⁴⁻, tin(II) and vanadium(IV) ions

The Fe(CN)₆⁴⁻ ions rapidly reduce Np(VII) in a 1 M NaOH solution¹⁴⁵ [the equilibrium of the reaction (150) is shifted to the left] and Pu(VII) in a 5 M NaOH solution.¹¹⁹ According to our estimation, the equilibrium constant of the reaction (150) in a 1.5 M KOH solution is 0.1 (*T* = 23 °C). We estimated the rate constant for oxidation [the equilibrium of the reaction (150) is shifted to the right] as 350 litre mol⁻¹ min⁻¹ in going from 10 to 23 °C. The rate constant for reduction was estimated at 3500 litre mol⁻¹ min⁻¹.

Tin(II) reduces Np(VII) in a 1 M NaOH solution¹⁴⁵ and Pu(VII) in 1.5–2.5 M NaOH solutions in the course of stirring.¹⁵²

At 20–80 °C, vanadium(IV) (20 mmol litre⁻¹) reduces Np(V) (0.2 mmol litre⁻¹) in 1–5 M NaOH solutions as a result of which Np(IV) precipitates and captures a portion of Np(V) from the solution.¹⁵³ Reduction slows down as the alkali concentration is increased and is accelerated as the temperature is raised.

k. Reduction with organic compounds

Neptunium(VII). The ascorbate ions rapidly reduce Np(VII).¹⁴⁵ The semiquantitative data on reduction of Np(VII) with other organic compounds are given in Table 4.

At 25 °C, Np(VII) does not virtually react with ethanol, acetate ions and oxalate ions both in 2 M and 0.1 M alkaline solutions. The resistance of Np(VII) to ethanol and oxalate ions is decreased (particularly, at a low concentration of the OH⁻ ions) when the temperature is raised to 65 °C. Formaldehyde rapidly reduces Np(VII) under all conditions being studied, whereas the other compounds react with Np(VII) at a moderate rate.

The kinetics of the reactions of Np(VII) with aliphatic alcohols, formaldehyde and formate ions in alkaline solutions was examined in the studies.^{154–159} For all systems, the reaction rate is governed by the equation

$$-\frac{d[\text{Np(VII)}]}{dt} = k[\text{Np(VII)}] = k_0[\text{Red}]^n[\text{OH}^-]^m[\text{Np(VII)}],$$

Table 4. Time of reduction of a half amount of Np(VII) ($\tau_{1/2}$) with organic compounds.¹⁴⁵

Reducing agent (Red)	[Red] ^a $\tau_{1/2}$ /min		[OH ⁻] = 0.1 mol litre ⁻¹		[OH ⁻] = 2 mol litre ⁻¹	
	25 °C	65 °C	25 °C	65 °C	25 °C	65 °C
Oxalate ion	0.070	> 100	32	> 100	> 100	> 100
Acetate ion	0.200	> 100	> 100	> 100	> 100	> 100
EDTA	0.010	75	1.1	> 100	45	
Citrate ion	0.090	12	0.4	—	22	
Formate ion	0.090	50	2.5	> 100	20	
Ethanol	1.500	> 100	5	> 100	30	
Formaldehyde	0.060	1.5	0.1	—	0.3	

^a In mol litre⁻¹.

where k_0 is the rate constant at [Red] = 1 mol litre⁻¹, [OH⁻] = 1 mol litre⁻¹, *T* = 25 °C. The kinetic parameters are given in Table 5.

Analysis of the data from Table 5 shows that the rate constant for oxidation decreases as the number of atoms in normal alcohols is increased. Oxidation products of alcohols are more reactive than alcohols as such.

Neptunium(V). In 1–5 M NaOH solutions containing up to 1 mol litre⁻¹ of HCOONa, Np(V) is not reduced at 60–90 °C during 5 h. Under the same conditions, the reactions performed in the presence of palladium salts afford palladium metal on which hydrated Np(IV) oxide precipitates. Platinum salts also exert a catalytic effect on Np(V) reduction, although this process is less efficient than that occurring in the presence of palladium salts. Reduction of neptunium(V) with the formate ions proceeds on its contact with an anion-exchange resin covered with palladium or platinum metal.¹⁶¹

Plutonium(VII). The ascorbate ions rapidly reduce Pu(VII).¹⁵² The semiquantitative data on the reactions with some other compounds, which react with Pu(VII) more slowly, are presented in Table 5.

It can be seen that the reaction of Pu(VII) with ethanol is less efficient than that with methanol and the rate constants for Pu(VII) reduction with these alcohols are much higher than the analogous constants for Np(VII).

Table 5. Effect of the nature of the reducing agent (Red) and the reaction conditions on stability of Np(VII) and Pu(VII).

Red	[Red] /mol litre ⁻¹	[KOH] /mol litre ⁻¹	<i>T</i> /°C	10 ² <i>k</i> /min ⁻¹	<i>n</i>	<i>m</i>	<i>E</i> _a /kJ mol ⁻¹	10 ⁴ <i>k</i> ₀	Ref.
Data for Np(VII)									
CH ₃ OH	16.4	1.0	28.2	3.84	0.74	−1.5	50.7 ± 3.4	44.0	154
C ₂ H ₅ OH	3.4	1.0	38.9	0.69	1.5	−1.1	49.7 ± 2.6	4.47	154
n-C ₃ H ₇ OH	0.28	1.0	60.4	0.80	0.9	−0.96	46.3 ± 3.0	34.5	155
n-C ₄ H ₉ OH	0.22	1.0	60.4	0.28	0.6	−1.0	58.4 ± 3.6	5.77	156
n-C ₅ H ₁₁ OH	0.10	1.0	60.4	0.14	0.8	−1.0	81.4 ± 4.5	2.71	156
iso-C ₃ H ₇ OH	0.26	1.0	55.6	0.37	0.8	−1.0	52.0 ± 2.0	16.4	157
iso-C ₄ H ₉ OH	0.22	1.0	55.6	0.23	0.8	−1.0	54.0 ± 2.0	10.9	157
iso-C ₅ H ₁₁ OH	0.11	0.5	60.4	0.40	1.0	−0.95	71.0 ± 3.0	9.0	155
CH ₂ O	0.0075	1.0	29.6	1.23	1.0	−1.0	59.0 ± 4.0	1.14 × 10 ⁴	158
(CH ₃) ₂ CO	0.27	1.0	30.3	0.42	0.9	−1.0	49.0 ± 2.0	96.0	158
HCOONa	0.01	0.2 ^a	65.0	1.45	0.6	−0.33	56.0 ± 2.0	93.0	159
Data for Pu(VII)									
CH ₃ OH	0.55	2.5	25.0	60.3	—	—	—	—	152
	0.034	0.95 ^a	25.2	0.26	1.5	−0.3	50.0 ± 4.0	4 × 10 ³	160
CH ₂ O	0.004	2.5	25.0	55.5	—	—	—	—	152
C ₂ H ₅ OH	0.55	2.5	25.0	39.6	—	—	—	—	152
	0.024	0.94 ^a	25.2	0.23	0.9	−0.8	44.0 ± 4.0	6.3 × 10 ²	160

^a NaOH was used as the medium.

I. Reduction with metals

Reduction of Np(VII), Pu(VI) and Am(VI) in alkaline solutions with aluminium metal was examined in the study.¹⁶² The reactions were carried out at room temperature. A 2–6 cm² aluminium plate was submerged in an alkaline solution of actinide, which was vigorously stirred. Reduction of neptunium(VII) (0.1–2 mmol · litre^{−1}) in a 0.1–2 M NaOH solution was completed in 8–20 min depending on the alkali concentration and the size of the plate. Neptunium (25%–50%) partially precipitated on the aluminium plate as a thin layer, which was firmly attached to the support. The precipitate contained only Np(V). Reduction of Pu(VI) was completed in 5–20 min to give a colloid of Pu(IV) and a precipitate of hydrated Pu(IV) oxide; 5–7 µg cm^{−2} of plutonium precipitated on the aluminium surface. The amount of the precipitate varied with the concentrations of plutonium and alkali.

A precipitate of Am(III) hydroxide rapidly formed upon reduction of Am(VI). The amount of americium precipitated on the aluminium surface was no higher than 6 µg cm^{−2}.

The reactions of Np(V) and Pu(VI) with zinc, chromium, tin and their alloys in 0.5–4 M NaOH solutions were examined under static and dynamic conditions (filtration of solutions through a column filled with metal granules).¹⁶³ Reduction of actinides and precipitation of hydroxides took place on the surface of metallic granules. In the case of plutonium, the best result was achieved on contact of chromium granules with a solution of Pu(VI) in 0.5 M NaOH at 60 °C for 2–5 h. The best sorption of neptunium from a 1 M NaOH solution was attained upon prolonged contact with chromium and zinc granules.

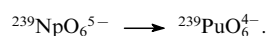
An increase in the alkali concentration and the addition of chromate ions and complex-forming agents slow down sorption of plutonium.

V. Conclusion

Abundant data were accumulated on redox reactions of actinides in carbonate and alkaline solutions. Procedures for oxidation of low-valence forms of neptunium, plutonium and americium and stability of high-valence forms of these elements were studied in detail. In many cases, the transitions between the oxidation states V, VI and VII proceed easily because they do not require substantial structural rearrangements of the ions. By contrast, the transition IV → V giving rise to an 'yl' group proceeds slowly. The proposed mechanisms of redox processes are consistent with the concepts of general chemistry. However, many of these mechanisms call for experimental or quantum-chemical verification.

Among the reactions to be studied, the following reactions, in our opinion, are of most interest: disproportionation of Pu(V) in a wide range of concentrations of bicarbonate and carbonate ions; the reactions of Np(IV), Pu(IV) and Am(IV) with ozone in carbonate solutions; oxidation of Np(V) and Pu(V) with ferricyanide ions in concentrated carbonate solutions; reactions of Np(VI) and Pu(VI) with hydrogen peroxide in bicarbonate-carbonate solutions; and disproportionation of Pu(VI) in concentrated alkaline solutions (if this process does not occur, it is necessary to establish the causes).

Problems of the preparation of macroamounts of curium(VI) (attempts to solve this problem were unsuccessful¹⁶⁴) and Pu(VIII) are of particular interest. It was suggested¹⁶⁵ that Pu(VIII) can be produced upon β decay of ²³⁹Np(VII) in the solid state



In this connection, the fundamental question arises as to the form of existence of Pu(VIII) and its stability. The estimated potential of the Pu(VIII)/Pu(VII) pair is higher than 3 V,¹⁶⁶ which excludes the existence of Pu(VIII) in solution or the gaseous phase. However, it was reported^{167, 168} that plutonium was oxidised with molecular oxygen to PuO₄ under the conditions of gas thermo-chromatography. This compound is comparable in volatility to octavalent osmium oxide (OsO₄). Undoubtedly, there is a need to

carry out further experiments on the determination of the composition of the volatile plutonium compound, including studies with the use of modern methods of analysis, which allow one to determine the structures and compositions of specimens with a weight of several nanograms (in particular with the use of X-ray synchrotron radiation).¹⁶⁹

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^d — *Russ. J. Phys. Chem. (Engl. Transl.)*

^e — *High Energy Chem. (Engl. Transl.)*

Cryogels on the basis of natural and synthetic polymers: preparation, properties and applications

V I Lozinsky

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Abstract. This review deals with cryotropic gelation in polymeric systems, which takes place on moderate freezing, storing in a frozen state and subsequent thawing of solutions or colloidal dispersions containing monomeric or polymeric precursors. The polymer materials formed under these conditions are termed as cryogels. They are macroporous heterophase gels in which poly-crystals of the frozen solvent act as porogens during gel formation. The current knowledge about the structure of moderately frozen solutions of low- and high-molecular-mass compounds is considered, the general regularities of the cryotropic gelation processes and their similarity to and differences from gelation at positive temperatures are discussed, the fields of application of cryotropic gelation techniques are described, and examples of using polymeric cryogel-based materials for solving applied problems are given. The bibliography includes 433 references.

I. Introduction

The applications of processes based on freezing are quite diverse. They include food technology,¹ ground freezing for the construction of underground utilities, the formation of cryobanks for storage of biological objects (blood, semen), ice preparation in sports centres, cryoconcentration of brines in chemical technology and fruit juices during processing of agricultural products, freeze-drying (lyophilisation) of drugs and many other. Branches of science such as low-temperature physics, cryobiology and cryo-medicine, geocryology, glaciology, *etc.*, are developing. Cryo-chemistry is in progress,² including those fields concerned with frost resistance of polymers, low-temperature polymerisation, cryoresistance of latexes, *etc.* This review is devoted to one line of research in polymer cryochemistry, namely, cryotropic gelation processes. Despite the fact that systematic studies along this line were started only in the 1970s, the number of patented processes and materials has already exceeded several hundred. However, no surveying papers have been published so far. All known reviews

are concerned either with particular cases of gelation (for example, radiation-induced polymerisation in frozen solutions giving rise to cross-linked gel materials³) or with only one type of gel [in particular, the macroporous gels resulting from freezing–thawing of concentrated solutions of poly(vinyl alcohol) (PVA)^{4–11}]. The main goal of this review is to summarise and describe systematically the information on the cryotropic gelation in general and on the specific features that distinguish it from the processes traditionally used to prepare chemical (covalently cross-linked) and physical (non-covalent) gels.

The explanation of the main notions and terms such as cryotropic gelation, cryostructuring and cryogel(s), *etc.*, can be found in the literature.^{6,9,10,12–14} In addition, the author proposes that the processes yielding gels of various natures would be termed by words with Greek or Latin roots constructed as follows: ‘... + tropic’ [from τροπος (tropos), which implies directed or induced¹²], *e.g.*, chemotropic — induced by the formation of chemical bonds between polymer chains and resulting in a three-dimensional covalent network of the gel; ionotropic — induced by ion exchange (the formation of ionic bonds); chelatotropic — induced by chelation; thermotropic — induced by heating; psychrotropic — induced by cooling without freezing [from ψυχρία (psychria), which means chill¹²], by analogy with the well-established terms such as psychrometer, a psychrophilic microorganism, *etc.*; cryotropic — induced by freezing; solvotropic (or solvatotropic) — induced by a change in the solvent properties (quality).

The notions of positive and negative temperatures (referred normally to 0 °C) and the notions of moderately frozen systems also require more accurate definition. As applied to the objects discussed in this review, positive temperatures are those above the freezing point of any solvent, while negative temperatures are those below this point. Systems are considered to be moderately frozen if they retain a fraction of non-frozen solvent (usually, this refers to a temperature region lower than the freezing point of the neat solvent by not more than several tens of degrees).

II. What are cryotropic gelation and cryogels?

The structured polymeric physical bodies called gels (or lyogels, in colloid chemistry) can be characterised as immobilised solvent–polymer systems, in which macromolecules are connected in a three-dimensional network by non-fluctuating bonds that are rather stable in time. The nature of these bonds and the network morphology (single-phase and heterophase systems are the 1st-

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and 2nd-kind gels, respectively, according to Papkov's classification¹⁵) are determined by the chemical structure and the method of preparation of the gel. The solvent retained by the cross-linked polymer plays a very important role, as it prevents the system from collapsing into a compact mass and ensures diffusion of soluble substances from the surrounding liquid medium into the gel and back.^{16–18} Gels, except for thixotropic ones, are normally able to undergo substantial reversible deformations in the absence of a flow.¹⁹

Two basic methods for the preparation of gels are known^{15,20} to exist (Fig. 1): first, swelling of either a polymer (as a block, a film, a fibre or a powder) or a xerogel (cross-linked polymer without a solvent) in an appropriate low-molecular-weight liquid; second, gel formation in a liquid medium (solution or colloid dispersion of the corresponding gel-forming agents).

In the former case, a gel is formed due to limited swelling of a non-cross-linked polymer or swelling (exhausting swelling, if the equilibrium is reached) of a xerogel, which, in turn, can be prepared by a solvent-free synthesis or by mere drying of a lyogel.

The latter case represents the most widely used route to gel formation. In this case, the initial system can be a solution of monomers in which branching polymerisation or polycondensation is initiated; or a solution of high-molecular-weight compounds containing appropriate cross-linking agents (ionotropic and chelotropic types of cross-linking are possible); or a solution of a polymer converted into a physical gel due to a change in the thermodynamic quality of the solvent (by which, one means its affinity towards the polymer) or to partial crystallisation of the polymer; or colloidal sol, which undergoes a phase transition to a gel-like state.

Starting from these precursors, one can prepare chemotropic (covalently cross-linked) gels, ionotropic and chelotropic gels (in which the three-dimensional network junction knots are stabilised by slightly dissociating salt or coordination bonds, respectively), and also thermotropic and psychotropic non-covalent (physical) gels. Ageing of colloidal sols usually gives gels of a sophisticated morphology (coagulation and condensation-crystallisation gels, according to Rebinder²¹).

It was shown²² that all types of gelation that take place in a solvent can also be realised in a cryogenic version for the corresponding initial systems using appropriate conditions for freezing, storing in the frozen state, and thawing (see Fig. 1). Thus, cryotropic gelation is a specific type of gelation that takes place upon cryogenic treatment of the initial systems potentially capable of forming a gel. A necessary condition for the processes resulting in the formation of cryogels is crystallisation (freezing) of

the main bulk of the low-molecular-weight liquid present in the initial system.

The polymer gel phase can be formed in one of the stages of cryogenic treatment: either directly during freezing of the initial system [this refers, for example, to colloid dispersions of gelatinised starch²³ or to aqueous solutions of polygalactomannan from the locust bean gum (LBG), which is a block polysaccharide giving rise to thermally reversible physical cryogels],^{24–26} or during storage of samples in the frozen state (this mainly refers to the formation of chemically cross-linked cryogels^{14,27–30}), or during thawing of the frozen specimens (this is typical of non-covalent cryotropic gelation of, for example, aqueous solutions of PVA^{9,31–34}). This will be considered in more detail below in the discussion of the cryotropic gelation kinetics.

First, we shall consider the structure and properties of moderately frozen solutions of low- and high-molecular-weight compounds in order to formulate the current views on the medium in which the cryogel formation proceeds.

III. The structure of frozen solutions of low- and high-molecular-weight compounds. The notion of non-frozen liquid microphase (NFLMP)

The freezing and melting (thawing) of frozen solutions of various substances are fairly complex phenomena dependent on a large number of factors. Although studies in this field have long been carried out, new data providing more precise and more in-depth understanding of the mechanisms of these processes constantly appear in scientific literature. The progress of these studies is promoted to a large extent by the advent of experimental instrumentation and involvement of new methods and theoretical approaches. It is noteworthy that the traditional views according to which frozen solutions are polycrystalline solids at temperatures below the eutectics cannot explain, for example, the occurrence of chemical reactions with diverse mechanisms in these systems. These views do not allow interpretation of the spectroscopic data (ESR, NMR) concerning the maintenance of the high mobility of some of the solute and solvent molecules down to temperatures tens of degrees lower than the freezing point of the initial system.

The cryotropic solidification of neat crystallisable liquids and solutions of low-molecular-weight compounds (LMWC) in such liquids has been studied most extensively, mainly under conditions close to equilibrium.^{35–37} However, freezing of these objects under conditions far from equilibrium brings about specific

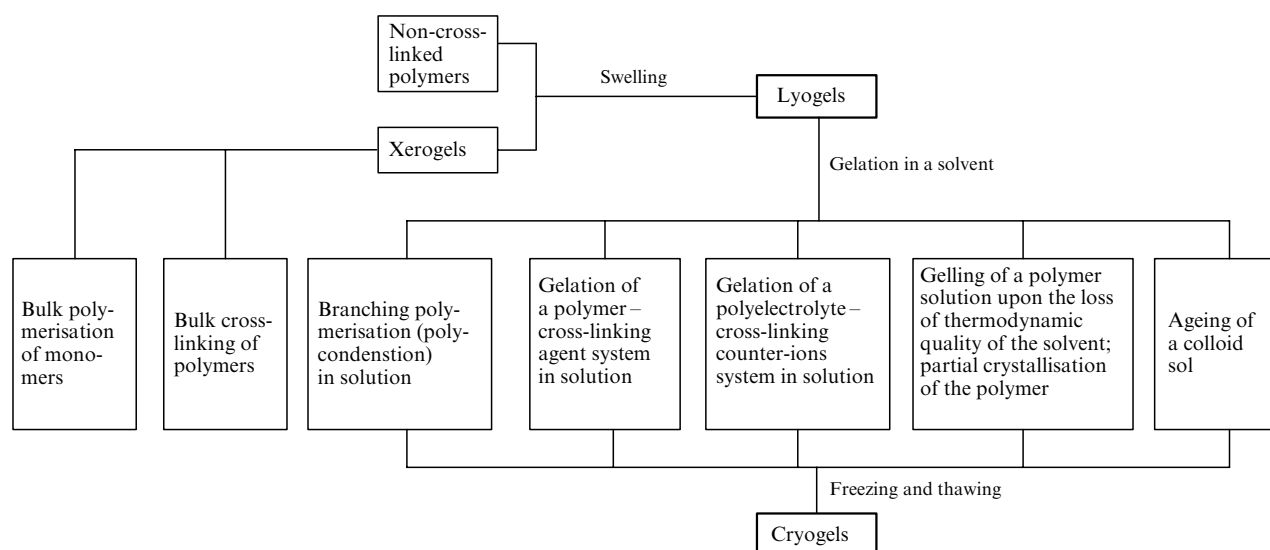


Figure 1. Generalised chart of the techniques for the formation of polymer gels.

effects, depending on the cooling rate, the specimen geometry, the vessel material, the duration of storage in the frozen state, and lots of other factors.^{38–41} The processes taking place during the cryogenic treatment of solvent–polymer, solvent–polymer–monomeric additive, and solvent–swollen gel systems are even more complex. The course of freezing or thawing of such systems is strongly influenced by the polydispersity of the polymers (an exception is represented by narrow homogeneous fractions of molecular-weight standards or purified protein specimens). This gives rise to non-equivalence of the liquid–solid phase diagrams for the same solvent–polymer pair characterised by different molecular weights (MW) or molecular-weight distributions (MWD) of the polymeric component. Due to the polymer polydispersity, Smith and Pennings⁴² proposed that the solvent–polymer systems subjected to freezing should be called pseudo-binary, to distinguish them from the solvent–LMWC binary systems. In addition, due to the slow relaxation processes in high-viscosity media, the attained phase states of the frozen specimens depend appreciably on the thermal pre-history during freezing. The capability for association in solutions at low temperatures, inherent in many polymers, results in the situation that the phase diagram of one system at the same negative temperature would depend in each particular case on the dynamics of cooling of the given specimen and the rate of solvent crystallisation.

In addition, high rates of liquid crystallisation in solutions and, especially, in swollen gels bring about the risk of mechanical destruction of polymer chains (so-called cryocracking) under the action of shear or wedging stresses in the zones of movement of the solvent crystallisation fronts (see, for example, Refs 43–46).

Below we mainly consider the phenomena that are significant for the cryotropic gelation processes. The anomalous depression of the freezing temperature of cross-linked gels^{44,47–52} or the effect of the polymer MW and concentration on the trend of its solution to undergo either crystallisation or glass transition on cooling⁵³ are beyond the scope of this review, as well as some other aspects concerning freezing of polymer solutions and gels but not related directly to cryostructuring processes.

1. The liquid microphase in frozen multicomponent solutions

The pioneering studies demonstrating the possibility of chemical reactions in moderately frozen solutions (*i.e.*, in systems retaining a fraction of non-frozen solvent) were published in the 1960s.^{54–60} Grant *et al.*⁵⁴ discovered a higher (compared to that at room temperature) degree of hydrolysis of the β -lactam ring in penicillin G and 6-aminopenicillanic acid in the presence of alkaline catalysts in frozen aqueous solutions of the reactants. The highest degree of conversion was observed at -18°C . Study of the reaction products showed⁵⁵ that after thawing, the solution of 6-aminopenicillanic acid contained 7–8-unit oligomeric peptides. These were not formed in a similar solution kept at 20°C for the same period. Thus, oligomerisation took place only on cryogenic treatment. Similar results have also been obtained in the synthesis of oligopeptides by polycondensation of *N*-carboxyanhydrides of several amino acids in frozen dioxane ($T_m = 11.4^\circ\text{C}$).⁵⁶ This process was most efficient in the crystallised reaction system at 1°C rather than at positive temperatures.

Butler and Bruce^{57,58} were, apparently, the first to suggest that the systems obtained by moderate freezing of multicomponent solutions of LMWC contain, after macrosolidification, apart from the solid phase, liquid regions between the solvent crystals in which the reactants are accumulated. Subsequently, this idea was further developed in Pincock's and Kiovisky's works (see, for example, reviews^{59,60}). Having studied the kinetics of some usual (*i.e.*, not involving oligomer or polymer formation) reactions of LMWC in frozen solvents (both water and organic solvents), the researchers concluded that these reactions proceed in 'liquid holes, present among the crystalline solid, which contain high concentrations of the reactants'.⁶¹

This early stage of investigation resulted in the following conclusions:⁶⁰

(1) moderate freezing of a solution of reactants in a crystallisable solvent does not terminate the reaction because substances are accumulated in the liquid regions; over a certain range of negative temperatures, this may even accelerate the reaction;

(2) if the total volume of the liquid inclusions remains unchanged during the reaction (the temperature does not change and the products and the reactants are in solution), the observed (apparent) rate (v_{obs}) of substance transformation can be described (with good agreement with experimental results) by the usual kinetic equation

$$v_{\text{obs}} = \frac{1}{V} \frac{dm}{dt}, \quad (1)$$

where V is the volume of the reaction phase, *i.e.*, the total volume of liquid inclusions; m is the number of moles of reactants in the reaction phase; and t is time. With v_{obs} determined by analytical methods, it is possible to estimate the V value;

(3) the dependence of the reaction rate on temperature for moderately frozen solutions does not obey the Arrhenius equation and passes through an extremum;

(4) reactions in moderately frozen media differ fundamentally from solid-phase reactions because the reactant molecules in the regions that remain liquid can execute forward motion, which is hardly possible in a solid (at both macroscopic and microscopic levels).

A significant contribution to the development of the concept of structural and phase inhomogeneity of multicomponent frozen solutions (in particular, at temperatures below eutectic ones) was made by Sergeev and Batyuk (see reviews^{2,62–64}). They confirmed that frozen solutions actually contain regions, the mobility of molecules in which is comparable with that in liquids, and developed kinetic models suitable for quantitative description of reactions proceeding in such systems.

Ultimately, it was established quite definitely that moderately frozen solvent–LMWC systems are not entirely solid not only in the phase diagram region between the liquidus and solidus lines but also well below this region. In non-solidified regions which Sergeev and coworkers called the 'non-frozen liquid microphase' (NFLMP), the molecules possess high mobility; this shows itself as narrow signals in high-resolution NMR spectra. If the reactants are readily soluble, they are accumulated (in the limiting case, completely) in the NFLMP. From the thermodynamic standpoint, the formation of the liquid microphase in multicomponent frozen systems stems from the fact that 'inclusion of dissolved substances in the crystal lattice of a solid solvent requires more energy than that spent for the increase in the chemical potentials upon an increase in the concentrations of components in the liquid microphase'.⁶²

The existence of NFLMP in frozen solutions of monomeric substances at temperatures below the eutectic point of the corresponding system can be detected, in particular, by examining the NMR spectra of dissolved substances^{66,67} or ESR spectra of spin probes.^{68–70} For example, the triplet signal for 2,2,6,6-tetramethyl-4-hydroxypiperidin-1-oxyl in liquid benzene ($T_m = 5.5^\circ\text{C}$) remains such in a frozen sample down to $\sim -50^\circ\text{C}$ and degenerates completely into a singlet only at liquid nitrogen temperatures, due to the fact that the solid microenvironment of the nitroxide probe suppresses its rotation.⁶² It was found⁷¹ that hydrolysis of *p*-nitrophenyl acetate in aqueous salt systems (solutions of Na_2HPO_4 or $\text{Na}_2\text{B}_4\text{O}_7$) with an eutectic composition prepared beforehand occurs at temperatures at least 10° lower than the eutectic point; the liquid-phase nature of this process was proved by special experiments.

After a thermodynamic equilibrium has been reached, frozen systems in which no reactions take place are characterised by the same NFLMP composition independent of the way of freezing of the initial solution.⁶⁵ However, during cooling of the initial system to a specified negative temperature, every instant of time is matched by a particular phase state, which depends on the conditions of cooling. The farther the cooling conditions from

equilibrium, the more pronounced the changes which occur in the frozen system during relaxation to the thermodynamic equilibrium. In solutions of polymers frozen under non-equilibrium conditions, relaxation proceeds much more slowly than that in LMWC systems. It is noteworthy that the liquid–solid diagrams constructed for such non-equilibrium conditions of freezing (this is almost always the case for chemical reactions carried out in moderately frozen solutions) are called non-equilibrium state diagrams rather than phase diagrams,³⁹ and the former can differ appreciably from the equilibrium diagrams. All these specific features of the phase state of systems subjected to freezing are especially important for those cryochemical processes whose rates are commensurable with the dynamics of crystallisation of the initial solution in which the amount (volume) and composition of the liquid microphase vary continuously during freezing until a phase equilibrium is reached.

Thorough experimental research of a number of cryochemical reactions in frozen multicomponent solutions and theoretical analysis of the results made it possible to derive kinetic equation (2), which differs from the above Eqn (1), referring to the simplest case, and allows the calculation of the reaction rates in these systems.^{2, 62–64}

$$v_{\text{obs}} = k^0 e^{-E/RT} \left[\frac{T_0 - T}{\Delta \sum_i C_i} \right]^{\left(\sum_j n_j - 1 \right)} \Pi_j C_j^{n_j}, \quad (2)$$

where k^0 is the pre-exponential factor; E is the activation energy of the reaction determined for the liquid medium; R is the absolute gas constant; T_0 is the crystallisation point for the neat solvent; T is the temperature of the frozen sample; Δ is the cryoscopic coefficient of the solvent; C_i is the concentration of substances (i components) in the initial solution; C_j is the concentration of a j th reactant in the non-frozen region of the system; n_j is the reaction order with respect to the j th reactant.

The structure–kinetic model, which underlies this theory of chemical processes in frozen multicomponent solutions, interprets the non-monotonic pattern of the temperature dependence of the rates of reactions (whose overall order is more than one) in these systems as being due to the competition of the opposite trends, namely, the increase in the reaction rate caused by cryoconcentration and the decrease in the rate following the decrease in the temperature.

For the temperature corresponding to the maximum reaction rate T_{max} , the following relation was derived:^{2, 62–64}

$$T_{\text{max}} = \left\{ \frac{E^2}{4R^2 \left(\sum_j n_j - 1 \right)^2} + \frac{ET_0}{R \left(\sum_j n_j - 1 \right)} \right\}^{0.5} - \frac{E}{2 \left(\sum_j n_j - 1 \right)}. \quad (3)$$

It can be seen from Eqn (3) that T_{max} decreases with an increase in the overall reaction order. In the case where all the reaction components are concentrated in the NFLMP, and conditions for fast attainment of T_{max} have been found, selective acceleration of one of the several reactions proceeding in parallel becomes possible (and this has been confirmed by experiments^{63, 64, 72, 73}).

The deviation of the physicochemical characteristics of the NFLMP (viscosity, density, dielectric constant, heat capacity, *etc.*) from those of non-frozen solutions caused by the change in the microenvironment has an influence on the reactivity of the solutes and their capacity for association. This, in turn, has an impact on the kinetics of cryochemical reactions in frozen multicomponent solutions. The data presented above lead to the conclusion that for a large number of moderately frozen solutions of individual substances and mixtures, NFLMP exists over a fairly broad range of negative temperatures. Both the initial compo-

nents and the reaction products (if any reactions proceed) are accumulated in this microphase (provided that they are sufficiently soluble). These reactions are liquid-phase processes, despite the fact that the frozen specimen as a macroscopic body looks like a solid.

The information concerning such cryochemical processes and their mechanisms available from the literature mainly deals with frozen solutions of LMWC. The behaviour of polymer–solvent systems under these conditions is much more complex; the polydispersity of polymers (see above) is not the only reason for this difference. Another reason is the fact that polymer macromolecules not only execute translational and rotational motions as a single whole. In addition, they (first of all, flexible-chain polymers) possess a large set of intramolecular conformational degrees of freedom, in particular, segmental mobility. This accounts for the high sensitivity of these systems to freezing regimes.

2. Non-frozen solvent in polymer solutions and gels at temperatures below the freezing point of the system.

In the subsequent Sections of this review we shall demonstrate, using a number of particular examples, how moderate freezing, storage in the frozen state and subsequent thawing of a gel-forming polymer system result in the formation of a cryogel. Even the mere formation of the gel indicates that the reactants present in a frozen system (including polymers) do not lose mobility after crystallisation of the main bulk of the low-molecular-weight solvent. At least, they retain sufficient mobility for participation in intermolecular interactions giving rise to cross-links (either covalent or not) to form the three-dimensional cryogel network. It is clear that this type of motion can occur only in the solvent region that has not crystallised (or vitrified), *i.e.*, in the NFLMP.

It is noteworthy that most of the publications dealing with the properties of NFLMP in frozen polymeric systems concentrate on the non-frozen solvent rather than on macromolecular components because the physical methods used in the studies [most often, NMR and DSC (differential scanning calorimetry)] provide information mainly about the solvent. However, in some recent publications, the behaviour of polymers under these conditions has also been studied (see below). Since the interest in this field is related, first of all, to the development of cryobiology, cryomedicine and food technology, aqueous systems were studied most often.^{1, 9, 22, 37, 39, 63, 64, 67, 70, 74–83} although Oikawa and Murakami^{52, 84} considered organic solvent–polymer frozen systems. It was found that, on moderate freezing of polymer solutions or gels, after crystallisation of the main bulk of the solvent, its certain fraction (which is, moreover, much greater than that in solvent–LMWC systems) is not incorporated into the solid phase. Further cooling of samples may result in freezing out of an additional amount of the liquid component but, nevertheless, some remains non-frozen.

Physicochemical studies (NMR, ESR, DSC) of these frozen polymeric objects show the presence of non-frozen solvent at temperatures several tens of degrees lower than the freezing point of the system. For example, this is manifested in the NMR spectra as relatively narrow signals of the corresponding nuclei.^{39, 77, 79, 81, 85–88} The ESR spectra of the spin probes introduced into the polymer solution before freezing are typical of the liquid microenvironment of the probe;^{70, 89–92} calorimetry also shows incomplete crystallisation of the initial liquid.^{39, 74, 76, 93–111} The fraction of the solvent which remains non-frozen can be rather high. For example, for aqueous polymeric systems (solutions of swollen slightly cross-linked networks), the amount of non-crystallised water reaches 0.4–1.0 g per g of the polymer, depending on the temperature, and the layer of non-frozen water firmly fixed by the polymer is ~ 1 nm thick, which corresponds to two or three molecular hydration shells.³⁹ This value is an average because it was obtained by dividing the amount of non-frozen liquid into the polymer weight in the initial system. This did not

take into account the preferred solvation by water of hydrophilic sites of the polymer chains and the tendency of hydrophobic regions to expel water, which is the case for heteropolymers such as proteins or so-called protein-like synthetic hydrophilic-hydrophobic copolymers.^{112–114} Therefore, the real sizes (volumes) of the areas which remain liquid after crystallisation of the main bulk of the solvent in water–polymer systems appear to be greater. This, in turn, creates conditions for the retention of mobility of chains or chain segments in the non-frozen region of the solvent. This is confirmed by high-resolution NMR spectra of frozen solutions of PVA in D₂O, which resembled the usual liquid-phase ¹H and ¹³C NMR spectra of PVA, although the signals were markedly broadened. Thus, under these conditions, the polymer retains, at least, segmental mobility.^{81, 87, 88} Analogous results were obtained for frozen aqueous solutions of polyacrylamide.⁶⁷

The data indicating that some enzymes do not lose activity in moderately frozen solutions^{2, 115–125} also attest to the maintenance of segmental mobility of polymer chains under these conditions, because the transformation of a substrate into a product normally requires a conformational change in the enzyme macromolecule (especially, in the vicinity of the active site).^{126, 127}

The volume of polymer-containing NFLMP in a particular range of negative temperatures can be estimated using a special procedure proposed by Mikhalev *et al.*^{70, 89–92} for processing of the ESR spectra of spin probes (stable nitroxides) introduced into the system subjected to freezing. Hysteresis phenomena were observed,⁷⁰ that is, the NFLMP volumes measured during freezing and thawing were unequal.

For frozen aqueous solutions of polyhydroxy polymers (in particular, polysaccharides), data on the properties of water molecules of the first solvation layer occurring in direct contact with the polymer OH groups have been obtained. These H₂O molecules connected to the polymer through hydrogen bonds do not participate in the crystallisation–melting phase transitions; when a definite negative temperature (so-called T_g' point) is attained, they are vitrified together with the polymer. This fraction of liquid is referred to as non-freezable solvent.^{93–99} Normally, each hydroxy group of the polymer chain retains approximately one water molecule.¹⁰⁸ In the case of polyelectrolytes, the ionic groups retain even larger amounts of non-freezable water due to Coulomb forces.⁹⁹ It should be emphasised that the non-freezable solvent is not identical to the non-frozen solvent (which failed to crystallise under particular conditions). The amount of the latter depends on the temperature and thermal pre-history of a particular specimen. For example, for the frozen D₂O–PVA system, the non-frozen solvent is responsible for a relatively narrow signal in the NMR spectrum down to a temperature 55 °C lower than the freezing point of the system. Only on further cooling, is it possible to record a broad signal from the non-freezable solvation water.⁸¹ In the general case, the non-freezable solvent is a constituent part of the non-frozen solvent.¹⁰²

As noted above, the amount of solvating non-freezable solvent depends on the conformation of macromolecules, for example, on the density of packing of the polypeptide chain in the protein globule. Thus it was found by NMR spectroscopy⁸⁵ that in a solution of serum albumin frozen at –35 °C, the amount of non-freezable water is 0.30 g per g of the protein. If the same macromolecules have been treated with urea, the packing of the polypeptide chains becomes loose and the quantity of non-freezable water increases to 0.44 g per g of the protein.

Thus, the higher the degree of solvation of the polymer in the initial solution, the greater the fraction of non-freezable solvent in the crystallised sample at negative temperatures, because in this case, more groups with high solvent affinity in the polymer become accessible for the solvent molecules.

Indeed, determination [by DTA (differential thermomechanical analysis), DSC and dilatometry] of the dependence of the non-frozen portion on the initial concentration of poly(*N*-vinylpyrrolidone) in aqueous solutions frozen at various temperatures

Table 1. Dependence of the weight of water non-frozen at –45 °C on the concentration of poly(*N*-vinylpyrrolidone) in the initial solution.¹²⁸

Concentration (%)	Weight of non-frozen water (%)	Relative fraction of non-frozen water /g of H ₂ O per g of the polymer
5.0	10.9	2.18
15.0	21.0	1.19
30.9	36.6	0.80
39.2	48.9	0.77
46.4	53.6	0.62

showed that the overall weight of the liquid that has not crystallised increases with an increase in the polymer content but the proportion of this liquid decreases to reach some limiting value, which corresponds to the amount of non-freezable solvent (Table 1).

In the case of freezing of swollen cross-linked polymers, the behaviour of the NFLMP has a number of specific features. For example, in cross-linked polyacrylamide hydrogels (PAAG), the amount of non-frozen water obeys an almost linear dependence on the temperature of the crystallised specimen in the –8 to –60 °C range.^{77, 129} In the subzero temperature range (0 to –8 °C), differences in the mobility of molecules in the liquid part of the solvent depending on whether the temperature of measurements was approached during cooling or heating of the specimen were detected by relaxation NMR spectroscopy.¹²⁹ In the case of system cooling, the spin–lattice relaxation time (T_1) measured at –6 °C was 4 times as long as T_1 found for the system obtained by heating of an identical PAAG specimen from a colder state, *i.e.*, the plot for the temperature dependence of T_1 has a hysteresis loop.¹²⁹ Nearly the same picture is observed at subzero temperatures for frozen gelatin or α_s -casein hydrogels.⁷⁹ One reason for these hysteresis phenomena may be the fact that during heating, the diffusion of water molecules from the crystalline to liquid phase is hampered due to the presence of the polymer network.⁷⁷ This demonstrates once again the important role of conditions (cooling or heating) used to prepare frozen specimens for phase equilibration.

These effects are inherent in not only aqueous systems. A certain mobility of polymer chains in moderately frozen lyogels can also be detected in cross-linked polymers swollen in organic solvents. For example, measurement of the spin–spin relaxation times (T_2) of protons in a cross-linked rubber swollen in deuterio-benzene ($T_m = 6.8$ °C) shows that down to ~ -33 °C, chain segments still execute thermal motion in the medium of the crystallised solvent.¹³⁰ It has been shown⁵² using NMR spectra of benzene-d₆ (solid-echo technique) that the mobility of the solvent molecules is still retained at temperatures lower by 15–18 °C.

It should be emphasised that various NMR techniques are most useful for investigations of frozen solvent–polymer systems.

To conclude this Section, we would like to summarise the important features of cryotropic gelation.

1. Crystallisation of a monomeric liquid during freezing of polymer solutions is accompanied by a minor temperature depression, which differs only slightly from the crystallisation point of the pure solvent.

2. In moderately frozen multicomponent solutions, some of the low-molecular-weight liquid remains non-crystallised at temperatures below the eutectic point. The non-frozen solvent molecules retain rather high mobility; these microregions (NFLMP) of the macroscopically frozen solutions accumulate the solutes, which also possess certain molecular (in the case of LMWC) or segmental (in the case of polymers) mobility.

3. The volume of the NFLMP depends on the system temperature, concentration of soluble (or swollen) components and, if

the phase equilibrium has not yet been established, on the instant of the measurement.

4. Due to cryoconcentration effects and some other factors (for example, the increase in the dielectric constant of the medium on cooling), acceleration of chemical reactions can be observed in a definite range of negative (for the used solvent) temperatures.

IV. Effects inherent in cryogel formation processes

As noted in the previous Section, moderate freezing of solvent–LMWC and solvent–polymer systems gives rise to phase inhomogeneous systems which include a non-frozen liquid microphase. If the initial specimen contains gel-forming agents, the polymer framework of the corresponding cryogel is formed exactly in these non-frozen microregions of the frozen material. This is sketched in Fig. 2.⁶

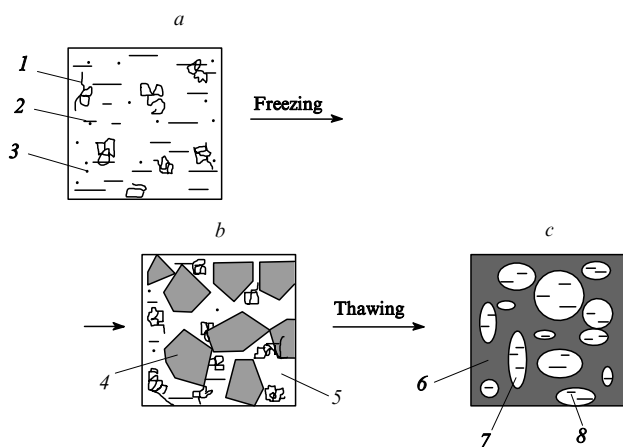


Figure 2. Basic diagram of cryotropic gelation.^{6,22}

(a) initial sample, (b) sample after freezing, (c) cryogel; (1) polymer precursors, (2) solvent, (3) low-molecular-weight compounds or monomer precursors, (4) polycrystals of the frozen solvent, (5) NFLMP, (6) polymer network of the gel phase of the heterophase cryogel, (7) macropores, (8) solvent.

The volume of NFLMP depends on numerous factors, in particular, on the nature of the solvent and the initial concentration and MW of the solutes (for polymers, also on the chain conformation), the system temperature, the regime of specimen freezing, the presence of soluble or insoluble admixtures, etc. In Fig. 2, all components are shown for clarity on an arbitrary (large) scale. It has been found^{67,70,80–83} for several gel-forming systems that the NFLMP volume (Fig. 2b) varies from fractions of a percent to several percent of the solvent volume in the initial specimen (Fig. 2a). Thawing of the specimen gives rise to a macroporous cryogel (Fig. 2c) containing large pores with variable size and geometry. The polycrystals of the frozen solvent (in some cases, crystal solvates or cryoprecipitate particles if these arise during cooling of the initial specimens) act as pore-forming agents (porogens) in this case. On melting or dissolution of these porogens after thawing, cavities filled with the melted solvent remain in the cryogel bulk. Due to the surface tension forces of the gel phase, the surface of the macropore walls is bent; the faceted shape of the walls, typical of the crystalline porogen particles, is replaced by a round shape. In addition, the wall material possesses its own (gel) porosity. Since this gel is formed at high concentrations of precursors, the resulting polymer phase is a dense network with a microporous structure.

A typical feature of various polymeric cryogels is heterophase and heteroporous (often, supermacroporous, spongy or cellular) morphology. The macropores in the cryogel thus formed are usually interconnected because during freezing, each crystal of the solvent grows, as a rule, from the vessel periphery towards the

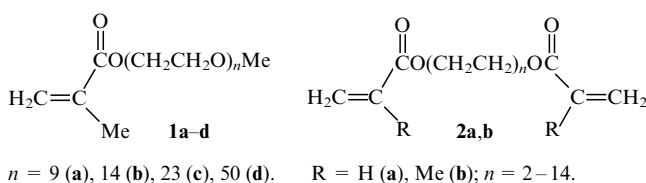
centre (if no directional freezing is involved) until it comes into contact with the face of another crystal.

An increase in the precursor concentrations in the NFLMP (with respect to that in the initial system), i.e., cryoconcentration is one of the main reasons for some specific effects typical of cryogel formation. A number of examples classified according to the types of gel-forming systems (see Fig. 1) are presented below.

1. Cryogels formed by polymerisation or polycondensation

The preparation of gel structures by polymerisation or polycondensation of monomer precursors is one of the most extensively used pathways to solvated polymer networks.^{15–18,131–134} Apparently, the first description of gels synthesised by polymerisation of unsaturated monomers in frozen media, i.e., polymerisation cryogels, was described in publications^{3,135–138} devoted to the γ -radiation-induced gelation of frozen aqueous solutions of 2-hydroxyethyl methacrylate (2-HOEMA). It was found that at -24°C and at an initial monomer concentration of 10%–40%, turbid cellular (spongy) cryogels containing interconnected micrometer-size macropores are produced. When the monomer concentration is increased to 50%–80%, a foam-plastic-like material with isolated macropores is formed, because the frozen system represents a vitrified matrix of the monomer with small ice crystals dispersed in it. When the initial content of water is low ($<10\%$), the process yields a transparent polymeric monolith because cooling of these specimens results in vitrification instead of ice crystallisation,¹³⁷ while polymerisation, evidently, occurs as a solid-phase process.¹³⁹ For the irradiation doses used (~ 1 Mrad) post-polymerisation does not occur in any of the systems, i.e., the polymer is formed only during irradiation. The fact that a monomer with one double bond is converted into a cross-linked gel points to a branching mechanism of polymerisation, i.e., chain transfer to a side functional group of the monomer takes place.

In addition to materials based on 2-HOEMA,^{3,4,138,140–165} a similar procedure is used to prepare macroporous cryogels based on oligo(ethylene glycol) methyl ether methacrylates **1a–d**¹⁶⁶ and oligo(ethylene glycol) diacrylates **2a** and dimethacrylates **2b**.^{167–169}



When the initial concentrations of the structurally related nine-unit mono-¹⁶⁶ and diacrylates¹⁶⁸ are identical, a lower swelling capacity is observed for cryogels based on the oligomer containing two double bonds, pointing to a higher degree of polymer cross-linking. The partial replacement of moderately hydrophilic 2-HOEMA in the initial composition by highly hydrophilic *N*-vinylpyrrolidone sharply increases the degree of swelling of the resulting cryogels in water and, as noted in a publication,¹⁷⁰ makes the polymer sponge 'softer'.

An interesting way of controlling the microporosity of the polymer phase in heterogeneous cryogels of this type has been reported.¹⁷¹ Oligo(ethylene glycol) with an MW of 1000 Da is introduced as a 'molecular' porogen into the initial solution of a mixture of acrylic acid and methyl methacrylate. After radiation-induced cryopolymerisation of the unsaturated monomers, this additive is washed out of the gel phase by a large excess of water. Apart from the usual micropores present in the polymer network, this gel contains additional (a sort of calibrated) pores.

In order to synthesise cryogels with reactive aldehyde groups, acrolein is added to a solution of 2-HOEMA [or poly(oxyethylene dimethacrylates)]. Irradiation of the frozen solution of the comonomers affords a functionalised macroporous carrier suitable for

covalent coupling of specific antibodies for the preparation of immunosorbents.¹⁷²

Thus, by varying the concentration and the nature of monomer precursors, one can change, over a wide range, the physical and chemical properties of the gels formed in the radiation-induced cryopolymerisation and used as carriers of immobilised enzymes,^{140, 142, 149–153, 158, 160–164, 171} antibodies,¹⁴³ non-proteinaceous biopolymers¹⁶⁵ and microbial cells^{141, 144–148, 156, 157, 159, 166} (see Section V).

Systematic studies of cryotropic gelation induced by polymerisation in frozen solutions induced by chemical initiators have been mainly carried out using polyacrylamide cryogels (cryo-PAAG).^{22, 29, 30, 173–177} The radical copolymerisation of acrylamide (AAM) with *N,N'*-methylenebis(acrylamide) (MBAAM) in water was initiated by the redox system used traditionally for this type of comonomer, namely, ammonium persulfate (APS)–*N,N,N',N'*-tetramethylethylenediamine (TMEDA), capable of generating radical ions, which initiate polymerisation even at low temperatures.¹⁷⁸

The critical concentration for gelation (CCG) at 20 °C for a mixture of the AAM and MBAAM monomers in the synthesis of polyacrylamide gels (PAAG) amounts to ~2% (depending on the monomer ratio).¹⁷⁸ However, if the reaction mixture is frozen immediately after addition of the initiator (for example, kept at –10 °C for several hours) and thawed, it is possible to obtain cryoPAAG at a twice lower initial concentration of the same comonomers (Table 2).^{22, 30} Thus, polymerisation cryogels can also be formed with chemical initiation; in this case, the CCG decreases. In reality, this decrease is only apparent, the main reason being the accumulation of reactants in the polymerisation region, *i.e.*, in the NFLMP. It is significant that this seeming decrease in the CCG is observed for any type of cryotropic gelation.

Table 2. Formation of polyacrylamide gels from low-concentration aqueous solutions of an AAM–MBAAM mixture at 20 and –10 °C in the presence of an initiator.^{22, 173}

Total concentration of AAM and MBAAM /g dl ^{–1}	The ratio [AAM]:[MBAAM] /mol mol ^{–1}	Formation of PAAG or cryoPAAG	
		20 °C	–10 °C
1.0	50:1	–	+
1.0	40:1	–	+
1.0	30:1	–	+
1.0	20:1	–	+
1.0	10:1	–	+
2.0	50:1	–	+
2.0	40:1	–	+
2.0	30:1	–	+
2.0	20:1	+ / –	+
2.0	10:1	+	+

Notes. Initiator: APS, 0.025 g dl^{–1} and TMEDA, 0.05 g dl^{–1}. The following designations are used: – means that the system remains liquid; + / – means that a very weak gel is formed; + means the formation of a gel or a cryogel.

Polyacrylamide cryogels have a spongy morphology, which is mainly dictated by the temperature regime of cryotropic gelation. Figure 3 presents the photomicrographs which show the structure of cryogels synthesised at –10 and –20 °C from identical solutions of comonomers frozen by different procedures: by placing the reactant solution into a cryostat with a specified temperature (freezing from above) (Fig. 3 *a, b*); and by initial fast freezing of the system in liquid nitrogen to –196 °C followed by transferring the specimens into a cryostat with a specified moderate negative temperature (Fig. 3 *c, d*). The latter procedure, which minimises the influence of the duration of cooling and

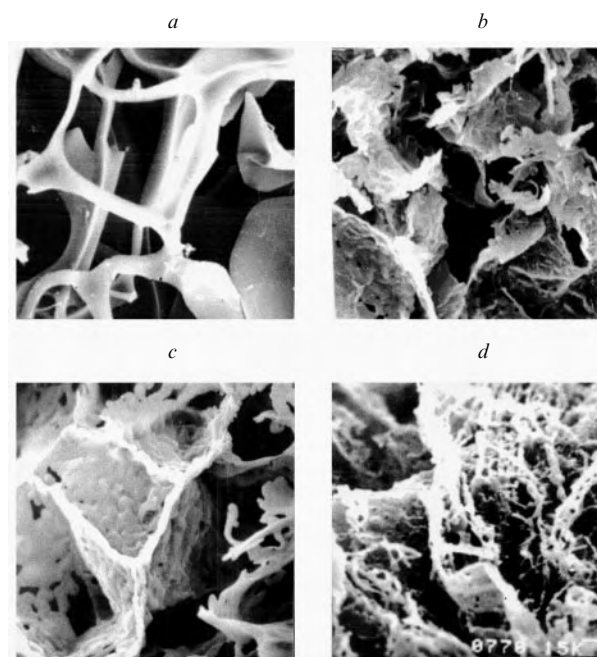


Figure 3. Electronic photomicrographs (scanning electron microscopy) of cryoPAAG specimens formed from aqueous solutions with a total comonomer concentration of 3% and [AAM]:[MBAAM] = 30:1 at different conditions of cryogenic treatment.^{22, 176}

(*a*) Freezing from above, –10 °C; (*b*) freezing from above, –20 °C; (*c*) low-temperature quenching, –10 °C; (*d*) low-temperature quenching, –20 °C. Scale: 20 μm to 1 cm.

freezing stages on the kinetics of cryochemical reactions, is sometimes called low-temperature quenching.

When cryogels are prepared by freezing from above, lowering of the synthesis temperature from –10 to –20 °C leads to a greater number of porogen particles (small crystals of ice) having, however, a smaller size; this has a noticeable influence on macropore diameter in the cryoPAAG (Fig. 3 *a, b*). In addition, the lower the temperature, the greater the amount of solvent that freezes out, *i.e.*, the NFLMP volume decreases, while the concentration of soluble substances in this phase grows. The walls of the macropores thus formed are thinner; however, according to measurements of the swelling capacity of the network material, they are built of a more concentrated gel.^{22, 175} When the low-temperature quenching procedure is employed, the cryoPAAG morphology changes (Fig. 3 *c*).^{22, 176} The cryogel architecture formed at –10 °C combines the porosity typical of the sample obtained by freezing from above at the same temperature and the structure of macropore walls inherent in the material prepared at –20 °C also by freezing from above. This means that, as the reacting system is warmed from –196 to –10 °C, the main structural elements of the gel phase have time to be formed during those several minutes when the system is at about –20 °C. Simultaneously, this indicates that polymerisation is rather fast under these conditions.

The porous structure of various cryogels can be characterised as an intricate three-dimensional maze. This is observed most often for aqueous systems due to the branched shape of ice polycrystals, which give rise to macropores of complex configurations in the specimen bulk. To prepare cryogels with a rather regular arrangement of macropores, it is necessary to use directional cooling and a solvent that forms oblong crystals on freezing. Thus formamide ($T_m = 2.8$ °C) crystallises as long thin needles. When cryoPAAG is prepared in this solvent and one end of the tube with the reaction solution is cooled, directional growth of formamide crystals takes place. The resulting cryogel contains long capillary channels oriented along the temperature gra-

dient.^{22, 174} Thus, the macroporosity of the polymer cryogels can be 'governed' to a certain extent by selecting the solvent and crystallisation regime.

The osmotic characteristics (swelling behaviour in various media) of spongy cryogels similar to cryoPAAG are mainly determined by the initial concentrations of precursors, the nature of the solvent used, and conditions of cryogenic treatment. The total volume of the liquid absorbed by a cryogel during swelling consists of two components, namely, the solvating solvent firmly kept by the polymer network and the capillary solvent which fills the macropore space and can be removed rather easily even by slight compression of the cryogel. It can be seen from the photomicrographs shown in Fig. 3 that the latter component is markedly greater than the former one as the internal volume of macropores accounts for the greater part of the cryogel volume. For example, for the cryoPAAG specimen formed at -10°C from a 3% solution of comonomers (in 40:1 molar ratio), the overall swelling capacity in water is ~ 80 ml per g of dry polymer, while the degree of swelling of the macropore wall material is only ~ 4 ml g^{-1} (see Ref. 173). The last-mentioned value corresponds to the swelling in water of usual PAAG prepared at positive temperatures from 10%–20% solutions of the same precursors. This indicates that the polymer network of the cryogel is formed in the NFLMP, *i.e.*, in the medium highly concentrated as compared to the initial solution.

In this connection, of interest is one more specific effect inherent in the cryotropic gelation dynamics. Figure 4 shows^{22, 176} the variation of the yield of the gel fraction during the PAAG and cryoPAAG formation at temperatures of 25 and 15°C and at -15 and -25°C . Cryopolymerisation was carried out using the freezing from above (Fig. 4*a*) and low-temperature quenching procedures (Fig. 4*b*). A mere decrease in the temperature of the process in the liquid solvent from 25 to 15°C decreases the rate of PAAG formation and the yield of the gel

fraction. Meanwhile, polymerisation in a moderately frozen system, in particular at -15°C , is much faster than, for example, at 25°C , and the final yield of cryogels is much higher. In other words, at definite negative temperatures, gelation is accelerated compared to the gelation of analogous specimens in a non-frozen medium. This phenomenon is typical of the formation of cryogels.

It is also noteworthy that the curves for the corresponding positive temperatures in Figs 4*a, b* follow nearly the same pattern. This implies that the low-temperature quenching itself has no influence on the given reacting system; after fast freezing in liquid nitrogen and the subsequent fast warming of the reaction mixture, the usual gelation kinetics does not change (*cf.*, for example, the curves corresponding to 25°C in Figs 4*a* and 4*b*).

The temperature dependences of the gelation rate in frozen media pass through extrema. The time it takes to reach the gel point (for given systems, this implies an approximately 10% yield of the gel fraction) actually reflects the process rate in the initial stage (Fig. 5). A decrease in the temperature in the positive region entails an increase in the gelation time, whereas in a certain range of negative temperatures in the frozen medium, the time required to reach the gel point sharply diminishes, *i.e.*, the rate of the formation of cryoPAAG increases. In the case of freezing from above, this temperature dependence has a clear-cut extremum, the initial gelation rate being a maximum in a fairly narrow range of negative temperatures. A somewhat different pattern is observed when low-temperature quenching is used, namely, the extremum is less pronounced and a high initial rate of the process is observed over a wider temperature range. This attests to non-equivalence of the conditions of copolymerisation of AAM with MBAAM in specimens brought to the reaction temperature along different routes. In other words, the process of formation of cryoPAAG depends on the method of freezing, although special experiments with a thermocouple embedded in the frozen specimen show^{22, 176} that during the fast warming-up from -196°C , the system temperature reaches a specified value before the gel point is attained. The non-equivalence of NFLMP characteristics in these reacting systems for the use of these freezing procedures is also indicated by NMR spectroscopy data,⁶⁷ which reveal the differences between the amounts of the solvent remaining in the liquid state in the specimens frozen by different procedures. Thus, in the case of relatively fast cryotropic formation of chemically cross-linked polymer networks, the regime of freezing of a reacting system is an important factor which influences, even at the stage of crystallisation, the properties and the formation dynamics of cryogels.

Nuclear magnetic resonance spectroscopy is one of the few physical methods that allow direct detection of chemical reactions

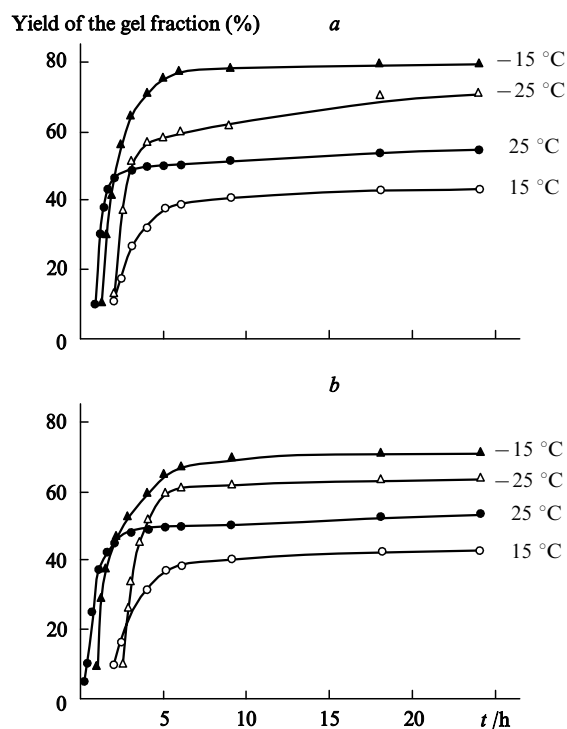


Figure 4. Dynamics of formation of PAAG and cryoPAAG (the temperature of synthesis is indicated near the corresponding curve) during freezing of the reacting system from above (*a*) and using the low-temperature quenching technique (*b*).^{22, 176} The initial total comonomer concentration is 3 mass %, [AAM]:[MBAAM] = 30:1.

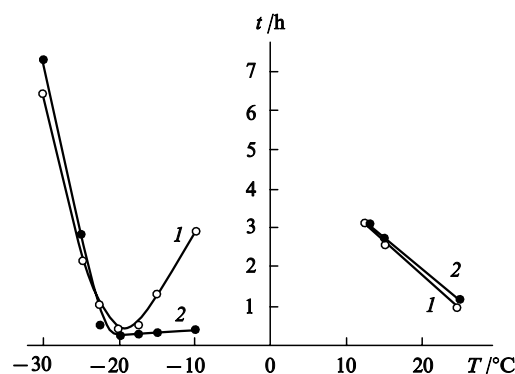


Figure 5. Time required for the formation of 10% of gel fraction in the reacting system *vs.* temperature of PAAG and cryoPAAG synthesis for freezing of the system from above (1) and for the low-temperature quenching version (2).^{22, 176} The initial total comonomer concentration is 3 mass %, [AAM]:[MBAAM] = 30:1.

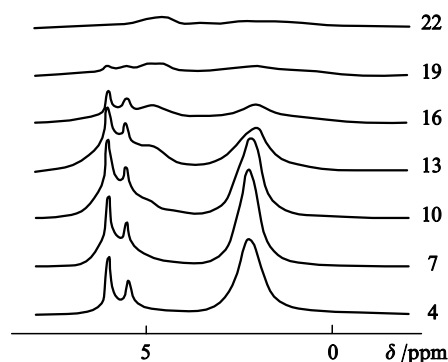


Figure 6. Evolution of the ^1H NMR spectra of a solution of a mixture of AAM, MBAAM, TMEDA, and APS in D_2O frozen using low-temperature quenching at -11.2°C .^{22,67} The initial total comonomer concentration is 3 mass %, $[\text{AAM}]:[\text{MBAAM}] = 30:1$. The digits near the curves represent the period of time (min) from the instant the system reaches a specified negative temperature to the instant of recording the spectrum.

in moderately frozen systems without thawing the sample. For instance, the evolution of the ^1H NMR spectra recorded at definite intervals (Fig. 6) for a solution of reactants (AAM–MBAAM–TMEDA–APS) frozen in D_2O proves unambiguously that in this case, cryopolymerisation in the frozen medium takes place but neither pre- nor post-polymerisation during freezing or thawing, respectively. For an initial period, the spectra of the frozen solution of the reactants remain identical to the spectra of a similar specimen that does not contain the initiator. Subsequently (starting from about the tenth minute of the process), the intensity of the narrow signals due to the monomer protons [6.15 and 6.03 ppm (CH_2), 5.60 ppm (CH)] starts to decrease, and a broad signal [~ 5 ppm (CH_2)] for the protons of the polymer chains appears.⁶⁷ In addition, NMR spectroscopy shows that the reactant ratio in the NFLMP differs from this ratio in the initial solution due to the partial crystallisation of AAM and MBAAM at temperatures below the eutectic point; therefore, the reaction medium is enriched in the initiator (the spectra contain an intense common signal for the protons of the CH_3 and CH_2 groups of TMEDA with a maximum at ~ 2 ppm). As polymerisation advances, the crystallised monomers are again dissolved in the liquid regions of the macrofrozen system and participate in the reaction, resulting ultimately in a high yield of the gel fraction. The measurement of spectroscopic characteristics of the non-frozen fraction of the solvent shows that an initial stage of polymerisation develops under conditions of increasing volume of the liquid microphase, and only when a certain degree of conversion of the monomers into polymeric products has been attained, does the solvent content reach a constant value.⁶⁷ Thus, depending on the cryopolymerisation temperature and freezing conditions, the composition and the volume of the reaction solution in the microreactor (non-frozen liquid microphase) can vary, which influences the gelation dynamics.

Since the variation of the temperature regimes of cryopolymerisation allows the macroporous morphology of gel materials to be controlled over certain limits, this approach has been used to prepare cryogels based on so-called stimuli-responsive⁷⁹ or sensitive¹⁸ polymers. In recent years, gel materials prepared from these polymers have attracted increasing attention both for fundamental research and for applied purposes. In particular, hydrogels that collapse reversibly upon a change in the environment parameters (temperature, pH, ionic strength, thermodynamic quality of the solvent, applied electric field, and so on) are considered to be promising materials for biomedical and biotechnological purposes.^{17, 18, 179–182} For example, in temperature-sensitive hydrogels in which the chains of the corresponding linear polymer undergo a reversible conformational change on passing through

the upper or lower critical solution temperature (UCST or LCST), substantial thermally induced reversible changes in the degree of swelling take place. Hydrogels based on cross-linked poly(*N*-isopropylacrylamide), poly(*N,N*-diethylacrylamide) (PDEAAM), poly(*N*-vinylcaprolactam) and so on are examples of thermally sensitive polymer systems.^{181–187}

Important characteristics of these materials which determine their performance characteristics include the temperature range in which the network collapses and the rate of system response to external treatment. Normally, the larger the specimen under study, the lower this rate, because the kinetics of collapse (or swelling) is controlled by heat transfer within the bulk of the gel and by the solvent diffusion and, hence, depends on the geometric dimensions of the specimen. However, if a macroporous structure is imparted to the material, the intrinsic response time of the macroporous specimen to a change in the temperature would decrease with respect to that observed for a fine-pored material, despite the fact that the weight and heat transfer rates in the gel phase remain the same. In this case, mass and heat transfer processes occur within the thin walls of macropores, *i.e.*, at short distances; as a consequence, the intrinsic time of collapse for this specimen is shorter than that for the microporous gel having the same total volume.

One approach to the synthesis of stimuli-responsive gels with enlarged pores is synthesis at temperatures above the collapse point of the cross-linked polymer (*i.e.*, above the LCST for the corresponding non-cross-linked polymer).^{188–190} In this case, phase segregation results in the formation of a coarser-pored gel (with pores of up to several hundred of Ångström) compared to that prepared from the same solution of monomer precursors but in the homogeneous medium at temperatures below the LCST (with pores of several tens of Å). The use of auxiliary porogens, for example foaming agents,¹⁹¹ at the stage of gel formation provides the possibility of producing an even coarser-pored material. In this case, some pores are closed but the rate of collapse or swelling of this gas-filled macroporous stimuli-responsive gel in reply to a change in the external conditions is much higher than that observed for homophase gel materials of the same chemical nature because the gel layer around each gas bubble is very thin.

As noted above, cryotropic gelation allows one to form gel systems with open interconnected capillary-sized macropores. Thus redox-initiated copolymerisation of *N,N*-diethylacrylamide or *N*-isopropylacrylamide with MBAAM in a frozen aqueous medium affords the corresponding macroporous (with pore size of several tens of micrometers) spongy temperature-sensitive cryogels.^{192,193} Gel materials of this type, in particular PDEAAM cryogels, collapse on heating much faster (Fig. 7a, curve 2) than usual PDEAAM gels formed in the liquid medium (Fig. 7a, curve 1).¹⁹² During the decrease in the swelling capacity, the main bulk of water retained by the cryogel is separated in the first 10–15 s. This includes almost all the capillary solvent and some fraction of the solvating liquid. The concentration of PDEAAM in the polymer phase of the cryogel (Fig. 7b) reaches very high values (50%–70%), whereas for a collapsed usual gel, these values are lower (17%–42%). In other words, during the thermally induced decrease in the swelling capacity, a cryogel displaces more liquid from the polymer phase than the usual gel. At temperatures above the LCST and in the shrunk state, PDEAAM cryogels retain not more than 3.5–5 water molecules per monomer unit, while the polymer network of a usual gel with the same composition retains up to 10–35 water molecules per unit. A unit of PDEAAM has three lone electron pairs (two at the carbonyl oxygen atom and one at the amide nitrogen atom) able to form hydrogen bonds with three water molecules. Hence, it can be concluded that the degree of hydration of PDEAAM cryogels after the collapse is close to the lowest possible value. Thus, the use of cryotropic gelation techniques allows one to create a new type of gel material combining the properties of a network of stimuli-responsive gels and a supermacroporous structure typical of cryogels.

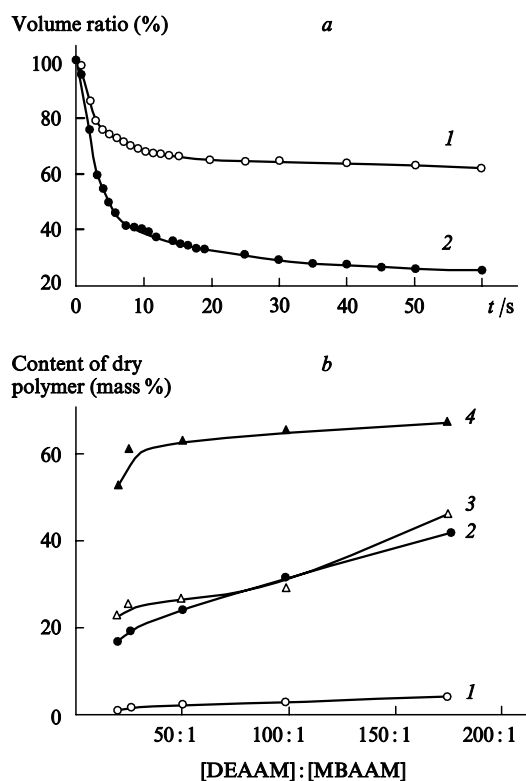


Figure 7. Properties of PDEAAM gels and cryogels.¹⁹² (a) dynamics of the thermally induced collapse of the PDEAAM gel (1) and cryogel (2); (b) content of the dry polymer in the gel phase at temperatures below (20 °C, curves 1, 3) and above (60 °C, curves 2, 4) the point of thermally induced collapse of the PDEAAM gel (1, 2) and cryogel (3, 4) for specimens with different initial ratios of the vinyl and divinyl comonomers and a constant total concentration (5.66%).

Unlike polymerisation cryogels, polycondensation analogues have been little studied, although actually, the only restriction hampering the synthesis of the latter may be the fact that many polycondensation reactions giving the corresponding polymers are endothermic and require heating of the monomer solution. In the case where the synthetic route chosen uses reactions with positive heats and the reactivity of monomers is rather high, the formation of polycondensation cryogels almost does not differ from the formation of polymerisation cryogels.

In particular, freezing is known^{194–199} to exert a structuring effect on hydrated sols of weak inorganic hydroxides (for example, iron hydroxide). The transformation of these sols into gels follows a polycondensation mechanism with water evolution to give a three-dimensional network of the inorganic oxide. The formation of silica gel on ageing of silicic acid sols is known^{200, 201} to proceed in a similar way; therefore, the cryogenic variant of this process can be regarded as polycondensation cryotropic gelation. Freezing of a silicic sol which liberates water during a chemical reaction, *i.e.*, forced dehydration of the system, should apparently shift the equilibrium towards the final product.

Preparation of silica cryogel is not an easy experimental task,²² because it requires a rather accurate acid titration of an alkaline solution of a silicate with cooling until a silicic sol is formed. Then the colloid system must be rapidly frozen to ensure that polycondensation (*i.e.*, ageing of the sol) occurs mainly in the NFLMP of the macrofrozen specimen. An interesting feature of the formation of silica cryogel is the fact that after thawing, the inorganic gel is obtained as scales rather than as a lump. The size of particles (2–5 mm) depends on the temperature of the cryogenic treatment. This is due to the fragility of silica cryogel, which is crushed by the growing ice crystals. In the preparation of elastic

cryogels based on organic polymers, sample destruction of this type is hardly ever observed.

The structure and properties of silica cryogels are mainly determined by the concentration of reactants and the temperature of freezing (Table 3). In particular, when the initial silicate concentration is above 0.5 mol litre⁻¹, the specific surface areas of the usual silica gel and silica cryogels formed at –10, –20, and –30 °C almost do not differ. However, cryogenic treatment of less concentrated systems affords silica cryogels whose specific surface areas are greater than that of the silica gel prepared from the reaction mixture with the same composition at a positive temperature. Silica cryogels formed at –10 °C possess a greater specific surface area than the specimens prepared at –20 and –30 °C. Unfortunately, the experimental data concerning inorganic cryogels of this type available to date are inadequate for a well-posed interpretation of this trend.

Table 3. Dependence of the specific surface area of silica gels and silica cryogels on the SiO₂ concentration in a silicic acid sol and on the gelation temperature.²²

Concentration of SiO ₂ in the silicic acid sol /mol litre ⁻¹	Specific surface area (m ² g ⁻¹) of the dry material formed at different temperatures			
	20 °C	–10 °C	–20 °C	–30 °C
0.7	90	102	96	94
0.5	350	375	370	360
0.4	510	600	550	530
0.3	590	750	690	645
0.25	630	875	810	740

^a Determined from adsorption of argon.

To the best of the author's knowledge, there are no publications dealing with polycondensation cryogels based on organic polymers. These cryogels are still to be prepared and comprehensively studied.

2. The formation of cryogels in solvent – polymer – cross-linking agent systems

Cross-linking in solutions of macromolecular precursors on treatment with appropriate cross-linking reagents has long been known and is widely used both in the laboratory and in industry for the preparation of lyogels. Moderate freezing of initial systems of this type, incubation in the frozen state for a required period of time and subsequent thawing lead to macroporous cryogels.

It is notable that cryostructures formed by cross-linking of polymer precursors in frozen media were known a long time ago. Indeed, the porous foodstuff 'kori-tofu', rather popular in Japan for several centuries, is nothing more than a cryogel based on soya proteins (so-called 11S-globulins) with covalent cross-linking by intermolecular disulfide bonds.²⁰² Moreover, cross-linking of polypeptide chains at cysteine residues takes place just during the cryogenic treatment.^{203, 204} Using model thiol-containing polymers (SH derivatives of carboxymethylcellulose and PAAM), it has been shown²⁰⁵ that atmospheric oxygen dissolved in the aqueous medium acts as the oxidant in these systems.

Thiol-containing water-soluble polymers proved to be very convenient objects for the study of the kinetics of cryotropic gelation of this type^{83, 206} because the course of the reaction can be monitored by highly sensitive spectrophotometric titration of the SH groups. Figure 8 shows the time variation of the concentration [calculated as the ratio of the current to initial SH titres expressed in per cent (Q_{rel})] of sulfhydryl groups in liquid and frozen aqueous solutions of the thiol derivative of PAAM at various temperatures. It can be seen that in frozen specimens (at –15 and –20 °C), the concentration of the SH groups decreases much faster than in liquid solutions; this markedly accelerates cryo-

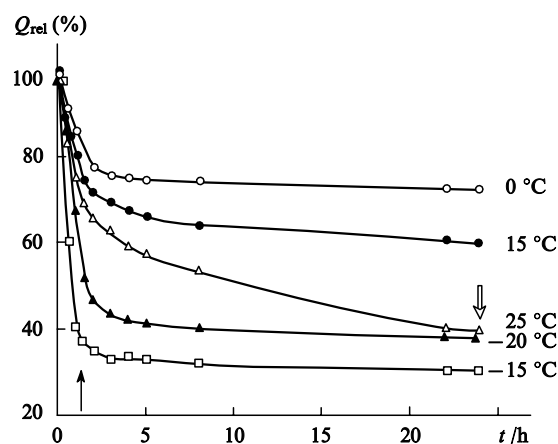


Figure 8. Kinetics of gelation of the SH derivative of PAAM at various temperatures in a liquid and frozen aqueous solution of the polymer (concentration 2 g dl^{-1} , pH 7.8).^{22, 83}

tropic gelation. For example, at -15°C , a cross-linked gel is formed over a period of approximately 1 h (shown by the black arrow), whereas at 25°C , this occurs only after 24 h (light arrow). In other words, for the cryostructuring of solvent–polymer–cross-linking agent systems, as for the formation of polymerisation cryogels, gelation in a definite range of negative temperatures is accelerated compared to that for non-frozen specimens.

At -5°C , an aqueous solution of SH-PAAM with a polymer concentration of 2 g dl^{-1} does not become frozen due to undercooling effects; therefore, the reaction is very slow under these conditions. When low-temperature quenching is used, the system is frozen at -5°C and the reaction rate is high owing to cryoconcentration (Fig. 9). The temperature dependence of the rate of variation of Q_{rel} in systems frozen by two different procedures passes through an extremum, which is typical of cryotropic gelation. Comparison of the pattern of variation of the SH-group concentration with the NMR data on the amount of mobile non-frozen solvent in the specimens shows⁸³ that after a specified negative temperature has been attained, the volumes and properties of liquid microphases in the specimens frozen in different ways are non-equivalent for a certain period of time. In the case of freezing from above, after crystallisation of the main bulk of the solvent, the reactions proceed initially under conditions of gradually decreasing volume of the liquid component, *i.e.*, with increasing concentrations of reactants. Conversely, in the speci-

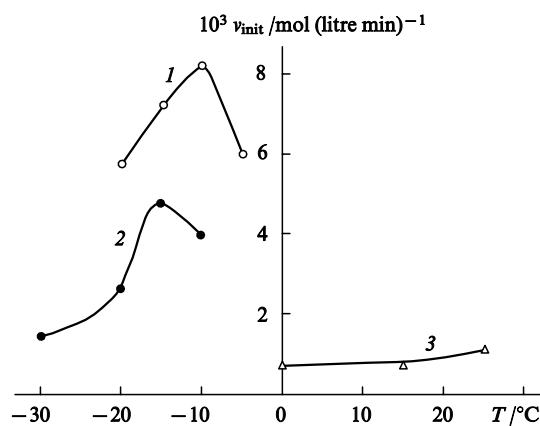


Figure 9. Initial rate (v_{init}) of gelation of the SH derivative of PAAM vs. temperature (concentration 2 g dl^{-1} , pH 7.8).^{22, 83} (1) Low-temperature quenching, (2) freezing from above, (3) variation of v_{init} for the region of positive temperatures.

mens frozen in liquid nitrogen and then heated to a specified negative temperature, the smallest volume of the microreactor and, hence, the greatest degree of substance concentration is attained almost simultaneously when the temperature of the environment (the cryostat refrigerating fluid) becomes equal to the temperature of the frozen reaction mixture. These dynamic differences between the phase states of the specimens brought to the temperature of a cryochemical reaction *via* different routes account for the non-equivalence of temperature dependences 1 and 2 in Fig. 9.

Cryotropic gelation in the solvent–polymer–cross-linking agent systems, like the synthesis of polymerisation cryogels, is accompanied by an apparent decrease in the CCG. For example, Fig. 10 shows the dependences of the yield of the gel fraction on the polymer concentration in the initial solution (Fig. 10a) and on the amount of the cross-linking agent (Fig. 10b) during the formation of normal gels and cryogels of chitosan [poly- β -(1 $\rightarrow$ 4)-D-glucosamine] cross-linked by glutaraldehyde at 25°C and in a moderately (-8°C) frozen medium. Cryogels are formed at substantially lower initial concentrations of both the polymer (Fig. 10a) and the cross-linking agent (Fig. 10b).^{13, 22} Undoubtedly, this decrease in the CCG is due to the cryoconcentration of the reactants in the NFLMP.

The normal gels of cross-linked chitosan are typical homophase hydrogels; in the swollen state, they are transparent and rather brittle, especially when the cross-linking degrees are relatively high. The whole bulk of the solvent present in the specimens swollen to equilibrium occurs in the bound (solvation) state. As in the case of other chemically cross-linked gels, it cannot be removed by squeezing out without disruption of the gel integrity. Conversely, cryogels formed from the same initial reaction solutions are heterophase spongy non-transparent materials in which the capillary-bound solvent can be separated rather easily by compression even at low mechanical loads.

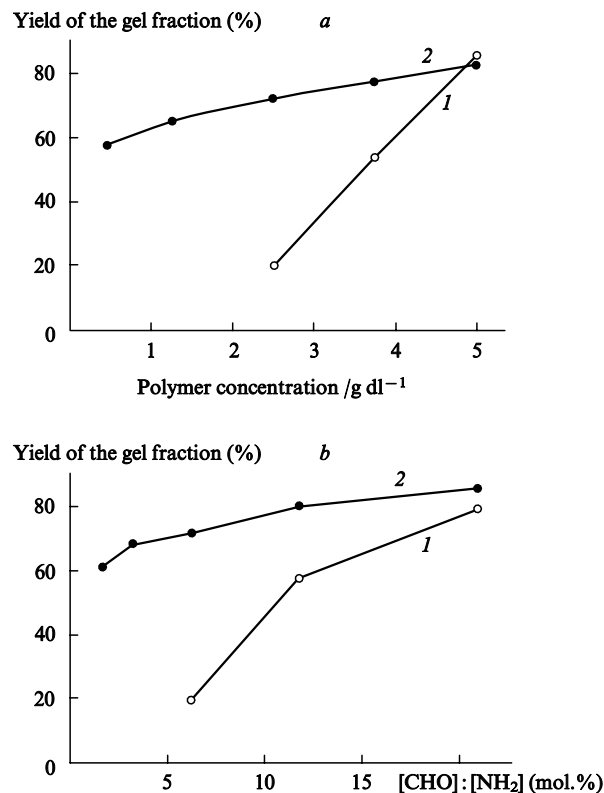


Figure 10. Yield of the gel fraction vs. the initial concentration of chitosan (a) and vs. the ratio of the number of glutaraldehyde CHO groups to the number of polymer amino groups for a fixed (2.5 g dl^{-1}) initial concentration of chitosan (b) ^{13, 22} at (1) 25°C , (2) -8°C .

The above examples refer to the synthesis of cryogels in frozen aqueous media. However, there are no obstacles preventing, in principle, the preparation of cryogels from precursors soluble in organic solvents. A necessary condition is that the organic solvent should undergo crystallisation rather than vitrification to ensure the separation of the solid and liquid phases and the formation of an NFLMP with an enhanced concentration of reactants.

Figure 11 shows the dependence^{22,30} of the yield of the gel fraction on the polymer concentration in the initial solution (Fig. 11 *a*) and on the temperature (Fig. 11 *b*) during the SnCl_4 -catalysed cross-linking of polystyrene with 1,4-xylylene dichloride according to the Friedel–Crafts reaction in liquid (13.5°C) and crystallised (-13.5°C) nitrobenzene ($T_m = 5.5^\circ\text{C}$). These data indicate that processes in organic solvents actually obey the same regularities as gelation in aqueous media, namely, the apparent decrease in the CCG for cryogenic processes (Fig. 11 *a*) and an extremal pattern of dependence of their efficiency on the temperature of the frozen system (Fig. 11 *b*). The polystyrene cryogels formed in crystallised nitrobenzene have a spongy morphology (similarly to cryogels based on hydrophilic polymers considered above) and during swelling absorb substantial amounts of organic solvents compatible with polystyrene, for example, benzene or toluene. The main bulk of the liquid absorbed by the cryogel is the capillary solvent which can be easily squeezed out. Thus, it can be concluded that the type of morphology of cryogels cross-linked by covalent bonds and the effects involved in their formation are rather general and do not depend on the nature of the crystallisable solvent used.

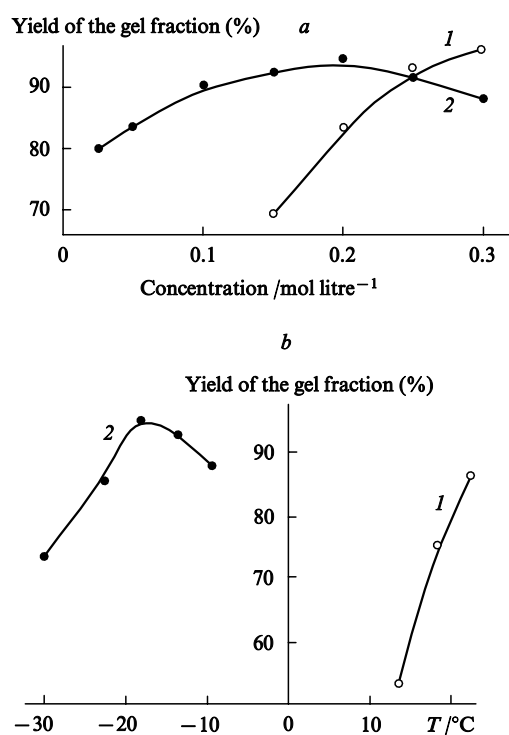


Figure 11. Yield of the gel fraction vs. the initial concentration of polystyrene expressed as the molar concentration of monomer units (*a*) and vs. the temperature (the initial concentration of monomer units of polystyrene is $0.3 \text{ mol litre}^{-1}$) (*b*);^{22,30} (1) formation of gels (13.5°C); (2) formation of cryogels (-13.5°C).

3. Ionic cryogels

Ionic, coordination, and coordination–ionic polymer gels represent special types of gel-like systems. On the one hand, they are thermally irreversible, like covalently cross-linked gels, and on the other hand, the change in the pH or the salt composition of the

liquid which surrounds the specimen can induce fast dissolution of swollen ionotropic and chelatotropic networks, which are converted again into the gel upon an appropriate change in the medium composition; this reversibility makes these systems similar to physical gels. A specific feature of many ionotropic gels is heterogeneity caused by impediments to the diffusion of new portions of counter-ions into deep regions of the gelling specimen through the gel membrane, which is formed rapidly at the sample surface (periphery).

Traditional ionotropic gels, *i.e.*, those formed at positive temperatures, can be divided conventionally into three groups.

The first group includes solvated networks based on polyelectrolytes whose macromolecules are cross-linked to give a three-dimensional structure through low-molecular-weight ions forming low-dissociated salt bridges with the ionogenic groups of the polyelectrolyte chains at the network junction knots. When complexing agents are used for cross-linking, a chelate (coordination) network is formed. These ionotropic and chelatotropic gels are capable of substantial repeated swelling after drying.

The second group includes polymer gels formed with the change in the charge of polyelectrolyte ionogenic groups, resulting in a decrease in the polymer solubility and phase separation. The gel-like systems formed in this case usually possess low mechanical strengths and, after drying, they are unable to swell to a substantial extent in the same medium as was used for gelation.

The third group comprises ionotropic gels formed during preparation of polyelectrolyte complexes (PEC). In essence, these systems represent swollen three-dimensional networks cross-linked by poorly dissociating salt bonds (similarly to the first-group ionic gels). However, in this case, it is often impossible to establish which of the PEC components (either polycation or polyanion) is the gel-forming and cross-linking component, especially if the MW and the initial concentrations of these compounds are similar.

Examples of preparation of ionotropic and chelatotropic cryogels that can be attributed (although with some reservations) to the first two groups have now been reported. Cryogels based on PEC have not yet been described.

The major obstacle faced during the formation of ionotropic cryogels is a too high rate of gelation, which proceeds even at the stage of component mixing. Indeed, if low-molecular-weight counter-ions inducing gelation are added to a polyelectrolyte solution in a concentration higher than the CCG, a lyogel is formed very rapidly. On subsequent freezing, the solvent crystallises in the gel phase, *i.e.*, it is virtually impossible to freeze the system when it still exists in the liquid state. This situation is encountered, for example, in the attempt to prepare a calcium alginate cryogel: the addition of a solution of a calcium salt to an aqueous solution of sodium alginate (the sodium salt of the linear block copolymer of D-mannuronic acid and L-guluronic acid) entails fast formation of a gel network, and the system loses fluidity. This specimen can be frozen, but this would not be accompanied by accumulation of precursors and by chain cross-linking in the NFLMP, peculiar to cryotropic gelation (Fig. 12, pathway *a*). Preparation of the cryogel by recharging the alginate carboxy groups is impossible either, because acidifying the solution results in fast formation of a thixotropic gel of alginic acid, whose freezing–thawing does not afford a macroporous material typical of cryogels (Fig. 12, pathway *b*).

Two approaches have been proposed to surmount these obstacles (Fig. 12, pathways *c* and *d*).

If a finely powdered salt having a negative temperature factor of solubility is added (as a source of cross-linking counter-ions) to a polyelectrolyte solution (Fig. 12, pathway *c*) and the resulting suspension is subjected to moderate freezing, gradual dissolution of this salt in the NFLMP and cross-linking of the polyelectrolyte chains take place at low temperature. After thawing, a macroporous ionotropic cryogel is produced. A crucial point is the choice of an appropriate salt because the solubility of most salts increases with increasing rather than decreasing the temperature.

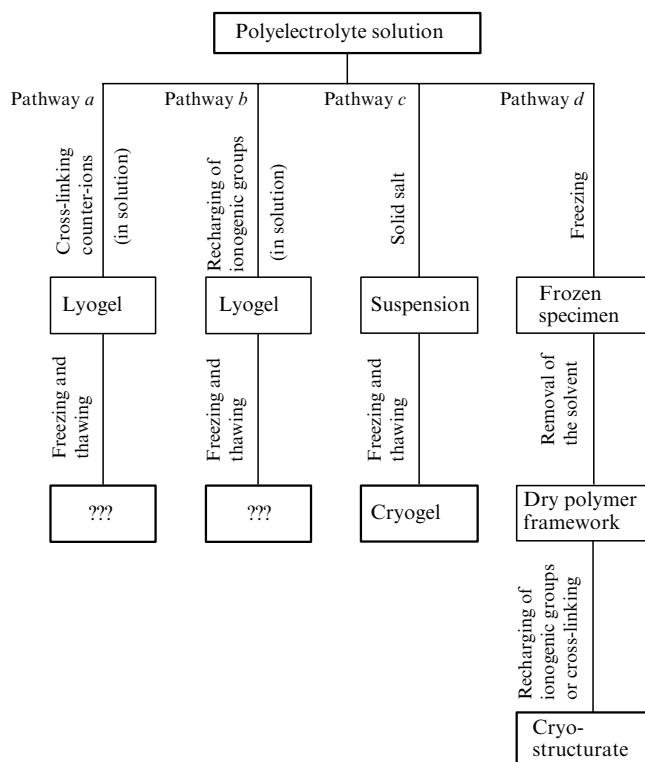


Figure 12. Basic diagram of the formation of ionic cryostructures.²²

The degree of salt grinding is also significant. This strategy has been employed to prepare an alginate cryogel^{22, 207, 208} using calcium salts with the solubility increasing upon decreasing temperature [in particular, calcium butyrate, pentanoate, succinate, glycerophosphate, and some other calcium salts have negative temperature factors of solubility in water (see Ref. 209, p. 1353)]. In this case, as in the formation of covalent cryogels, the properties of the final material depend not only on the precursor concentrations and the temperature of cryogenic treatment but also on the time of keeping the specimens in the frozen state. In particular, when the initial concentrations of sodium alginate and calcium glycerophosphate are 0.5 mass %, keeping frozen specimens at -10°C for 1.5 h gives ultimately (*i.e.*, after thawing, washing and drying) a cryogel with a rupture strength of 250 kg cm^{-2} . An increase in the duration of the cryogenic treatment to 3 h leads to a material with a rupture strength of 420 kg cm^{-2} , and incubation of the sample in the frozen state for 24 h makes this parameter about twice as high (800 kg cm^{-2}).^{22, 208} These data indicate that cross-linking and structuring of alginate require a certain time for dissolution of the solid cross-linking agent and for slow diffusion of calcium ions into the high-viscosity medium of the liquid microphase.

However, this strategy for the preparation of ionotropic cryogels is subject to numerous restrictions, related, most of all, to the admissible concentrations of precursors. Above a definite concentration of either the polyelectrolyte or the salt, too fast gelation taking place at positive temperatures prevents the formation of a 'true' cryogel.

Almost no limitations of this type are involved in the procedure shown as pathway *d* in Fig. 12. This strategy allows the preparation of macroporous ionotropic cryogels by both the recharge of ionogenic groups and cross-linking with appropriate counter-ions, although cryotropic gelation does not actually occur in this case.^{22, 210, 211} To prepare the target material, a polyelectrolyte solution with any desired concentration limited only by the polymer solubility is merely frozen at a required temperature. This is followed by removal of the crystallised solvent without thawing,

for example, by vacuum sublimation (freeze-drying) or cryoextraction (treatment at a negative temperature with a liquid which acts as a solvent for the crystalline phase but a non-solvent for the polyelectrolyte). Finally, cryogenically structured macroporous polymeric framework is obtained, which is then transformed into an insoluble state either by treatment with cross-linking counter-ions or by recharging ionogenic groups. The last-mentioned operation is also carried out in the polymer non-solvent and this no longer requires low temperatures.

For instance, freezing of a solution of sodium alginate and freeze-drying of the specimen thus formed followed by immersion of the porous material into an ethanol solution of calcium acetate results in an ion exchange reaction in which the material structure is fixed by poorly dissociating salt bridges. This yields a calcium alginate cryostructure²¹⁰ which is not dissolved in a physiological salt solution for several days, whereas a usual alginate gel prepared from the same precursors at a positive temperature loses its integrity in several minutes and is promptly dissolved. When substances capable of forming poorly dissociating coordination (more precisely, coordination – ionic) bonds with alginate groups, for example, chromium salts, are used as cross-linking agents, this procedure leads to chelotropic cryostructures.²²

Treatment of plates or grains of a frozen solution of sodium alginate with acidified acetone in the cold (*e.g.*, at -20°C) induces cryoextraction of ice with simultaneous transformation of the polymer network into alginic acid due to recharge of ionogenic groups. The final macroporous polymer is insoluble in water but is wetted by water and readily swells.²¹⁰

A similar strategy can be utilised to prepare a macroporous material from a polymeric base. A specimen prepared by freezing a solution of a macromolecular salt followed by removal of the solvent is treated, for recharge of ionogenic groups, with an alkaline reagent in a medium that is a non-solvent for the polymer.²¹¹ For example, dropwise addition of a solution of chitosan in dilute acetic acid to cooled (*e.g.*, to -15°C) octane results in frozen spherical particles, treatment of which with a saturated solution of NaOH in acetone or methanol at a negative temperature affords granulated macroporous chitosan base. This material is stable in alkaline or neutral media and is capable of coordinating heavy metal ions (for example, its capacity with respect to Cu^{2+} or Co^{3+} ions equals $5.2\text{--}5.5\text{ mmol g}^{-1}$).^{22, 211}

Thus, it is possible to carry out cryogenic structuring of polyelectrolytes, although it requires more sophisticated approaches, and to prepare ionic or coordination polymer materials possessing macroporous morphology, typical of cryogels.

4. Cryogels with a physical network of the polymer phase

As has been noted in the Introduction, non-covalent (physical) cryogels are the best known and investigated gel materials formed by the freezing–thawing strategy. This refers most of all to PVA cryogels. A detailed analysis of publications (by the end of 1997) devoted to the formation of PVA cryogels, the influence of cryogenic treatment parameters on these gels, and their properties has been given in a review.⁹ In this Section, we consider only the general fundamental items of non-covalent cryotropic gelation and the data on physical cryogels based on other polymers. However, at the end of the Section, some other results concerning PVA cryogels (published in 1998–2001) are also considered.

Generally, non-covalent physical gels form a very extensive class of gel systems produced in both aqueous and organic media (see, for example, the publications^{15, 20, 212}). In principle, non-covalent gels can be prepared by either cooling (if the solvent–polymer system has an UCST) or heating (if the system has an LCST). In the former case, one deals with psychrotropic gels, and in the latter case, thermotropic gels are involved. It is clear that the latter cannot be cryogels. But in the case of psychrotropic gel-forming systems, it is not always possible to prepare a physical cryogel by mere freezing. When the polymer concentration is above the critical point and the rate of material solidification on cooling is high, then, as in the case of polyelectrolytes with cross-

linking counter-ions (Section IV.3), fast gelling takes place. In this case, the system that undergoes freezing is no longer a solution but a gel; therefore, the structure of the polymeric material after thawing differs from that obtained in the case of 'standard' cryotropic gelation. An example of such a system is an aqueous solution of agarose (neutral polysaccharide, the major component of agar-agar), which is converted into a gel over a period of several minutes even at 40–30 °C when the polymer concentration is above 1%. An agarose macroporous cryogel can be prepared only from relatively dilute (<0.2%) solutions of the polymer. However, strength characteristics of such a cryogel are poor.

Solutions of PVA (in water or DMSO),^{9, 31–34, 213} amylopectin,²¹⁴ maltodextrin (a mixture of partially depolymerised starch polysaccharides with MW < 20 kDa),²¹⁵ starch,^{23, 216–219} or LBG^{23–26} are more convenient for the formation of non-covalent cryogels because they belong to systems gelling rather slowly on decreasing the temperature. They can be frozen without complications, stored for a required period at a specified negative temperature and then thawed to give the corresponding cryogels. The cryogels based on these polymers are thermally reversible: they fuse at elevated temperatures and repeated freezing–thawing of the solution results again in a cryogel.^{22, 31, 220}

Depending on the type and initial concentration of the polymer and the regimes of cryogenic treatment, this gives either spongy cryostructures with moderate strength similar to cryo-PAAG, described in Section IV.1, or elastic non-spongy cryogels (which are exemplified by PVA cryogels). Most likely, these distinctions in the morphology of materials are related to the amount of free (unbound) solvent able to crystallise at a chosen negative temperature and to the size of porogen polycrystals thus formed. In some cases, the same solvent–polymer system with different contents of the macromolecular component can be converted in both spongy and non-spongy cryogels.

For example, dilute (0.05–0.75 g dl⁻¹), semidilute (0.75–2.0 g dl⁻¹) and concentrated (>2.5 g dl⁻¹) aqueous solutions of LBG remain liquid at room temperature for several months.²²¹ Freezing–thawing (–10 to –30 °C) of these solutions gives very weak spongy cryostructures in the first case, good polymeric sponges in the second case, and elastic non-spongy cryogels in the third case.^{23–26}

Aqueous solutions of maltodextrin containing less than 15–20 g of the polymer per dl (the concentration depends on the MW) cannot be transformed into a gel without cryogenic treatment. Concentrated aqueous solutions of PVA containing no residual acetyl groups form gels very slowly, whereas the freezing–thawing procedure always gives cryogels.^{9, 22, 31–34, 213, 215} Thus, thermally reversible physical cryogels are obtained at lower initial concentrations of the macromolecular precursors and often much faster than without freezing. This indicates that non-covalent cryotropic gelation, like the formation of covalently cross-linked cryogels, is subject to the effects of the apparent decrease in the CCG and accelerated gelation.

The chemical nature of the intermolecular bonds stabilising the junction knots of the three-dimensional polymer network in physical cryogels depends on the structure of the gel-forming polymer material. Usually, these are either hydrogen bonds (the predominant type of contacts between the chains in thermally reversible cryogels, similar to cryogels based on PVA, starch, and other polyhydroxy polymers)^{222–224} or hydrophobic interactions, which play an important role in the formation of new protein cryogels,^{82, 225} or various weak (but cooperative) dispersion interactions. For PVA cryogels, the formation of microcrystallinity zones acting as junction knots in the supramolecular network has been shown experimentally.^{226–228} The sizes of microcrystallites are determined by the temperature conditions of cryostructuring and the number of freezing–thawing cycles. At these knots, syndiotactic sites of PVA chains form numerous hydrogen bonds.^{9, 22} Apparently, microcrystallinity zones function as the physical network junction knots also in the structure of cryogels formed from starch, maltodextrin, and LBG polysaccharides.

The macro- and micromorphology and physicochemical and thermal properties of non-covalent cryogels depend appreciably on some characteristics of the polymer precursors, which are not so important in the case where cryogels are formed through covalent cross-linking of macromolecules. For example, in the cryotropic gelation of PVA solutions, apart from essential properties of the polymer such as the MW and chain tacticity, the number of residual *O*-acyl groups [*O*-acetyl groups for the PVA prepared from poly(vinyl acetate)] is also a significant factor, as the presence of even ~5 mol. % of these substituents is sufficient for inhibiting the complementary ('side-by-side') interaction of neighbouring chains.^{213, 229–232} In other words, *O*-acyl groups act as sort of distance bars preventing the formation of numerous intermolecular hydrogen bonds and thus interfering with the formation of PVA cryogels. In the case of starch cryogels, an important parameter is the ratio of the linear to branched polysaccharides (amylose and amylopectin) in the system subjected to freezing, which depends on the type of starch used and, in some cases, on the procedure of its pretreatment.^{23, 214–219, 233–236} When non-covalent cryogels such as albumin cryogels are formed through hydrophobic interactions, the accessibility of hydrophobic regions for intermolecular contacts becomes the crucial factor. This is determined by the conformation of chains, in particular, by denaturation-related changes in the macromolecules of these globular proteins, which are specially induced by pretreatment (prior to freezing) such as the addition of chaotropic agents (which destroy the cluster structure of water), heating, or high-pressure treatment.^{82, 237–243} Thus, as in the case of 'usual' psychrotropic gelation, for the formation of physical cryogels, too, the chemical structure and the degree of exposure of the chain groups involved in intermolecular interactions are important factors.

The conditions of all stages of cryogenic treatment are highly significant for the objects considered. Whereas in the synthesis of cryogels cross-linked by covalent or ionic bonds, the conditions of thawing of specimens usually have little influence on the properties of final gels, the parameters of non-covalent cryogels are often fairly sensitive to the thawing conditions.^{9, 10, 14, 26, 31–34, 214, 215, 235, 244}

For example, Fig. 13 shows the variation of the apparent instantaneous modulus of elasticity (E_0) and the fusion temperature (T_f) of the LBG cryogels vs. the thawing rate of the specimens (the v_{th} values are laid-off along the abscissa axis on a logarithmic scale).^{22, 26} The specimens were prepared by freezing aqueous solutions of a polysaccharide (2.0 g dl⁻¹) at –20 °C for 18 h. It can be seen that the lower the thawing rate, the greater the rigidity and the thermal stability of these physical cryogels. This trend is typical of those thermally reversible cryogels in which hydrogen bonding is the predominant type of intermolecular contacts stabilising the polymer network junction knots (cryogels

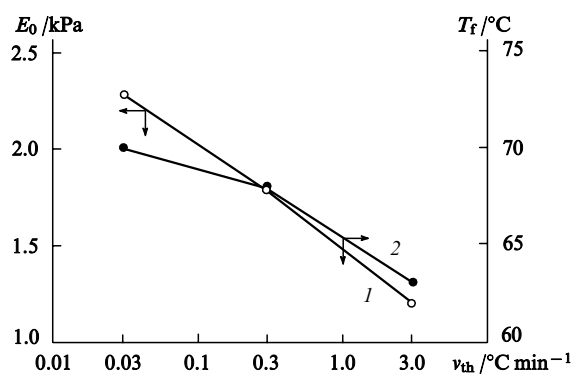


Figure 13. Properties of LBG cryogels vs. v_{th} .^{22, 26}
(1) Apparent instantaneous modulus of elasticity, (2) cryogel fusion temperature.

based on PVA, LBG, starch polysaccharides, gelatin, agar-agar, *etc.*, are examples of such systems).

The nature of this effect has been studied in most detail for PVA cryogels.^{9, 22, 31, 33, 34, 80, 244, 245} The data of Table 4 indicate that the shear modulus (G_0) of PVA cryogel specimens prepared from aqueous solutions with different polymer concentrations increases severalfold as the thawing rate decreases from 0.3 to 0.03 °C min⁻¹.^{34, 245} Conversely, in the case of high thawing rates (> 5–10 °C min⁻¹), PVA cryogels cannot be prepared at all, as, instead of an elastic gel, thawing gives a muddy thick liquid.^{31, 33, 34} These data indicate that the formation of PVA cryogels takes place exactly at the thawing stage. One can follow the kinetics of gelation and choose the temperature range corresponding to the highest intensity of this process (Fig. 14) using the following procedure: aqueous solutions of PVA are first frozen, for example, at –20 °C, then the specimens are transferred into a cryostat with a specified subzero temperature and, after incubation over particular periods of time, selected specimens are rapidly thawed (at a rate of ~3 °C min⁻¹) in order to eliminate the effect of the thawing rate.^{22, 34}

Table 4. Effect of the thawing rate on the rheological properties of PVA cryogels.^{22, 34, 245}

Concentration of PVA in the initial solution /g dl ⁻¹	Rate of thawing of frozen specimens /°C·min ⁻¹	Shear modulus of PVA cryogel specimen /kPa
3.0	0.30	< 0.3
3.0	0.03	< 0.3
5.0	0.30	< 0.3
5.0	0.03	1.73
7.0	0.30	1.80
7.0	0.03	3.93
10.0	0.30	4.94
10.0	0.03	10.6
10.0 ^a	3.0	1.40
10.0 ^a	0.30	3.20
10.0 ^a	0.03	9.40

Note. The materials were prepared by freezing at –20 °C for 18 h a completely deacetylated PVA with MW of 115 kDa. ^a PVC deacetylated to 99% with MW of 69 kDa.

The 0-h points in the plots correspond to the onset of incubation of frozen specimens at a specified subzero temperature (which is written near the corresponding curves in Fig. 14a). Figure 14b shows the duration of this incubation. The shear modulus of the PVA cryogels prepared using this technique increases rather weakly whilst keeping the frozen specimens at –10 °C. At higher negative temperatures, gelation becomes much more intense. The observed temperature dependence is non-monotonic, the process being faster in the –2 to –3 °C range than at –1.5 °C. Thus, in this case, the regularities are qualitatively analogous to the features of covalent cryotropic gelation during the synthesis of cryogels by polymerisation of monomer precursors (see Fig. 5) or by chemical cross-linking of polymer precursors (see Fig. 8b and Fig. 11b), *i.e.*, the temperature dependence of the efficiency of formation of non-covalent PVA cryogels at negative temperatures passes through an extremum.

Study of frozen solutions of PVA by ESR and NMR spectroscopy shows^{70, 81} a sharp increase in the amount of the mobile solvent above a certain threshold temperature range, which is 4–6 °C below the crystallisation point of the system. At these temperatures, together with firmly bound non-freezable water, an additional amount of liquid water appears in the solid, frozen specimen. This partial melting of ice increases the NFLMP volume; therefore, the mobility of macromolecules (or their segments) and the efficiency of polymer–polymer interactions

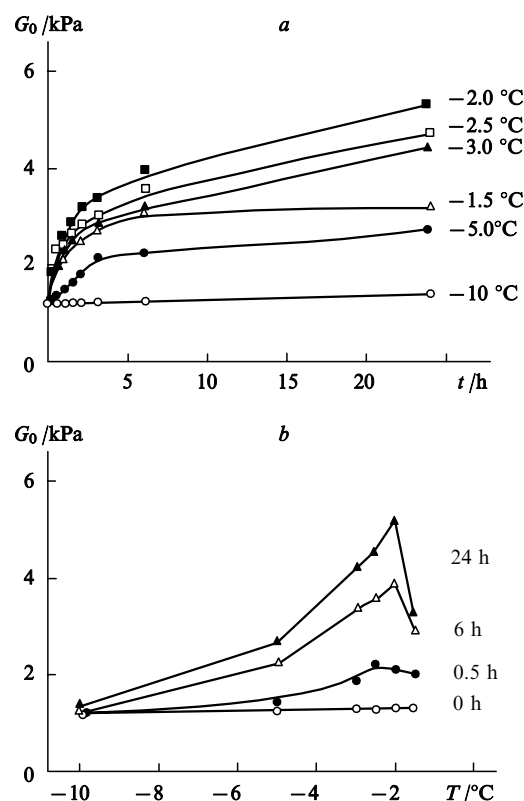


Figure 14. Dynamics of formation of PVA cryogels (completely deacetylated PVA with MW of 115 kDa, initial concentration 7 g dl⁻¹, freezing at –20 °C over a period of 24 h) at subzero temperatures.^{22, 34} (a) Time variation of rigidity of PVA cryogels; (b) temperature dependences of the rigidity of specimens kept in the subzero region.

increase. Finally, this results in the formation of microcrystallites which act as junction knots of the cryogel network. In particular, this mobility can be detected in ¹³C NMR spectra: ~8 °C below the melting point of the main bulk of the solvent, the resonance peaks for the carbon atoms of PVA virtually cannot be detected but when the temperature rises by ~3 °C, quite resolved, although weak signals arise. On further increasing the temperature (2–3 °C prior to thawing of the specimen), a real ¹³C NMR spectrum for the polymer solution is recorded. From this it follows that a temperature 5–6 °C below the system's thawing point corresponds to a boundary of retardation of the fast (on the NMR time scale) motions of the PVA carbochain backbone. Estimation of the spin–lattice relaxation correlation times for the carbon nuclei in the polymer, which serve as the criterion for the mobility of kinetic chain segments, shows that reorientation of the ¹³C nuclei in the PVA methylene groups in a system frozen at subzero temperatures occurs ~100 times more slowly than that in the initial liquid solution. This points to a very high viscosity of the NFLMP.⁸¹

On the basis of these data, it is possible to interpret the influence of the thawing rate or the duration of incubation of frozen specimens at moderate negative temperatures on the properties of PVA cryogels (see Fig. 14). The slower the thawing and the closer its conditions to equilibrium, the longer the period the specimen is at the temperatures optimal for gel network formation. Therefore, slow warming-up during thawing of the preparations is equivalent, in a sense, to storing the specimen for a long period at temperatures where the strongest cryogels are formed. Although a high polymer concentration in the NFLMP is favourable for gelation, this requires a fairly long period of time due to substantial viscosity of the NFLMP and low mobility of chains. The extremal dependence of the physicochemical properties of PVA cryogels on the cryostructuring temperature (see

Fig. 14 b) is due to the competition of factors favourable and unfavourable for gel formation. On the one hand, at temperatures above the extremum point, the amount of mobile solvent is greater, *i.e.*, the specific concentration of the gel-forming reagent in the NFLMP is lower, so is the probability of formation of effective intermolecular contacts (intensification of thermal motions in the system also counteracts stabilisation of the contacts). On the other hand, at temperatures below the extremum, the amount of mobile solvent decreases, the polymer becomes poorly solvated and retains only the firmly bound water, *i.e.*, the liquid medium in which the motion bringing together the interacting sections of the neighbouring chains takes place is no longer present.

Since concentrated aqueous solutions of PVA usually do not freeze in the subzero temperature range, *i.e.*, at temperatures of most intense gelation, due to undercooling effects, the initial specimens always need to be frozen at lower temperatures. The properties of PVA cryogels can be varied by varying the rate of thawing or the time of storage of the frozen materials at subzero temperatures.

Figure 15 shows the pattern of porosity of specimens of PVA cryogels thawed at rates of 0.3 and 0.03 °C min⁻¹. The photomicrographs of thin sections of cryogels dyed by Congo Red were taken using optical microscopy; the dark areas represent the gel phase and the light areas are macropores.^{22, 245} Whereas in the first specimen (Fig. 15 a), the macropore size and arrangement are rather irregular, the specimen of the PVA cryogel formed under slow thawing conditions (Fig. 15 b) possesses quite a perfect morphology with a clear-cut alternation of oblong macropores and strands of the gel phase. Undoubtedly, higher rigidity of slowly thawed cryogels of PVA of this type compared to the specimens thawed more rapidly (see Table 4) is due, among other factors, to the more regular macrostructure of the former.

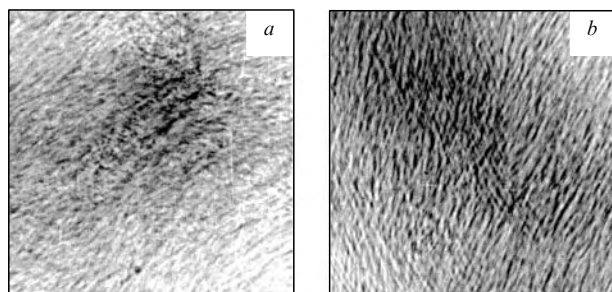


Figure 15. Photomicrographs (optical microscope) of thin sections of specimens of PVA cryogels formed from an aqueous solution (12 g dl⁻¹) of a polymer (MW 69 kDa, degree of deacetylation 99 mol. %) on freezing at -20 °C for 18 h followed by thawing at a rate of 0.3 (a) or 0.03 °C min⁻¹ (b) (see Refs 22, 34). Scale: 40 µm to 1 cm.

It is worth noting that the morphology of PVA cryogels has been studied most often by electron microscopy techniques, which imply dehydration of specimens,^{4, 22, 226, 246–253} resulting inevitably in some changes in the dimensions and shapes of the structural units of these objects.^{246, 249, 250, 253} The use of optical microscopy for these studies is more legitimate because it permits one to observe the real structure of a swollen cryogel.^{226, 245, 253–255}

Yet another interesting feature of non-covalent cryogels is an increase in the rigidity upon freezing and thawing repeated many times.^{4, 5, 9, 11, 25, 32, 226–228, 230–232, 256–258} For example, the dynamic modulus of elasticity of a PVA cryogel prepared from a 15% aqueous solution of the polymer (MW 75 kDa) is an order of magnitude higher after four cycles of cryogenic treatment (each cycle includes 24 h freezing at -20 °C and 7 h thawing at 15 °C) than after one such cycle.²⁵⁹ According to the data of X-ray diffraction analysis and DSC,^{226–228, 260} every subsequent freezing–thawing procedure increases the content and the size of

crystallites in the PVA cryogel. Apparently, repeated occurrence of the system in the temperature of the most intense gelation gives rise to new additional intermolecular contacts and extends those present previously. This is manifested, in particular, as numerous thickened regions observed through an optical microscope.²²⁶ In addition, the possible compaction of the supramolecular strands of the cryogel network, which approach one another under the action of growing ice crystals, cannot but be taken into account.

Thus, various procedures of cryogenic treatment of the water–PVA system make it possible to vary the properties and morphology of non-covalent cryogels of a given polymer over wide limits,^{9, 88, 245, 261–268} the duration of the occurrence of the frozen specimen at moderate negative temperatures being the crucial factor determining the efficiency of non-covalent cryotropic gelation.

This conclusion is also true for the formation of other physical cryogels. An important role of thawing or incubation at subzero temperatures was demonstrated for the cryotropic gelation of LBG,²⁶ maltodextrin,²¹⁵ amylopectin,²¹⁴ and mixtures of amylopectin with amylose.²³⁵ However, individual features of each of these polymers also make a contribution to the observed regularities.

For instance, in the case of highly crystalline starch polysaccharides, the primary cryogel is formed immediately during freezing, while thawing conditions influence the further formation (adjustment) of intermolecular contacts.^{214, 235} This can be clearly seen in a study of dilute systems in which the freezing–thawing cycle affords a cryoprecipitate rather than a cryogel over the whole specimen bulk. The precipitate can be readily separated from the solution and the yield of the gel fraction can be measured. This parameter shows that a decrease in the rate of thawing results in a substantial increase in the structuration efficiency compared to that in rapidly thawed preparations.²³⁵

To conclude this Section, it should be noted that non-covalent intermolecular interactions play an important role also in the formation of cryogels based on colloidal dispersion systems: suspensions, pastes and colloid sols. Such cryostructures are often produced on freezing–thawing of dispersions of food biopolymers; they are formed as coagulates upon cryogenic treatment of latexes, and so on. However, subtle physicochemical mechanisms of these processes have not yet been adequately studied, although the need for these studies is obvious.

Generally, the formation of non-covalent (physical) polymeric cryogels is characterised by the same effects as covalent cryostructuring, *i.e.*, the formation of macroporous gel-like bodies, apparent decrease in the CCG, acceleration of gelation over a definite range of negative temperatures and extremal temperature dependences of process rates. The main difference between non-covalent cryotropic gelation and the processes of formation of covalently cross-linked cryogels is the important role of the thawing stage (incubation at subzero temperatures) in the former case.

V. Applications of cryotropic gelation processes and materials based on polymeric cryogels

In recent years, the interest in polymeric cryogels as not only objects of scientific research but also promising materials for the solution of applied problems has constantly increased. The range of applications of the cryotropic gelation techniques and the gel materials is fairly broad. The unique porous structure of cryogels proves to be useful in many cases. An especially large number of publications including reviews^{3, 4, 6, 10, 11, 269} have been devoted to the use of various cryogels as materials for biomedical and biotechnological purposes. The development of cryogenic processes for the production of new food forms, new sorbents, filters, mechanochemical gel actuators (manipulator mechanisms), leather-like materials, catalyst systems, and many other things is in progress. The data demonstrating the fields and branches in which diverse cryogels have already been successively used are summarised in Table 5. It should be emphasised that the range of

Table 5. Fields of application of cryotropic gelation processes and materials based on polymeric cryogels.

Gel-forming reagents	Cryogel type	Application of a material or cryotropic gelation procedure	Ref.
2-HOEMA	IV.1(<i>r</i>)	carriers for enzyme immobilisation	3, 140, 142, 149–153, 158, 160–164
2-HOEMA + acrolein	IV.1(<i>r</i>)	carriers for antibody immobilisation and preparation of immunosorbents	143, 172
2-HOEMA + hyaluronic acid	IV.1(<i>r</i>)	gel matrices for controlled drug release	165
Hydroxy- and methoxyoligoglycol methacrylates	IV.1(<i>r</i>)	carriers for immobilisation of microbial cells	141, 144–148, 156, 157, 159, 166
Oligoethylene glycol monomethacrylates and dimethacrylates	IV.1(<i>r</i>)	gel matrices for cultivation of animal cells	168
AAM + MBAAM	IV.1(<i>c</i>)	carriers for immobilisation of microbial cells	22, 270, 271
	IV.1(<i>c</i>)	gel bases for supermacroporous bioaffinity sorbents	269, 272
AAM + MBAAM + allyl glycidyl ether	IV.1(<i>c</i>)	gel bases for supermacroporous bioaffinity sorbents	269, 272
Cryo(silica gel)	IV.1(<i>pc</i>)	carriers for immobilisation of microbial cells	22, 273
Gelatin + formaldehyde	IV.2	immobilisation of yeast cells	274
Serum albumin + glutaraldehyde	IV.2	immobilisation of photosynthetically active cell organelles of lettuce	275–278
	IV.2	immobilisation of the submembrane fraction of photosystem II of spinach cells	279, 280
	IV.2	immobilisation of photosynthetically active cyanobacteria	281
	IV.2	immobilisation of thermophilic bacterial cells	282
Polystyrene–polybutadiene block copolymer + Pd or Rh salts	IV.2	preparation of heterogeneous catalysts containing zerovalent metal nanoparticles	283
Collagen + dialdehyde (diepoxide, epichlorohydrin, diisocyanate, etc.)	IV.2	collagen materials for medical purposes	22, 284–287
A dispersion tanned by heavy metal salts of leather-processing wastes in the presence of cross-linking agents	IV.2	leather-like materials for domestic and technical purposes	22, 288–290
Sodium alginate + calcium gluconate	IV.3	polymeric scaffold of implants containing adsorbed hepatocytes	291, 292
Sodium alginate + calcium salt with a negative temperature factor of solubility	IV.3(<i>c</i>)	alginate sponges for medical purposes	22, 208, 209
Chitosan + β -tricalcium phosphate	IV.3(<i>c</i>)	polymer matrix of bone tissue implants	293
Polymeric acids	IV.3(<i>d</i>)	highly porous adsorbents for preconcentration of volatile bases	210, 294
Polymeric bases	IV.3(<i>d</i>)	highly porous adsorbents for preconcentration of volatile acids	211
PVA	IV.4	gel materials for calibration of NMR tomographs	266, 295, 296
	IV.4	immobilisation of AOT micelles containing enzymes	262
	IV.4	preparation of composites containing supported catalyst particles as fillers	297–299
	IV.4	gel matrices for controlled drug release	11, 300–306
	IV.4	carriers for enzyme immobilisation	307–325
	IV.4	carriers for immobilisation of microbial cells	6, 10, 22, 224, 252, 326–381
	IV.4	carriers for immobilisation of animal cells	382
	IV.4	gel bases for solid nutritional media for microbe cultivation	6, 22, 383
	IV.4	gel bases for solid nutritional media for plant cell cultivation	6, 22, 384
	IV.4	Support for the preparation of immunosorbents meant for isolation, purification, and modification of viruses	385, 386
	IV.4	chromatographic materials	387
	IV.4	protective coatings for frozen fish and meat	388–392
	IV.4	composite ice as a structural material	22, 393
	IV.4	thawed soil densification	22, 394
	IV.4	artificial baits for sports and amateur fishing	395
	IV.4	biocompatible materials for medical purposes	396–405
	IV.4	macroporous membranes	406, 407
PVA + chitosan or dextran	IV.4	biocompatible gel materials	408, 409
PVA + polyacrylic acid	IV.4	gel matrix for controlled drug release	168, 261, 410
PVA + alginate	IV.4	support for immobilised microbial cells	411–413
PVA + polyelectrolyte	IV.4	gel materials for mechanochemical actuators	7, 414–422
PVA + gellan	IV.4	gel matrix for controlled drug release	423
PVA + collagen fibres	IV.4	biocompatible gel materials	248, 424, 425
PVA + Fe salts	IV.4	gel dosimetric system	426
Solutions and dispersions of food biopolymers	IV.4	production of structured food forms	236–243, 427–433

problems solved using cryogels is permanently extending. In Table 5, types of cryogels are designated according to the numbers of the Sections of the review in which these cryogels are considered:

IV.1 are cryogels formed upon polymerisation (r implies radiation initiation, c means chemical initiation) or polycondensation (pc);

IV.2 are cryogels prepared by covalent cross-linking of polymeric precursors;

IV.3 are ionic cryogels (the letters correspond to the pathways of cryogel formation presented in Fig. 12);

IV.4 are non-covalent cryogels with a physical network of the polymeric phase.

VI. Conclusion

To summarise the discussion on the most important features of cryotropic gelation of polymeric systems, the properties of the gel specimens thus formed and some applications of these materials, several conclusions can be drawn.

1. Cryotropic gelation and concomitant chemical reactions (including the non-covalent interactions between the precursor molecules) are liquid-phase processes occurring in the non-frozen liquid microphase of moderately frozen (macroscopically solid) specimens.

2. Cryotropic gelation can take place in both aqueous and organic frozen media provided that the solvent used and the conditions of cooling ensure crystallisation rather than vitrification of the system.

3. The final products of cryotropic gelation (cryostructuring) are macroporous, often spongy gel-like materials called cryogels (cryostructures). The role of the porogen in the formation of these polymeric materials is played by crystals of the frozen solvent; therefore, the pattern of porosity of the cryogels is determined by conditions of freezing, incubation in the frozen state, and, in some cases, thawing of the gelling system. The polymeric network of the gel phase (walls of macropores) possess intrinsic microporosity.

4. Due to the accumulation of soluble components in the non-frozen liquid microphase, cryotropic gelation is characterised by an apparent decrease in the CCG with respect to that observed for the gelation in the same initial systems at positive temperatures.

5. As a rule, moderate freezing of the initial system accelerates gelation.

6. The temperature dependences of the rate and efficiency of cryotropic gelation usually pass through an extremum due to the competition between factors that favour (cryoconcentration effects) and hamper (low temperature, high viscosity, and so on) the process.

7. The properties of the polymeric cryogels are determined by the temperature of the cryogenic process, the nature of the solvent used, the type (monomer or polymer precursors) and the concentration of gel-forming reagents, the presence of other soluble materials and insoluble fillers, the rate of freezing, the duration of storage in the frozen state, thawing dynamics, and some other factors.

8. A unique combination of a number of properties, first of all, high porosity and interconnection of macropores and the facility of the process technology for the preparation of gel materials with this type of morphology allow cryogels to be regarded as a new type of polymer systems interesting in both scientific and applied aspects. The cryotropic gelation technique opens up prospects for the perfection of existing materials and development of new materials for various practical applications.

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Synthesis of 2'-O-alkylnucleosides

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Abstract. The published data on the synthesis of 2'-O-alkylnucleosides are reviewed. The known methods are systematised and their advantages and disadvantages are discussed. The bibliography includes 174 references.

I. Introduction

Synthesis of modified oligonucleotides is a popular trend in the modern organic chemistry of nucleic acids. The introduction of modified fragments into the oligonucleotide chain allows one to solve diverse problems, such as the enhanced transport of DNA fragments through cell membranes, the increase in their resistance against nucleases and the increase in thermodynamic stabilities of various NA duplexes. The introduction of chemically reactive groups into oligonucleotides allows the preparation of various conjugates with peptides, dyes, *etc.* Post-synthetic random modifications or modifications at the 3'- and/or 5'-ends of oligonucleotides are possible in principle, but direct incorporation of a modified unit into a predetermined position of an oligomeric chain in the course of oligonucleotide synthesis is the most versatile approach.

This review surveys the synthesis of modified nucleosides containing alkoxy groups at positions 2' of the carbohydrate moieties. These compounds are used as precursors of monomeric components in oligonucleotide synthesis. Preparation of now commercially available building blocks for the oligoribonucleotide synthesis, of conformationally locked nucleic acids (LNA)

(their synthesis is not confined to the alkylation of the 2'-hydroxy group) and 2'-O-(β -D-ribofuranosyl)nucleosides (for reviews see Refs 1 and 2) are not considered here.

Modified oligonucleotides containing an alkoxy group at the 2'-position of the carbohydrate moiety cannot be prepared by modification of natural oligonucleotides. The only possible approach is the synthesis of a modified monomer and its incorporation into the oligonucleotide chain in the course of automated oligonucleotide synthesis.

2'-O-Methyladenosine was isolated for the first time from a natural source in 1959;³ approaches to the synthesis of this class of compounds were developed soon thereafter (in 1965–1966).^{4–6}

In the past decade, modified oligonucleotides containing an alkoxy group in position 2' of the carbohydrate fragment are actively employed as antisense probes. The results of these studies are summarised in several books^{7–9} and reviews.^{10–13} It was demonstrated that 2'-O-methyloligonucleotides form duplexes with RNA which are kinetically and thermodynamically more stable and simultaneously more sensitive to mismatches than non-modified oligoribonucleotides,¹⁴ which makes them indispensable tools in antisense biotechnology. Besides, 2'-alkyloligonucleotides are used in the design of ribozymes¹⁵ which are more resistant to nuclease digestion than their natural counterparts, and in studies of the processing of genetic material.^{16–19} 2'-O-(3-Aminopropyl)-oligonucleotides are especially resistant against 3'-exonucleases due to the interaction of the amino group with the metal-binding domain. This was demonstrated by X-ray diffraction analysis using the Klenow fragment from *E. coli* as an example.²⁰ 2'-O-(2-Aminoethyl)oligonucleotides are the most potent inhibitors of the *in vivo* gene expression according to the antigenic mechanism, *viz.*, the formation of a triplex with genomic DNA, in comparison with other known modified analogues of nucleic acids.^{21,22} Oligonucleotides containing chemically reactive groups in position 2' of the carbohydrate fragment are used for conjugation with various compounds, *e.g.*, fluorophores²³ (these conjugates are used for structural analyses of various RNAs), electrochemically active compounds²⁴ (design of DNA analysers), metal ion complexes²⁵ (chemical nucleases), DNA and RNA duplexes with covalently linked chains.^{26,27}

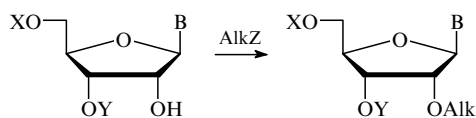
The alkylation of the 2'-hydroxy group of nucleosides usually follows a nucleophilic substitution mechanism.

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X, Y are H or protective groups; B is a heterocyclic base; AlkZ is an alkylating reagent.

Blocking of reaction centres of heterocyclic bases, 3'- and 5'-hydroxy groups to avoid side reactions is the central problem in the synthesis of 2'-*O*-alkylnucleosides. The choice of suitable protective groups still remains a topical problem. The majority

Table 1. Alkylation of the 2'-hydroxy group of nucleosides with diazomethane in the H₂O–DME system.

Nucleoside	Yield (%)	Ref.
 (Ado)	40	4
	27	28
	38	29
	20	30
	22 ^a	33
 (Cyd)	25	28
 (1a)	30–40	32
 (1b)	37	31
 (1c)	0	34
 (2)	90 ^b	35

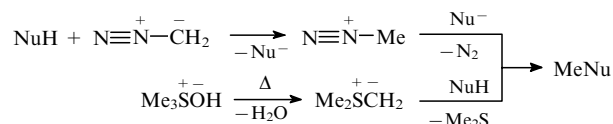
Note. Hereinafter, Tr = Ph₃C. ^a The alkylation by diazoethane gave a mixture of ethyl and methyl derivatives (~ 1 : 1); ^b the yield of 2'-*O*,3-*N*-dimethyl-3',5'-di-*O*-tritylarabinouridine is indicated.

of currently known alkylation procedures imply the use of strong organic or inorganic bases, therefore classical protective groups are not always compatible with the reaction conditions.

The review considers recent advances in the synthesis of 2'-*O*-alkylnucleosides and historically significant methodologies. Such a choice of literature sources is determined by the fact that the main approaches to the synthesis of 2'-*O*-alkylnucleosides have been known since the 1970's–1980's. However, modified 2'-*O*-alkyloligonucleotides came into use only in the early 1990's. Studies in this field have led to the development of novel methods for the synthesis of 2'-*O*-alkylnucleoside and optimisation of the existing methods.

II. Alkylation of nucleosides with diazomethane and trimethylsulfonium hydroxide

The alkylation procedures of nucleosides with diazomethane and trimethylsulfonium hydroxide have been proposed at different times, but here we consider them together because these reactions follow similar mechanisms. In addition, both these methods have only a historical significance at present.

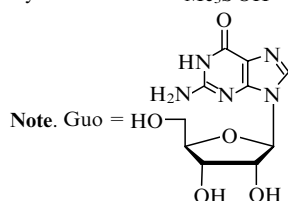


Broom and Robins⁴ have synthesised 2'-*O*-methyladenosine by treatment of adenosine with diazomethane in aqueous dimethoxyethane (Table 1) and these results were reproduced by different authors.^{28–35} Later, diazomethane was used for the alkylation of other nucleosides (Cyd, **1a–c**, see Table 1). The reaction with diazoethane proceeds in a similar way,³³ but a mixture of methyl and ethyl derivatives is formed in a ~ 1 : 1 ratio. The formation of methyl ethers is rationalised by solvent participation. Alkylation of 3',5'-di-*O*-tritylarabinouridine (**2**) under similar conditions led to the dialkylation product, viz., 2'-*O*,3-dimethyl-3',5'-di-*O*-tritylarabinouridine.³⁵ With 3-deazaauridine (**1c**), the reaction proceeded selectively with the heterocyclic base (see Table 1).³⁴

The use of trimethylsulfonium hydroxide as an alkylating reagent in the synthesis of 2'-*O*-methylnucleosides was proposed and developed by Kinoshita *et al.* in 1978–1980^{36–38} (Table 2).

Table 2. Alkylation of the 2'-hydroxy group of nucleosides with oxonium derivatives and trimethyl phosphate in DMF at 110 °C.

Nucleoside	Alkylating reagent	Yield (%)	Ref.
Cyd	Me ₃ S ⁺ OH [–]	30	36, 37
Cyd	Me ₃ S ⁺ OH [–]	28	38
Ado	Me ₃ S ⁺ OH [–]	20	38
Guo	Me ₃ S ⁺ OH [–]	11	38
Ado	Me ₃ PhN ⁺ OH [–]	6	39
Cyd	Me ₃ PhN ⁺ OH [–]	26	39
Ado	(MeO) ₃ PO	22	40
Cyd	(MeO) ₃ PO	28	40
Ado	Me ₃ S ⁺ OH [–] (see ^a)	5–10	41
Cyd	Me ₃ S ⁺ OH [–] (see ^a)	5–10	41



^a The reaction was carried out in DMSO with B(OH)₃ addition at 110 °C.

This alkylating reagent is less reactive than diazomethane; therefore, the reaction is carried out in DMF at 110 °C. The alkylation with trimethylanilinium hydroxide³⁹ and trimethyl phosphate⁴⁰ gave similar results. An attempt to use trimethylsulfonium iodide³⁸ resulted in compounds in which only the heterocyclic base was alkylated. The addition of boric acid to trimethylsulfonium hydroxide also led to the alkylation of heterocyclic bases.⁴¹

The main disadvantage of both methods is their low selectivity, since the alkylation products of both the sugar residue and the heterocyclic base are formed. These possess similar chromatographic mobilities, which impedes separation of the reaction products. The yields of the target products are usually low.

III. Alkylation of nucleosides with methyl iodide in the presence of silver(I) oxide

Historically, the alkylation of nucleosides with methyl iodide in the presence of Ag₂O was the first method for the preparation of 2'-O-methylnucleosides. Furukawa *et al.*⁶ performed the alkylation of 3',5'-di-*O*-trityluridine (**3a**) devoid of protective groups in the heterocyclic base; therefore, the reaction partly involved the uracil residue (Table 3). This method was not further used until the early 1980's when this was rekindled for the alkylation of nucleosides with 3'- and 5'-hydroxy groups blocked by the 1,1,3,3-tetraisopropylidisiloxane-1,3-diyl protective group (TIPDS, the Markiewicz protection) and the protected heterocyclic base (Table 3, compounds **3b–f**, **4a,b**, **5**).

Beigelman *et al.*⁵¹ made an attempt to synthesise 2'-*O*-methylcytidine from 5'-*O*-dimethoxytrityl-3'-*O*-*tert*-butyldimethylsilyl-*N*⁴-isobutyrylcytidine (**4c**), which is an intermediate product in the preparation of building blocks for the oligoribonucleotide synthesis. This attempt was unsuccessful, since the alkylation was accompanied by the 3'→2' migration and partial removal of the silyl protective group; 2',3'-di-*O*-methylcytidine

and 3'-*O*-methylcytidine were formed as side products. Hodge and Sinha⁵² have synthesised 2'-*O*-methyl-, -ethyl-, -allyl-, -propyl and -pentyl nucleoside derivatives **4d,f** (the reaction was carried out in the presence of 0.1–0.2 equiv. of pyridine). The yields of 2'-*O*-alkynucleosides decreased with an increase in the size of the alkyl group but remained at a sufficiently high level. Special mention should be made of the fact that this approach is suitable for large-scale (tens of grams) syntheses (see Table 3, compound **4d**).⁵²

Today, the alkylation with methyl iodide in the presence of silver(I) oxide has proved to be a fairly efficient approach to the synthesis of pyrimidine 2'-*O*-alkynucleosides. At the same time, it is seldom used for the synthesis of purine derivatives. It is of note that the methylation of partially protected 2-thiouridine (**6**)⁵³ gave a complex mixture, which may be due to the interaction of Ag₂O with the thioketone group and subsequent alkylation of the heterocyclic base.

IV. Alkylation of nucleosides in the presence of bases

1. The use of alkali metal hydroxides

There are two approaches to the alkylation of nucleosides in the presence of alkali metal hydroxides: the reaction may be carried out in non-aqueous or in aqueous media.

In the mid-1960's, Reese *et al.*⁵ performed the alkylation of 3',5'-di-*O*-trityluridine (**3a**) with benzyl chloride in the presence of potassium hydroxide in dry dioxane, which resulted in protected 2'-*O*-benzyluridine (**7**) (Table 4).

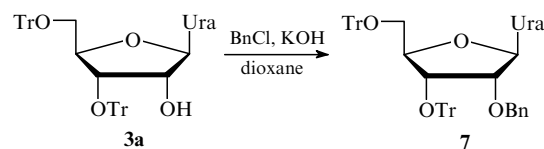
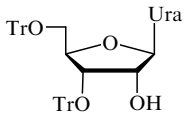
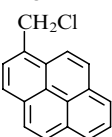
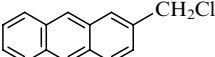
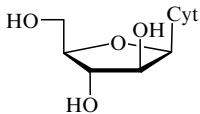
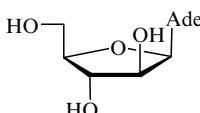
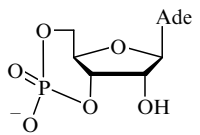
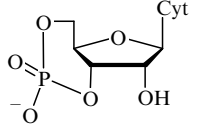


Table 3. Alkylation of the 2'-hydroxy group of nucleosides with methyl iodide in the presence of Ag₂O.

Nucleoside	R ¹	R ²	R ³	Compound No.	Nucleoside : MeI : Ag ₂ O	Reaction conditions	Yield (%)	Ref.
	Tr	Tr	H	3a	1 : 15 : 5	Me ₂ CO, 20 °C, 72 h	50	6
	TIPDS	TIPDS	Cl ₃ CCMe ₂ OC(O)	3b	1 : 100 : 5	40 °C, 7 h	93	42
	TIPDS	TIPDS	Bz	3c	1 : 15 : 10	Me ₂ CO, 20 °C	86	43
	TIPDS	TIPDS	Bz	3c	1 : 26 : 2.9	PhH, 40 °C, 16 h	85	44, 45
	TIPDS	TIPDS	Bz	3c	1 : 26 : 2.9	PhH, 40 °C, 16 h	40	46
	TIPDS	TIPDS	2,4-(NO ₂) ₂ C ₆ H ₃ S	3d	1 : 10 : 8	Me ₂ CO, 20 °C, 16 h	94	47
	TIPDS	TIPDS	2-NO ₂ C ₆ H ₄ S	3e	1 : 10 : 8	Me ₂ CO, 20 °C, 16 h	92	47
	TIPDS	TIPDS	4-MeOC ₆ H ₄ C(O)	3f	1 : 7 : 8	40 °C, 5 h	100	48
	TIPDS	TIPDS	2-NO ₂ C ₆ H ₄ O	4a	1 : 20 : 10	Me ₂ CO, 20 °C, 72 h	81	49
	TIPDS	TIPDS	BzNH	4b	1 : 26 : 2.9	PhH, 40 °C, 4 h	69	44, 45
	TIPDS	TIPDS	BzNH	4b	1 : 20 : 3	PhH, 20 °C, 2 h	98	50
	DMTr	TBDMS	Pr ⁱ CONH	4c	—	—	26	51
	DMTr	H	BzNH	4d	1 : 25 : (1.5–2.5)	PhMe, 0 °C, 5–17 h	see ^a	52
	DMTr	H	4-Bu ^t C ₆ H ₄ OCH ₂ C(O)NH	4f	1 : 25 : (1.5–2.5)	PhMe, 0 °C, 5–17 h	see ^a	52
	TIPDS	TIPDS	Cl	5	1 : 26 : 2.9	PhH, 40 °C, 1 h	66	44, 45
	TIPDS	TIPDS	Cl	5	1 : 26 : 2.9	PhH, 40 °C, 4 h	40	46
	TIPDS	—	—	6	—	—	see ^b	53

Note. Hereinafter, DMTr = (4-MeOC₆H₄)₂PhC, TBDMS = Bu^tMe₂Si. ^a The yields of the alkylation products with methyl, ethyl, propyl, allyl and pentyl iodides are 93%, 83%, 75%, 79% and 50%, respectively; ^b the product was not isolated from the reaction mixture.

Table 4. Alkylation of the 2'-hydroxy group of nucleosides in the presence of alkali metal hydroxides.

Nucleoside	Compound No.	Alkylating reagent	Nucleoside : alkylating reagent : sodium hydroxide	Reaction conditions	Yield (%)	Ref.
	3a	BnCl	1 : 1.2 : 5	dioxane, Δ	60	5
			1 : 1.1 : 10	benzene–dioxane, Δ , 2 h	65 ^a	54
			1 : 1.1 : 10	benzene–dioxane, Δ , 2 h	48 ^a	55
Cyd		(MeO) ₂ SO ₂	1 : 30 : 100	H ₂ O, 20 °C, 5 h	22	56
		(MeO) ₂ SO ₂	1 : 10 : 50	H ₂ O, 20 °C, 5 h	12	57
Ado		(MeO) ₂ SO ₂	1 : 6 : 30	H ₂ O–DME, 20 °C, 7 h	25	58
	8	(MeO) ₂ SO ₂	1 : 30 : 100	H ₂ O, 20 °C, 5 h	5	59
		(MeO) ₂ SO ₂	1 : 2 : 45	H ₂ O, 20 °C, 10 h	8 ^b	60
		(EtO) ₂ SO ₂	1 : 2 : 45	H ₂ O, 20 °C, 10 h	6 ^b	60
		(MeO) ₂ SO ₂	1 : 6 : 30	H ₂ O–DME, 20 °C, 7 h	20 ^b	61
	9	(MeO) ₂ SO ₂	1 : 6 : 30	H ₂ O–DME, 20 °C, 7 h	10	62
	10a	MeI	1 : 10 : 3	H ₂ O–DMF, 20 °C, 3 h	50	63
		EtI	1 : 10 : 3	H ₂ O–DMF, 20 °C, 3 h	40	63
	10b	MeI	1 : 10 : 3	H ₂ O–DMF, 20 °C, 3 h	62	63
		EtI	1 : 10 : 3	H ₂ O–DMF, 20 °C, 3 h	30	63

Note: Hereinafter, Ura is the uracil residue, Cyt is the cytosine residue, Ade is the adenine residue. ^a The yield over two steps (alkylation and detritylation) is indicated; ^b the yield over two steps (protection of 5'- and 3'-hydroxy groups and alkylation) is indicated.

The advantage of this method is that the heterocyclic base is not alkylated; however, the yields of the steps of the synthesis of the starting compound (3',5'-di-*O*-trityluridine) do not exceed 30%–45%. Later, in the 1990's, the alkylation was performed with more complex alkyl halides.^{54, 55}

In the early 1970's, it was proposed⁵⁶ to use dialkyl sulfates as alkylating reagents in the presence of alkali metal hydroxides in aqueous media (see Table 4, compounds **8**, **9**). It was shown⁵⁶ that at pH > 13, no alkylation of the heterocyclic base occurs. The alkylation of adenosine and cytidine 3',5'-cyclophosphates (**10a**, **b**) with alkyl halides in water–organic media has been described.⁶³ No side alkylation products at the 5'- and 3'-hydroxy groups were formed, which resulted in higher yields and facilitated the chromatographic isolation of the reaction products.

As can be seen from Table 4, the alkylation of the nucleoside **3a** in non-aqueous media gives fairly good yields even in the case of rather complex alkyl halides, but drastic reaction conditions significantly restrict the use of this method. Alkylation by dialkyl sulfates and alkyl iodides in aqueous and water–organic media proceeds as a rule with low yields and is of low practical value.

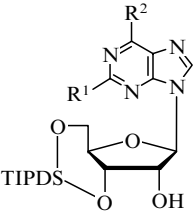
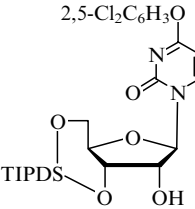
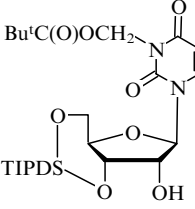
2. The use of organic bases

Alkylation of nucleosides in the presence of organic bases was first proposed by Sproat *et al.*^{64–70} (Table 5). The alkylation of

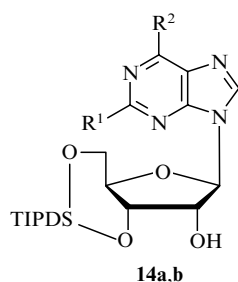
partially protected nucleosides with alkyl halides was carried out in the presence of 2-*tert*-butylimino-2-diethylamino-1,3-dimethylperhydro-1,3,2-diazaphosphorine (BDDDP) (see Ref. 71). This reaction and subsequent extraction are not accompanied by the formation of hydroxides; therefore, the protective groups of heterocyclic bases are preserved. It is of note that in addition to the known groups, *e.g.*, compounds **11a**, **b**, **d**, **12**, novel protective groups were introduced, *viz.*, the pivaloyloxymethyl group (compound **13**) for the protection of the N³-position of uracil and the *tert*-butyldiphenylsilyl group (compound **11c**) for the blocking of the O⁶-position of guanine (see Table 5). The pivaloyloxymethyl protective group is more stable than the conventional benzoyl group. In addition, the N³-pivaloyloxymethyl derivative **13** is obtained in a higher yield than the N³-benzoyl derivative. The use of the *tert*-butyldiphenylsilyl protective group made it possible to increase the total yield and to reduce the number of steps in the synthesis of 2'-*O*-propargylguanosine, since the 3'- and 5'-hydroxy groups and the O⁶ atom of the heterocycle are deprotected simultaneously under the action of tetrabutylammonium fluoride.⁶⁴

The alkylation of compound **14a** was accompanied by a side reaction at the exocyclic amino group; compound **14b** did not undergo alkylation under these conditions.⁶⁴

Table 5. Alkylation of the 2'-hydroxy group of nucleosides in the presence of BDDDP.

Nucleoside	R ¹	R ²	Compound No.	Alkylating reagent	Nucleoside : alkyl halide : BDDDP	Reaction time /h	Yield (%)	Ref.
	H	2,5-Cl ₂ C ₆ H ₃ O	11a	MeI	1 : 1.2 : 1.2	6	63	65
	H	2,5-Cl ₂ C ₆ H ₃ O	11a	MeI	1 : 1.2 : 1.2	6	—	66
	H	2,5-Cl ₂ C ₆ H ₃ O	11a	HC≡CCH ₂ Br	1 : 1.25 : 1.2	2	57	68
	H	2,5-Cl ₂ C ₆ H ₃ O	11a	MeCH=CHCH ₂ Br	1 : 1.2 : 1.2	6	70–75 ^a	68
	Cl	2,5-Cl ₂ C ₆ H ₃ O	11b	MeI	1 : 1.2 : 1.2	6	68	65
	Cl	2,5-Cl ₂ C ₆ H ₃ O	11b	MeI	1 : 1.2 : 1.2	6	70	66
	Cl	2,5-Cl ₂ C ₆ H ₃ O	11b	MeCH=CHCH ₂ Br	1 : 1.2 : 1.2	6	70–75 ^a	66
	NH ₂	TBDPS–O	11c	MeI	1 : 2.5 : 5	3	48	67
	NH ₂	TBDPS–O	11c	MeI	1 : 2 : 2	3	49	64
	NH ₂	TBDPS–O	11c	CH ₂ =CHCH ₂ Br	1 : 2.5 : 5	3	51	67
	NH ₂	TBDPS–O	11c	CH ₂ =CHCH ₂ Br	1 : 2 : 2	3	51	64
	NH ₂	TBDPS–O	11c	HC≡CCH ₂ Br	1 : 2 : 2	3	51	64
	NH ₂	TBDPS–O	11c	N≡CCH ₂ Br	1 : 2 : 2	3	47	64
	NH ₂	TBDPS–O	11c	EtO ₂ CCH ₂ Br	1 : 2 : 2	3	48	64
	Cl	2-NO ₂ C ₆ H ₄ O	11d	MeI	1 : 2 : 2	3	61	64
	Cl	2-NO ₂ C ₆ H ₄ O	11d	CH ₂ =CHCH ₂ Br	1 : 2 : 2	3	51	64
	Cl	2-NO ₂ C ₆ H ₄ O	11d	HC≡CCH ₂ Br	1 : 2 : 2	3	71	64
	Cl	2-NO ₂ C ₆ H ₄ O	11d	N≡CCH ₂ Br	1 : 2 : 2	3	70	64
	Cl	2-NO ₂ C ₆ H ₄ O	11d	N≡CCH ₂ Br	1 : 2 : 2	3	61	69
	Cl	2-NO ₂ C ₆ H ₄ O	11d	EtO ₂ CCH ₂ Br	1 : 2 : 2	3	62	64
		2,5-Cl ₂ C ₆ H ₃ O	12	MeI	1 : 1.2 : 1.2	6	—	66
			12	HC≡CCH ₂ Br	1 : 1.25 : 1.2	2	61	68
			12	N≡CCH ₂ Br	1 : 2 : 2	3	64	69
			12	EtO ₂ CCH ₂ Br	1 : 2 : 1.5	1	90	70
			13	HC≡CCH ₂ Br	1 : 1.25 : 1.2	2	48	68
			13	N≡CCH ₂ Br	1 : 2 : 2	3	65	69

Note. The yield of compound **11c** is indicated over two steps (alkylation and desilylation). Hereinafter, TBDPS is Bu^tPh₂Si; ^a the yields over two steps (alkylation and reduction of the crotyl residue to the butyl residue) are indicated.



R¹ = NH₂, R² = Ph₂NCO₂ (**a**); R¹ = PrⁱCONH, R² = Ph₂NCO₂ (**b**).

It was also shown⁶⁴ that the introduction of the carbamoyl protective group at the exocyclic N² atom of guanosine decelerates the alkylation reaction and strongly decreases the yields.

Nearly all the works from Sproat's laboratory are methodologically flawless: as a rule, all reactions proceed with high yields and result in the formation of single products. The syntheses are multistep, but the total yields are rather high. The main disadvantage of this method is the high cost of BDDDP; therefore, the preparation of compounds in gram quantities using this method is hardly possible. These works are also interesting with respect to

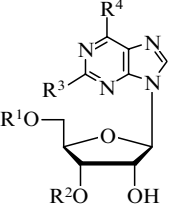
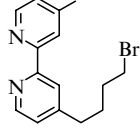
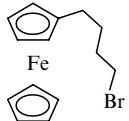
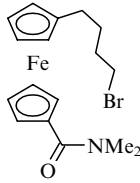
the application of novel protective groups for the heterocyclic bases.

3. The use of alkali metal hydrides

With alkali metal hydrides as the bases, the alkylation may be carried out with both the unprotected and the partially protected nucleoside. In the former case, the selectivity of the reaction involving the 2'-hydroxy group is due to its higher acidity in comparison with the 3'- and particularly the 5'-hydroxy group.⁷² Nevertheless, this is accompanied by the formation of side products including the 3'-isomer with similar chromatographic mobilities; therefore, protected adenosine derivatives are sometimes used (Table 6). In the case of other (especially, pyrimidine) nucleosides, the alkylation partly involves the heterocyclic base. The use of alkali metal hydrides as the bases demands careful selection of protective groups, since some of them are unstable under the reaction conditions. In addition, post-synthetic workup results in the formation of alkali metal hydroxides, which precludes the application of certain standard protective groups. Nevertheless, at present this approach is one of the most popular ones.

The method proposed by Robins *et al.*³² back in 1966 and recently employed by Yano *et al.*⁷³ in which 2-amino-6-chloro-

Table 6. Alkylation of the 2'-hydroxy group of nucleosides in the presence of sodium hydride.

Nucleoside	R ¹	R ²	R ³	R ⁴	Alkylating reagent ^a	Nucleoside : alkylating reagent : sodium hydride	Reaction conditions	Yield (%)	Ref.
	H	H	H	NH ₂	MeI	1 : 1.15 : 0.75	DMF, 0 °C, 4 h	42	73
	H	H	H	NH ₂	MeI	1 : 1.03 : 1.2	DMF, 0 °C, 3.5 h	23	74
	H	H	H	NH ₂	MeI	1 : 1.1 : 1.6	DMF, 0 to 20 °C, 10 h	25 ^b	75
	H	H	H	NH ₂	EtI	1 : 21 : 1	DMF, 0 to 20 °C, 10 h	3.5 ^b	75
	H	H	H	NH ₂	AllBr	—	—	—	76
	H	H	H	NH ₂	AllBr	1 : 1.1 : 1	DMF, 20 °C, 18 h	66 ^c	77
	H	H	H	NH ₂	EtO ₂ CCH ₂ Br	—	—	—	78
	H	H	H	NH ₂	EtO ₂ CCH ₂ Br	—	DMF	22 ^d	79
	H	H	H	NH ₂	PhthN(CH ₂) ₃ Br	1 : 1.15 : 1.5	DMF, 30 °C, 17 h	17	80
	H	H	H	NH ₂	PhthN(CH ₂) ₅ Br	—	DMF, 0–5 °C	21 ^b	81
	H	H	H	NH ₂	PhthN(CH ₂) _{2–4} Br	—	DMF	—	82
	H	H	H	NH ₂	Me(CH ₂) ₈ Br	—	DMF	—	82
	H	H	H	NH ₂	Im(CH ₂) ₃ Br	—	DMF	—	82
	H	H	H	NH ₂	TsS(CH ₂) ₆ Br	—	DMF	23	83, 84
	H	H	H	NH ₂	Ph(CH ₂) ₂ OTs	1 : 1 : 1.2	DMF, 0 °C, 3 h; 60 °C, 16 h	15	85
	H	H	H	NH ₂		1 : 1.2 : 1.3	DMF, –5 °C, 24 h	18	86
	H	H	H	NH ₂		1 : 1.1 : 0.5	DMF, 20 °C, 18 h	45	87
	H	H	H	NH ₂		1 : 0.9 : 0.5	DMF, 35 °C, 48 h	30	88
	H	H	NH ₂	NH ₂	AllBr	1 : 1.1 : 1	DMF, 20 °C, 18 h	77 ^c	77
	H	H	NH ₂	NH ₂	BnO(CH ₂) _n Br (<i>n</i> = 2, 3)	—	DMF	48, 50	89
	H	H	NH ₂	NH ₂	PhthN(CH ₂) ₃ Br	1 : 1.15 : 1.5	DMF, 30 °C, 17 h	—	80
	H	H	NH ₂	NH ₂	C ₄ H ₉ Br	—	DMF, 5 h	—	90
	H	H	NH ₂	NH ₂	C ₇ H ₁₅ Br	—	DMF, 5 h	—	90
	H	H	NH ₂	NH ₂	C ₁₀ H ₂₁ Br	—	DMF, 5 h	—	90
	H	H	NH ₂	NH ₂	C ₁₆ H ₃₃ Br	—	DMF, 5 h	—	90

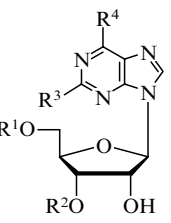
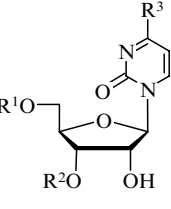
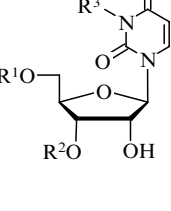
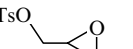
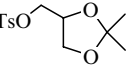
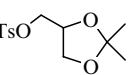
Nucleoside	R ¹	R ²	R ³	R ⁴	Alkylating reagent ^a	Nucleoside : alkylating reagent : sodium hydride	Reaction conditions	Yield (%)	Ref.
	H	H	NH ₂	NH ₂	MeO((CH ₂) ₂ O) _n (CH ₂) ₂ I (<i>n</i> = 0, 1, 2, 4)	—	DMF, 5 h	—	90
	H	H	NH ₂	OH	AllBr	—	—	—	76
	H	H	NH ₂	Cl	MeI	—	DMF, −20 °C	45 ^e	91
	H	H	NH ₂	2-NO ₂ C ₆ H ₄ (CH ₂) ₂ O	MeI	1 : 1.9 : 0.9	DMF, −45 to 20 °C, 3 h	22	75
	H	H	NH ₂	2-NO ₂ C ₆ H ₄ (CH ₂) ₂ O	EtI	1 : 8 : 0.9	DMF, −50 to −15 °C, 6 h	13	75
	Tr	H	H	OMe	BnCl	1 : 42 : 1.5	PhH–dioxane, 20 °C	41	92
	2,4-Cl ₂ C ₆ H ₃ CH ₂	2,4-Cl ₂ C ₆ H ₃ CH ₂	H	OMe	MeO(CH ₂) ₂ Br	1 : 1.15 : 1	THF, Δ	78	93
	2,4-Cl ₂ C ₆ H ₃ CH ₂	2,4-Cl ₂ C ₆ H ₃ CH ₂		OBn	MeO(CH ₂) ₂ Br	1 : 1.15 : 1	THF, Δ	93	93
	H	H	NH ₂	—	MeI	1 : 1.03 : 1.2	DMF, 0 °C, 3.5 h	—	74
	H	H	NH ₂	—	MeI	1 : 1.1 : 1.6	DMF, 0 to 20 °C, 10 h	25 ^b	75
	H	H	NH ₂	—	EtI	1 : 21 : 1	DMF, 0 to 20 °C, 10 h	14 ^b	75
	H	H	NH ₂	—	BnCl	1 : 30 : 5	DMF, 20 °C	12	94
	Tr	TIPDS	NHCOPr ⁱ	—	MeI	—	DMF	79	95
	Tr	Tr	NHBz	—	BnCl	1 : 2 : 2	PhH–dioxane, 20 °C	48	96
	DMTr	H	NC(CH ₂) ₂	—	MeI	1 : 8 : 1.6	DMF, −50 to −15 °C, 6 h	33	75
	2,4-Cl ₂ C ₆ H ₃ CH ₂	2,4-Cl ₂ C ₆ H ₃ CH ₂	BnOCH ₂	—	MeI	1 : 1.15 : 1	THF, Δ	98	93
	2,4-Cl ₂ C ₆ H ₃ CH ₂	2,4-Cl ₂ C ₆ H ₃ CH ₂	BnOCH ₂	—	AllBr	1 : 1.15 : 1	THF, Δ	88	93
	2,4-Cl ₂ C ₆ H ₃ CH ₂	2,4-Cl ₂ C ₆ H ₃ CH ₂	BnOCH ₂	—	PrBr	1 : 1.15 : 1	THF, Δ	67	93
	2,4-Cl ₂ C ₆ H ₃ CH ₂	2,4-Cl ₂ C ₆ H ₃ CH ₂	BnOCH ₂	—	Pr ⁱ Br	1 : 1.15 : 1	THF, Δ	20	93
	2,4-Cl ₂ C ₆ H ₃ CH ₂	2,4-Cl ₂ C ₆ H ₃ CH ₂	BnOCH ₂	—	EtO ₂ CCH ₂ Br	1 : 1.15 : 1	THF, Δ	97	93
	2,4-Cl ₂ C ₆ H ₃ CH ₂	2,4-Cl ₂ C ₆ H ₃ CH ₂	BnOCH ₂	—		1 : 1.15 : 1	THF, Δ	72	93
	2,4-Cl ₂ C ₆ H ₃ CH ₂	2,4-Cl ₂ C ₆ H ₃ CH ₂	BnOCH ₂	—	 R-isomer	1 : 1.15 : 1	THF, Δ	34	93
	2,4-Cl ₂ C ₆ H ₃ CH ₂	2,4-Cl ₂ C ₆ H ₃ CH ₂	BnOCH ₂	—	 S-isomer	1 : 1.15 : 1	THF, Δ	35	93
	2,4-Cl ₂ C ₆ H ₃ CH ₂	2,4-Cl ₂ C ₆ H ₃ CH ₂	BnOCH ₂	—	PhthN(CH ₂) ₄ Br	1 : 1.15 : 1	THF, Δ	64	93
	2,4-Cl ₂ C ₆ H ₃ CH ₂	2,4-Cl ₂ C ₆ H ₃ CH ₂	BnOCH ₂	—	MeO(CH ₂) ₂ Br	1 : 1.15 : 1	THF, Δ	83	93

Table 6 (continued).

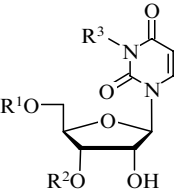
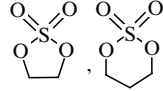
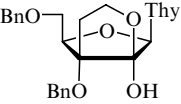
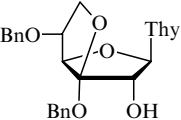
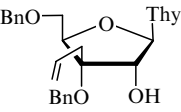
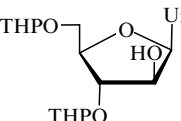
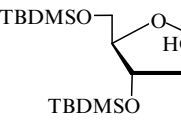
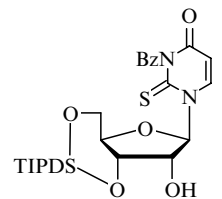
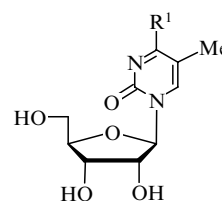
Nucleoside	R ¹	R ²	R ³	R ⁴	Alkylating reagent ^a	Nucleoside : alkylating reagent : sodium hydride	Reaction conditions	Yield (%)	Ref.
	2,4-Cl ₂ C ₆ H ₃ CH ₂	2,4-Cl ₂ C ₆ H ₃ CH ₂	BnOCH ₂	—	MeO((CH ₂) ₂ O) _n (CH ₂) ₂ Br (<i>n</i> = 1, 2, 3)	1 : 1.15 : 1	THF, Δ	89, 76, 24	93
	2,4-Cl ₂ C ₆ H ₃ CH ₂	2,4-Cl ₂ C ₆ H ₃ CH ₂	BnOCH ₂	—	C ₁₀ H ₂₁ O((CH ₂) ₂ O) ₃ (CH ₂) ₂ Br	1 : 1.15 : 1	THF, Δ	61	93
		TIPDS	BnOCH ₂	—	MeI	1 : 10 : 1.2	DMF, 0 °C, 2 h	71 ^f	97
		TIPDS	BnOCH ₂	—	EtO ₂ CCH ₂ Br	1 : 5 : 2.2	DMF, −5 °C, 1.5 h	98	98
		TIPDS	TrS	—	Bu ^t O ₂ CCH ₂ Br	1 : 4 : 4	THF, 18 h	78	99
	H	H	BnOCH ₂	—		—	DMF, −45 to 20 °C	63, 50	100, 101
	Tr	Tr	H	—	BnCl	1 : 20 : 10	DMF, 20 °C	33 ^g	102
	Tr	Tr	H	—	BnCl	1 : 20 : 0.9	DMF, 20 °C	60	103
	—	—	—	—	MeI	1 : 7.4 : 2	CH ₂ Cl ₂ , 36 °C, 23 h	62	104
	—	—	—	—	MeI	1 : 2.6 : 7.5	CH ₂ Cl ₂ , 20 °C, 48 h	62	105
	—	—	—	—	MeI	1 : 5 : 3	THF, 0 °C, 2 h	84	106
	—	—	—	—	AllBr	1 : 2 : 2	THF, 20 °C, 17 h	40	107, 108
	—	—	—	—	AllBr	1 : 2.5 : 2.5	THF, 20 °C, 16 h	32	107, 108

Table 6 (continued).

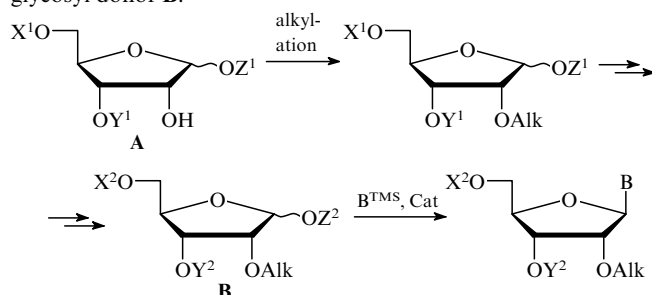
Nucleoside	R ¹	R ²	R ³	R ⁴	Alkylating reagent ^a	Nucleoside : alkylating reagent : sodium hydride	Reaction conditions	Yield (%)	Ref.
	—	—	—	—	MeI	—	PhH	—	53
	NH ₂ OH	— —	— —	— —	AllBr AllBr	— —	— —	— —	76 76

Note. ^a Abbreviations: Im, imidazolyl, Phth, phthaloyl; ^b The yield for a three-step synthesis (protection of the heterocyclic base, dimethoxytritylation, alkylation) is indicated; ^c the yield of a mixture of 2'- and 3'-isomers is indicated; ^d the yield over two steps (Markiewicz protection and alkylation) is indicated; ^e the total yield over two steps is indicated; ^f the yield over two steps (alkylation and desilylation) is indicated; ^g the yield of 2'-*O*-benzyl-3',5'-di-*O*-trityl-3-benzyluridine is indicated.

purine riboside was used as the starting compound seems to be a very promising approach to the large-scale synthesis of 2'-*O*-alkylguanosine derivatives. The total yield of alkylation and hydrolysis to 2'-*O*-alkylguanosine is ~ 45%; the use of expensive reagents is avoided.

V. Preparation of 2'-*O*-alklynucleosides by glycosylation of heterocyclic bases

The data on the synthesis of 2'-*O*-alklynucleosides by glycosylation of heterocyclic bases are summarised in Tables 7 and 8. This involves two steps, *viz.*, the alkylation of a partially protected carbohydrate and the glycosylation itself. In some cases, the alkylation of the 2-hydroxy group of the carbohydrate **A** is followed by a series of transformations in order to obtain the glycosyl donor **B**.



B^{TMS} is a silylated heterocyclic base;

$X^1, X^2, Y^1, Y^2, Z^1, Z^2$ are protective groups.

The synthesis of 2'-*O*-alklynucleosides by glycosylation of heterocyclic bases was proposed in the early 1970's by Haines.¹⁰⁹ 2'-*O*-Methyluridine was synthesised starting from the partially protected β -D-ribofuranoside **15**, the total yield being as low as 5%.

In the early 1980's, Imbach *et al.*^{110, 111} performed the synthesis of pyrimidine 2'-*O*-methylnucleosides (total yield 50% – 55%) starting from the accessible 1,3,5-tri-*O*-benzoyl- β -D-ribofuranose (**16**). Later, this approach was used by Cook *et al.*¹¹² for the synthesis of 2'-*O*-methyluridines containing various substituents at C⁵. The use of $CF_3SO_3SiMe_3$ instead of $SnCl_4$ as a glycosylation catalyst made it possible to increase the yields of target nucleosides in some cases (see Table 8).

Keller and Haner¹¹³ carried out the alkylation of the partially protected β -D-ribofuranoside (**17**) with *tert*-butyl bromoacetate in the presence of sodium hydroxide under conditions of phase-transfer catalysis. The desilylation with methanol and sulfuric acid was accompanied by transesterification of the *tert*-butyl ester and partial anomerisation. The glycosylation of thymine and adenine derivatives was stereoselective, the total yield was 15%.

Parmentier *et al.*¹¹⁴ have succeeded in obtaining methyl 2-*O*-methyl-D-ribofuranoside in four steps without the isolation of intermediate products (yield ~ 75%). If the intermediate products had to be isolated in each step, the total yield decreased to 8%.

Cook *et al.*^{78, 79} have performed the alkylation of the partially protected methyl β -D-ribose (**19**) (see Table 7) with ethyl bromoacetate. Subsequent glycosylation according to Vorbrüggen¹²¹ gave the target nucleoside (see Table 8).

Table 7. Synthesis of protected 2-*O*-alkylcarbohydrates as precursors of 2'-*O*-alklynucleosides.

Blocked carbohydrate	Compound No.	Alkylating reagent	Yield of the alkylation product (%)	Ref.
	15	CH_2N_2	88	109
	16	$CH_2N_2, BF_3 \cdot Et_2O$ $CH_2N_2, BF_3 \cdot Et_2O$	74 71	110, 111 112
	17	$BrCH_2CO_2Bu^t, NaOH, BnBu_3N^+Cl^-$ MeI, NaH $BrCH_2CO_2Et, NaH, DMF, 20^\circ C, 3 h$	67 ^a 75 74	113 114 115
	18	MeI, NaH 1) $HC \equiv CCH_2Br, NaH$; 2) $B_{10}H_{14}$	80 55	42 116
	19	$BrCH_2CO_2Et, NaH, DMF$	95	78, 79
	20	$MeI, BDDDP$ MeI, NaH	42 ^b 96 ^a	117, 118 117, 118
	21	MeI, NaH $CH_2=CHCH_2OC(O)Cl, DMAP,$ $Pd(OAc)_2, Ph_3P$	70 87	119 119

^a The yield for the alkylation of the β -anomer is indicated; ^b the yield for the alkylation of the α -anomer is indicated.

Table 8. Glycosylation of heterocyclic bases with 2-*O*-alkylcarbohydrates.

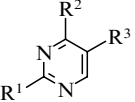
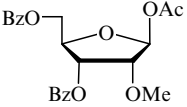
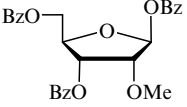
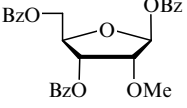
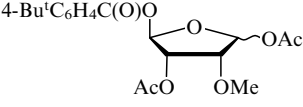
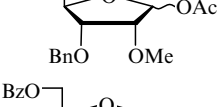
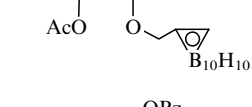
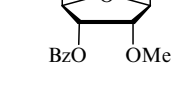
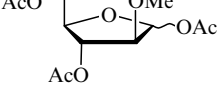
Heterocyclic base	R ¹	R ²	R ³	Glycosyl donor	Reaction conditions	Yield of the β-nucleoside (%) (α : β ratio)	Ref.
	OTMS	OTMS	H		SnCl ₂ , (CH ₂ Cl) ₂ , 20 °C, 24 h	24	109
	OTMS	OTMS	H		SnCl ₄ , 20 °C	74 70	110 111
	OTMS	OTMS	H		TMS – OTf, MeCN, 20 °C, 0.5 h	75	112
	OTMS	OTMS	H		20 °C, 16 h	55–70	42
	OTMS	OTMS	H		TMS – OTf, MeCN, 20 °C, 2–3 h	65 (1 : 4)	114
	OTMS	OTMS	H		TMS – OTf, MeCN, 20 °C, 4 h	71	116
	OTMS	OTMS	Me		TMS – OTf, MeCN, 20 °C, 0.5 h	55	112
	OTMS	OTMS	Me		TMS – OTf, (CH ₂ Cl) ₂ , 20 °C, 9 days	37 (2 : 3)	117, 118

Table 8 (continued).

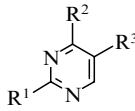
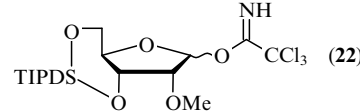
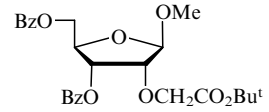
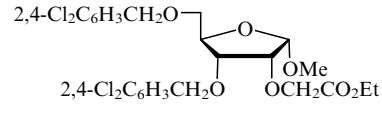
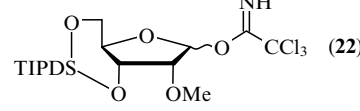
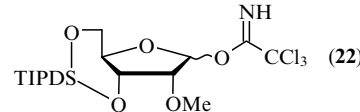
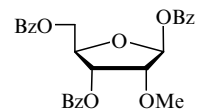
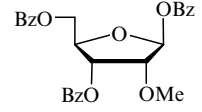
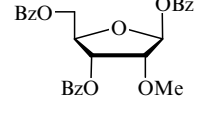
Heterocyclic base	R ¹	R ²	R ³	Glycosyl donor	Reaction conditions	Yield of the β-nucleoside (%) (α : β ratio)	Ref.
	OTMS	OTMS	Me		TMS–OTf, MeCN, 20 °C, 5 min TMS–OTf, (CH ₂ Cl) ₂ , 20 °C	94 93	119 121
	OTMS	OTMS	Me		TMS–OTf, 20 °C, 30 min	79	113
	OTMS	OTMS	Me		BSA, TMS–OTf, (CH ₂ Cl) ₂ , Δ	44	78, 79
	OTMS	OTMS	CH ₂ N ₃		TMS–OTf, MeCN, 20 °C, 5 min	62	120
	OTMS	OTMS	CH ₂ NPhth		TMS–OTf, MeCN, 20 °C, 5 min	61	120
	OTMS	OTMS	CF ₃		TMS–OTf, MeCN, 20 °C, 30 min	62	112
	OTMS	OTMS	F		TMS–OTf, MeCN, 20 °C, 30 min	68	112
	OTMS	OTMS	NO ₂		TMS–OTf, MeCN, 20 °C, 30 min	56	112

Table 8 (continued).

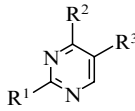
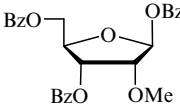
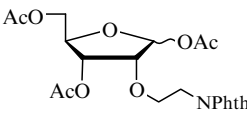
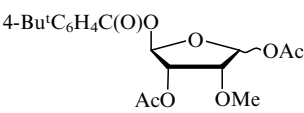
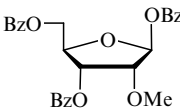
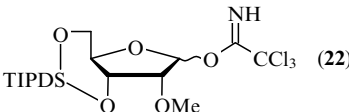
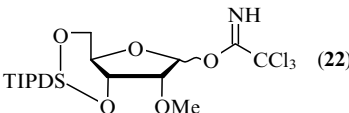
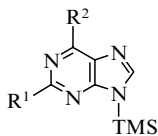
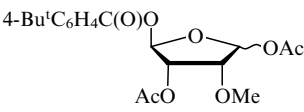
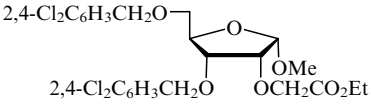
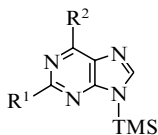
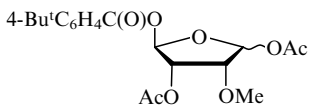
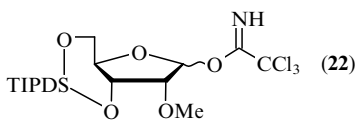
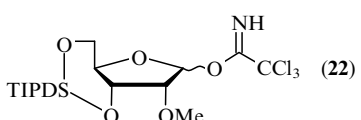
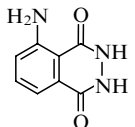
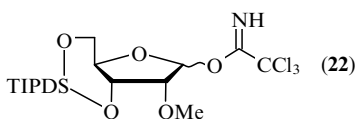
Heterocyclic base	R ¹	R ²	R ³	Glycosyl donor	Reaction conditions	Yield of the β-nucleoside (%) (α : β ratio)	Ref.
	OTMS	OTMS	CN		TMS–OTf, MeCN, 20 °C, 30 min	88	112
	OTMS	OTMS	I		TMS–OTf, (CH ₂ Cl) ₂ , –20 to 0 °C, 3 h	82 (1 : 2)	115
	OTMS	NHAc	H		20 °C, 16 h	55–70	42
	OTMS	NHBz	H		SnCl ₄ , 20 °C	70	110, 111
	OTMS	NHBz	Me		TMS–OTf, MeCN, 20 °C, 5 min	95	119
	STMS	OTMS	Me		TMS–OTf, MeCN, 20 °C, 5 min	71	120
	H	NHBz	—		TMS–OTf, MeCN, Δ, 3–5 h	55–70	42
	H	NHBz	—		SnCl ₄	63	113

Table 8 (continued).

Heterocyclic base	R ¹	R ²	R ³	Glycosyl donor	Reaction conditions	Yield of the β -nucleoside (%) (α : β ratio)	Ref.
	NHC(O)CH ₂ OPh	NH ₂	—		TMS–OTf, MeCN, Δ, 3–5 h	55–70	42
	NHC(O)CH ₂ OPh	H	—	 (22)	TMS–OTf, MeCN, 20 °C, 5 min	77	119
	NHC(O)Bu ^t	4-NO ₂ C ₆ H ₄ (CH ₂)O	—	 (22)	TMS–OTf, MeCN, 20 °C, 5 min	86	119
	—	—	—	 (22)	TMS–OTf, MeCN, 20 °C, 5 min	80	119

Note. Abbreviations: TMS–OTf, trimethylsilyl trifluoromethanesulfonate; BSA, *N,O*-bis(trimethylsilyl)acetamide.

Both anomers of 1-*N*-(2-*O*-methyl-D-arabinofuranosyl)thymine were prepared from the blocked carbohydrate **20** by Gotfredsen *et al.*^{117, 118} (see Table 7). It should be noted that no alkylation of the α -anomer of the monosaccharide derivative occurred in the presence of sodium hydride, whereas the yield of the alkylation product in the presence of BDDDP was only 42%. In the case of the β -anomer, the reaction with sodium hydride as a base was virtually quantitative.

In 1994, Chanteloup *et al.*¹¹⁹ published a paper, which described conversion of compound **21** into the *O*-trichloroacetimidate **22**. The latter served as a stereoselective and a high-

yielding donor (see Table 8). The total yield was 35%–45%. Later, the glycosylation of compound **22** was studied in more detail.¹²⁰ It is known¹²² that glycosylation with β -D-ribofuranose *O*-trichloroacetimidates follows the S_N2 mechanism with inversion of configuration of the C¹ atom. This suggests that the synthesis of the target β -nucleoside requires the α -anomer of the *O*-trichloroacetimidate. However, the thermodynamically and kinetically more stable β -anomer [yields 39% (α : β = 7:93) and 77% (α : β = 1:99), respectively] is predominantly formed in the presence of NaH and DBU (diazabicycloundecene). The α -anomer was predominantly formed only with K₂CO₃ as the base (total yield 71%, α : β = 93:7). Hence, this approach can be used for the synthesis of both α - and β -nucleosides.

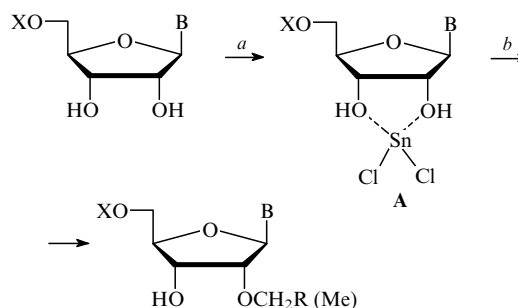
An elegant synthesis of 2'-*O*-alkynucleosides **23** and **24** (total yields 35%–40%) from the commercially available allofuranose derivative **18** has been described (Scheme 1).^{51, 116}

Although glycosylation is rather tedious and is seldom used, it is appropriate for the synthesis of 2'-*O*-alkylated ribothymidine^{78, 79, 112, 113, 118–120} and large-scale syntheses of modified 2'-*O*-alkynucleosides.

Glycosylation is the limiting step. It often proceeds non-stereoselectively and yields a mixture of α - and β -anomers. In addition, it strongly depends on the nature of the substituent at the C(2') atom and does not always give satisfactory yields of target products in the case of purine bases.

VI. Alkylation of the activated *cis*-diol group of nucleosides in the presence of transition metal compounds

In the alkylation of the *cis*-diol group of nucleosides with alkyl halides or diazoalkanes in the presence of transition metal compounds (Tables 9–11), the transition metal is activated due to complex formation. In this case, the reaction may be carried out with nucleosides with non-protected 2'- and 3'-hydroxy groups. The main advantage of this approach is that the reaction proceeds in the absence of a base, which eliminates the necessity to protect the imino groups of the heterocyclic bases and functional groups of alkyl halides. However, the alkylation by this method yields considerable amounts of 3'-isomers which are hardly separable from the target 2'-*O*-alkynucleosides owing to their similar chromatographic mobilities. In some cases, the isomeric mixture can be separated by crystallisation; more often, the modified nucleoside is first subjected to 5'-*O*-dimethoxytritylation and then to chromatography. The best ratio of the 2'- and 3'-isomers was achieved by alkylation of nucleosides in the presence of tin chloride^{123–134} (see Table 9). In this reaction, it is the tin derivative **A** initially formed that undergoes alkylation.



B = Ura.

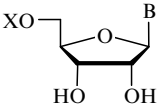
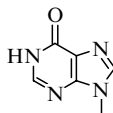
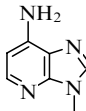
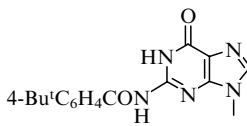
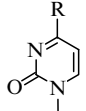
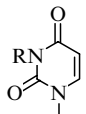
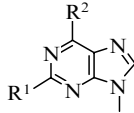
B = Ura, Cyt^{Ac}, Ade^{Bz}, Gua^{PheAc}.

(a) NaH, BzCl ; (b) B₁₀H₁₄; (c) H⁺; (d) BzCl; (e) NaIO₄; (f) Py, H₂O; (g) Ac₂O, Py; (h) B^{TMS}, TMS–OTf; (i) MeONa, MeOH; (j) MeI, NaH; (k) 4-Bu^tC₆H₄COCl, Py; (l) NaOH.

(a) SnCl₂; (b) RCHN₂ or MeI.

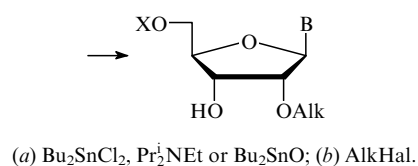
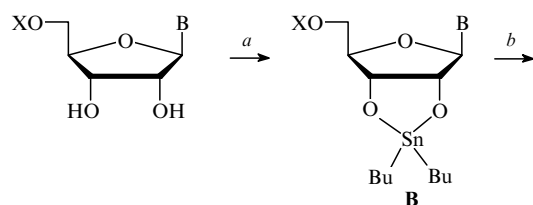
Yet another alkylation procedure in the presence of tin derivatives was proposed by Wagner *et al.*¹³⁵ The starting compound is treated consecutively with dibutyltin dichloride and dibutyltin oxide and alkyl halide with 2',3'-*O*-dibutylstannylene nucleosides **B** as intermediates. Later, this method was used for

Table 9. Alkylation of the activated *cis*-diol group of nucleosides with diazomethane in the presence of SnCl₂.

Nucleoside	X	B	Nucleoside : alkylating reagent : SnCl ₂	Reaction conditions	Yield of the 2'-isomer (%) (2' : 3' ratio)	Ref.	
Ado			1 : 3 : 0.18	MeOH – DME, 20 °C	38 (1.7 : 1)	123	
			1 : 3 : 0.06	MeOH – DME, 20 °C	30 (1 : 2)	124	
			1 : 3 : 0.02	DME, 20 °C, 8 h	27 ^a	125	
Urd			1 : 3 : 0.06	MeOH – DME, 20 °C	40 (~ 2 : 1)	124	
			1 : 3 : 0.02	DME, 20 °C, 8 h	30 ^a	125	
Cyd			1 : 3 : 0.18	MeOH – DME, 20 °C	74 (2 : 1)	123	
			1 : 3 : 0.06	MeOH – DME, 20 °C	35 (5 : 1)	124	
			1 : 3 : 0.02	DME, 20 °C, 8 h	34 ^a	125	
			1 : 3 : 0.2	MeOH – DME, 20 °C	67 (6.2 : 1) ^b	126	
Guo			1 : 3 : 0.06	MeOH – DME, 20 °C	15 (1 : 1)	124	
			1 : 3 : 0.02	DME, 20 °C, 8 h	16 ^a	125	
1a			—	EtOH – DME, 20 °C	34 ^c	127	
			1 : 3 : 0.02	DME, 20 °C, 8 h	21 ^a	125	
1c			1 : 3 : 0.11	MeOH – DME, 20 °C	40 (5 : 1)	35	
	H		1 : 3 : 0.02	DME, 20 °C, 8 h	21 ^a	131	
	TBDPS	Gua	1 : 3 : 0.18	MeOH – DME, 50 °C	22 (1 : 2)	128	
	DMTr	Ura	1 : 3 : 0.2	DMF, 50 °C, 8 h	41	129	
	H		1 : 3 : 0.2	MeOH – DME, 20 °C, 8 h	20 (2 : 1)	130	
	DMTr	Ade	1 : 1.6 : 0.04	DMA ^d , DMSO, CH ₂ Cl ₂ , dioxane, –10 °C, 45 min	63 (2 : 1)	131	
	DMTr		1 : 3 : 0.2	DMF, 50 °C, 8 h	43	129	
	DMTr		R = NHBz R = NPEOC(O)NH ^e	1 : 3 : 0.2 1 : 1.6 : 0.04	DMF, 50 °C, 8 h DMA, DMSO, CH ₂ Cl ₂ , dioxane, –10 °C, 45 min	49 87 (14 : 1)	129 131
	DMTr		R = H R = Bz	1 : 1.6 : 0.04 1 : 1.6 : 0.04	DMA, DMSO, CH ₂ Cl ₂ , dioxane, –10 °C, 45 min DMA, DMSO, CH ₂ Cl ₂ , dioxane, –10 °C, 45 min	74 (4.3 : 1) 65 (2.2 : 1)	131 131
	H		R ¹ = NH ₂ ; R ² = OEt	—	—	7	132
	H		R ¹ = R ² = NH ₂	1 : 3 : 0.2	DMF, 50 °C, 24 h	51 (~ 1 : 1)	133
	DMTr		R ¹ = H; R ² = NHBz	1 : 3 : 0.2	DMF, 50 °C, 8 h	36	129
	DMTr		R ¹ = NPEOC(O)NH; R ² = ONPE	1 : 1.6 : 0.04	DMA, DMSO, CH ₂ Cl ₂ , dioxane, –10 °C, 45 min	79 (4 : 1)	131
	Tr		R ¹ = H; R ² = NHTr	1 : 1.1 : 0.25	DMF, 0 °C, 18 h	21 ^f	134

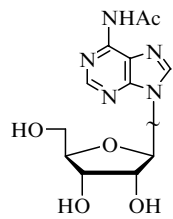
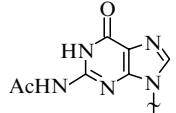
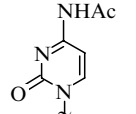
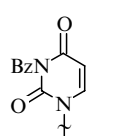
Note. ^a Alkylation with PhCHN₂; ^b alkylation with MeI; ^c the yield over two steps (alkylation and amination) is indicated; ^d DMA, dimethylacetamide; ^e NPE = 4-NO₂C₆H₄(CH₂)₂; ^f alkylation with Me₃SiCHN₂.

the synthesis of various 2'-*O*-alklynucleosides^{135–145} (see Table 10).



The intermediate tin derivative **B** is much more stable than the derivative **A**. In addition to tin salts, other metal salts were

Table 10. Alkylation of the activated *cis*-diol group of nucleosides in the presence of equimolar amounts of dibutyltin dichloride or dibutyltin oxide.

Nucleoside	Alkylating reagent	Nucleoside : alkylating reagent	Reaction conditions	Yield of the 2'-isomer (%) (2' : 3' ratio)	Ref.
Urd	MeI	1 : 2	DMF, 20 °C, 18 h	35 (2 : 1)	135
	MeI	1 : 2	DMF, 20 °C, 18 h	7	136
	H ₂ C=CHCH ₂ Br	see ^a	DMF, Bu ₄ NBr, 20 °C	49 (1.8 : 1)	137
	HC≡CCH ₂ Br	1 : 2	DMF, 120 °C, 6 h	~ 50 (~ 1.5 : 1)	138, 139
	PhthN(CH ₂) ₃ Br ^b	—	—	16.8	80
	PhthN(CH ₂) ₃ Br ^b	—	DMF, 130 °C	14	140, 141
	ClCH ₂ O(CH ₂) ₃ Br	1 : 1.3	(CH ₂ Cl) ₂ , 70 °C, 15 min	38 (1.25 : 1)	142
	BnCl	1 : 2	DMF, 100 °C, 1 h	31 (2 : 1)	135
Cyd	PhthN(CH ₂) ₃ Br ^b	—	—	16.8	80
	ClCH ₂ O(CH ₂) ₃ Br	1 : 1.3	(CH ₂ Cl) ₂ , 70 °C, 15 min	51 (2.5 : 1)	142
	ClCH ₂ O(CH ₂) ₃ Br	1 : 1.3	(CH ₂ Cl) ₂ , 70 °C, 15 min	60 (1.25 : 1)	142
	ClCH ₂ O(CH ₂) ₃ Br	1 : 1.3	(CH ₂ Cl) ₂ , 70 °C	45 (1 : 0.4)	142
	2-(BrCH ₂)AQ ^c	see ^d	DMF, CsF, 20 °C, 48 h	31 (1.8 : 1)	143
	2-(BrCH ₂)AQ ^c	see ^d	DMF, CsF, 20 °C, 48 h	30 (1.8 : 1)	144
	2-(BrCH ₂)AQ ^c	1 : 2	DMF, 20 °C, 48 h	35 (1.4 : 1)	145

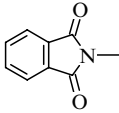
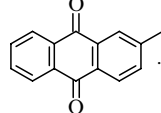
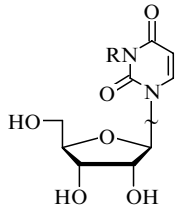
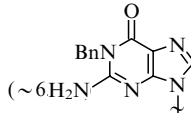
^a The nucleoside : AllBr : Bu₄NBr ratio is 1 : 1.2 : 1.1; ^b PhthN = . ^c AQ = . ^d the nucleoside : 2-(bromomethyl)anthraquinone : CsF ratio is 1 : 2 : 2.5.

Table 11. Alkylation of the activated *cis*-diol group of nucleosides by trimethylsulfonium hydroxide in the presence of acetylacetonates.

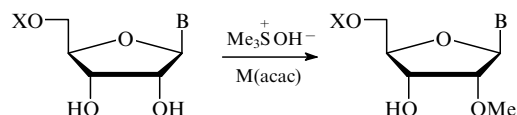
Nucleoside	M(acac)	Yield of the 2'-isomer (%) (2' : 3' ratio)	Ref.	Nucleoside	M(acac)	Yield of the 2'-isomer (%) (2' : 3' ratio)	Ref.
Cyd	Cu(acac)	60 (~ 3 : 1)	148				
	Mg(acac)	43 (10 : 1)	149				
Ado	Cu(acac)	45 (1 : 1)	148		R = Me	18 (~ 1.2 : 1)	148
	Mg(acac)	21 (~ 2 : 1)	149		R = Me	65 (20 : 1)	149
	Sr(acac)	75 (10 : 1)	91 ^a		R = Bn	62	149
Guo	Cu(acac)	18 (~ 1.2 : 1)	148				
Urd	Mg(acac)	21 (20 : 1)	149				
						Ag(acac)	70 91 ^b

Note. The reactions were carried out with the nucleoside : Me₃S⁺OH⁻ : M(acac) ratio of 1 : 2 : 0.5 in DMF (70 °C, 1 h). ^a The nucleoside : Me₃S⁺OH⁻ : Sr(acac) ratio in DMF (75 °C, 30 min) is 1 : 1.3 : 1.3; ^b the nucleoside : Me₃S⁺OH⁻ : Ag(acac) ratio in DMF (70 °C, 2 h) is 1 : 1.3 : 1.3.

tested,^{131, 146} but the degree of conversion in the alkylation and the ratio of the 2'- and 3'-isomers could not be increased.

It should be noted that sometimes the alkylation of the *cis*-diol group in the presence of cesium fluoride¹⁴⁷ affords larger amounts of the 2'-isomer. However, the addition of CsF in the alkylation of 2',3'-*O*-dibutylstannylene-*N*³-benzoyluridine slightly increased the selectivity, but the total yield of the reaction products decreased^{144, 145} (see Table 10).

The methylation of nucleosides with trimethylsulfonium hydroxide in the presence of transition metal acetylacetonates (Cu, Co, Zn, *etc.*) (see Table 11) is less popular.^{148, 149}



acac is the acetylacetonate residue, M is the transition metal.

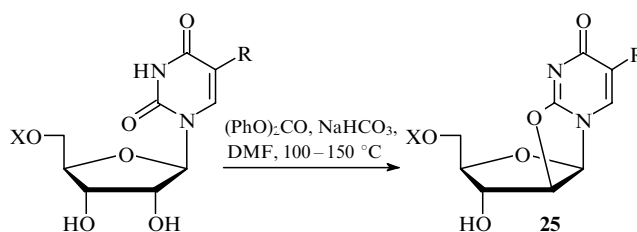
This approach eliminates the alkylation of heterocyclic bases (except for uracil) and provides high yields in certain cases. Later, it was shown⁹¹ that the maximum selectivity of nucleoside alkylation is achieved in the presence of silver acetylacetonates (for protected guanosine), strontium acetylacetonate (for adenosine) and magnesium acetylacetonate (for cytidine and protected uridine).¹⁴⁹ Nevertheless, this procedure is hardly suitable for the introduction of other alkyl groups into nucleosides.

VII. Synthesis of pyrimidine 2'-*O*-alkynucleosides from O²,2'-anhydronucleosides

In addition to direct alkylation of ribonucleosides, pyrimidine 2'-*O*-alkynucleosides are synthesised starting from O²,2'-anhydronucleosides. This approach is attractive because the synthesis of the anhydronucleoside results in both the activation of the C(2') atom and elimination of the possibility of the reaction of the N³ atom of the heterocyclic base.

The synthesis of the now commercially available O²,2'-anhydrouridine and its derivatives is performed using different methods.^{150, 151} Most often, this involves heating of uridine and its derivatives with diphenyl carbonate in the presence of sodium hydrogen carbonate as base. The O²,2'-anhydrouridine deriva-

tives **25** are easily purified by recrystallisation; the yields are ~ 90% (Table 12).



X is H or protective groups; R = H, Me.

It has been shown¹⁵² that no alkoxylation of nucleosides with magnesium alkoxides occurs in the presence of blocked 3'-hydroxy groups, presumably due to the necessity of its involvement in the coordination of magnesium. Similar conclusions were made by Ross *et al.*¹⁵⁴ for the alkoxylation with trialkyl borates. It is suggested that if magnesium alkoxides are used, the 5'-hydroxy group was protected with the dimethoxytrityl group. Later,¹⁵³ the alkoxylation of anhydrouridine containing a non-protected 5'-hydroxy group with magnesium methoxide was carried out under similar conditions. If aluminium alkoxides and trialkyl borates are used, the alkoxylation at the C(2') atom occurs with a free 5'-hydroxy group.^{154, 157} Blommers *et al.*¹⁵⁸ did not synthesise alkoxides beforehand, but carried out a reaction with an alcohol in the presence of tetra(isopropoxy)titanium.

The alkoxylation of O²,2'-anhydrouridine with trimethyl borate was successfully employed by other authors.^{91, 159} Besides, the 2'-*O*-methylated product was obtained by the reaction of the fluorescent uridine analogue 1-(β-D-ribofuranosyl)-2,2'-anhydrobenzo[*g*]quinazoline-2,4(3*H*)-dione **26** with a twofold excess of (MeO)₃B [(MeO)₃CH, NaHCO₃, MeOH].¹⁶⁰

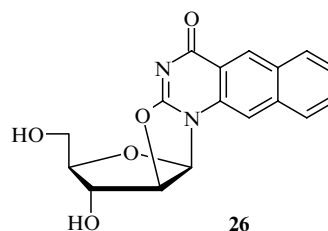
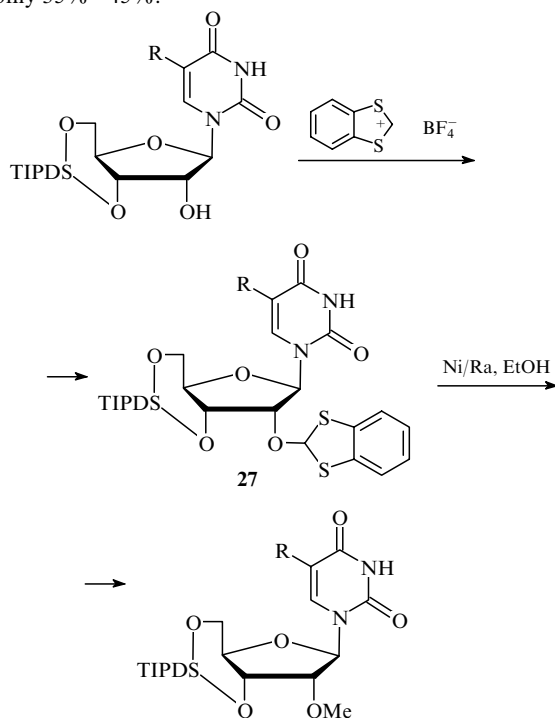


Table 12. Synthesis of pyrimidine 2'-*O*-alkynucleosides from O²,2'-anhydronucleosides.

R ¹	X	(R ² O) _n E	Nucleoside: (R ² O) _n E ratio	Reaction conditions	Yield (%)	Ref.
H	DMTr	(MeO) ₂ Mg	1 : 4	DMF, 100 °C, 4 h	88	152
H	DMTr	(EtO) ₂ Mg	1 : 6	DMF, 100 °C, 16 h	61	152
H	DMTr	(Pr ⁿ O) ₂ Mg	1 : 6	DMF, 100 °C, 16 h	62	152
H	DMTr	(AlO) ₂ Ca	1 : 40	DMF, 100 °C, 16 h	42	152
H	H	(MeO) ₂ Mg	1 : 4	MeOH, Δ, 5 h	92	153
H	H	(MeO) ₃ B	1 : 2	(MeO) ₃ CH, NaHCO ₃	86–97	154
Me	H	(MeO) ₃ B	—	MeOH	93	154
H	H	[PhthN(CH ₂) ₃ O] ₃ B	—	—	18	154
Me	H	[PhthN(CH ₂) ₂ O] ₃ B	1 : 2	THF, 150 °C, 24 h	21	155
Me	TBDPS	[PhthN(CH ₂) ₃ O] ₃ B	1 : 2	BH ₃ ·THF, (CH ₂ OH) ₂ , NaHCO ₃ , 150 °C, 16 h	50	77, 156
H	H	[MeO(CH ₂) ₂ O] ₃ Al	1 : 3	MeO(CH ₂) ₂ OH, Δ, 48 h	91	157
H	DMTr	PhthN(CH ₂) ₂ OH	1 : 5.8	Ti(OPr ⁱ) ₄ , NaHCO ₃ (cat), THF, 140 °C, 48 h	32	158

VIII. Other methods for the synthesis of 2'-O-alkynucleosides

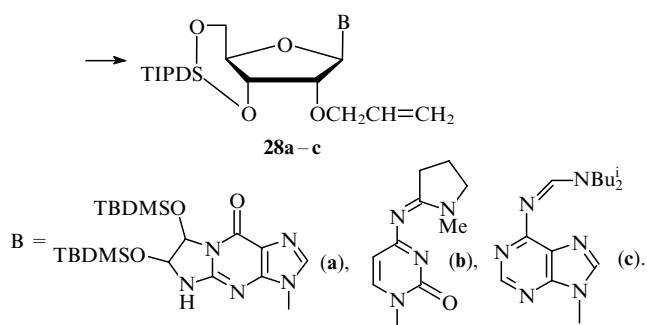
A modified procedure for a two-step methylation of nucleosides involving alkylation with 1,3-benzodithiolium tetrafluoroborate and subsequent reduction of the intermediate product **27** over Raney nickel was proposed by Sekine *et al.*¹⁶¹ This excludes the necessity of protecting the heterocyclic base and the amino groups additionally introduced into the heterocycle, but the overall yield is only 35%–45%.



R = H, CH₂N(Bn)CH₂CO₂Et.

Sproat *et al.*¹⁶² have succeeded in developing an efficient procedure for the synthesis of 2'-O-alkynucleosides by alkylating nucleosides with 3'- and 5'-hydroxy groups protected (the Markiewicz protective group) with allyl ethyl carbonate in the presence of a Pd(0) complex. A 2,5-dichlorobenzyl protective group was used to protect the OH group of the heterocycles.⁶⁶ The degree of conversion in the allylation of compounds **11a,b** and **12**¹⁶³ was 90% in 30 min and no side products were formed. However, this reaction can only be used for the synthesis of allyl ethers, since it proceeds *via* the intermediate allylpalladium(0) complexes. Later, this approach was used by Froehler *et al.*¹⁶⁴ for the preparation of 2'-O-allyl derivatives of 5-(propyn-1-yl)uridine and 5-(propyn-1-yl)cytidine.

Sproat *et al.*¹⁶⁵ have designed novel protective groups for heterocyclic bases which made it possible to reduce the number of steps in the synthesis of the 2'-O-allyl derivatives **28a–c** and to increase the overall yields of the target products, especially, in the case of the guanosine derivative **28a**.

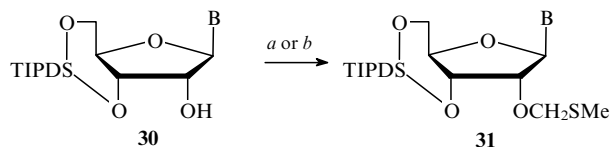


Direct allylation of the TIPDS-protected cytidine and adenosine derivatives (**29b,c**) is also possible, whereas earlier alkylation of uridine and inosine derivatives followed by transamination had to be performed.

A similar allylation procedure in which tetrakis(triphenylphosphine)palladium was used as a catalyst was proposed by Kumar *et al.*¹⁶⁶ This procedure allowed the alkylation of nucleosides bearing only the 5'-hydroxy protected group. With a 2.5-fold excess of allyl ethyl carbonate, the yields of the target allylation products of 5'-O-dimethoxytrityluridine and 5'-O-dimethoxytrityl-N⁴-benzoylcytidine were ~60%, whereas in the case of the stoichiometric ratio of the reactants the reaction involved predominantly the heterocyclic base (90%).

Subsequent modification of the allyl derivatives leading to the introduction of the aldehyde groups was repeatedly employed in different laboratories.^{167–170}

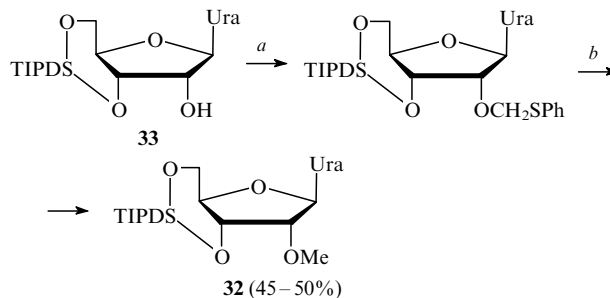
The alkylation of compounds **30** with dimethyl sulfide in the presence of dibenzoyl peroxide (yield 55%–70%) has been carried out.^{171,172} Later,¹⁷³ compounds **31** were prepared by the reaction with DMSO and acetic anhydride in the presence of acetic acid.



B = Ura, Cyt^{Bz}, Ade^{PhOAc}, Gua^{Buⁱ}.

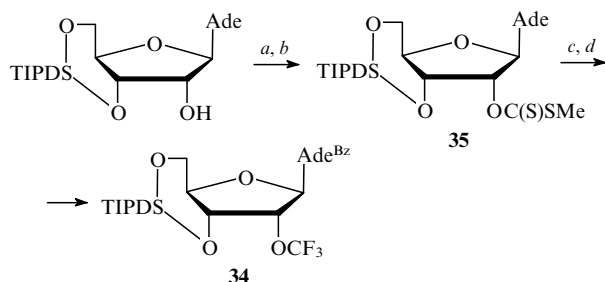
(a) Me₂S, Bz₂O₂, 2,6-lutidine; (b) DMSO, Ac₂O, AcOH.

This approach was used⁵¹ in a two-step synthesis of the 2'-O-methyluridine derivative **32** by alkylation of compound **33** with methyl phenyl sulfide and subsequent desulfurisation.



(a) MeSPh, Bz₂O₂, dimethylaminopyridine; (b) Bu₃SnH, Bz₂O₂.

Matsuda *et al.*¹⁷⁴ have synthesised 2'-O-trifluoromethyladenosine **34** *via* the intermediate 2'-methyl xanthate **35**.



(a) BuLi, CS₂, -78 °C; (b) MeI, -78 °C; (c) BzCl, Py;

(d) HF, Py, 1,3-dibromo-5,5-dimethylhydantoin.

The yield calculated over two steps was as low as 24% due to the formation of side products and partial removal of the Markiewicz protective group under the reaction conditions.

IX. Conclusion

The data considered above suggest that currently the methods for the synthesis of 2'-O-alkylnucleosides are well-developed, especially for the simplest representatives of this type of modified nucleoside, viz., 2'-O-methylnucleosides. Presumably, the main application of 2'-O-alkylnucleosides consists in their incorporation into oligonucleotides. The majority of modified oligonucleotides prepared from 2'-O-alkylnucleosides meet the major requirement, viz., the ability to form stable duplexes with the complementary regions of nucleic acids.

At present, the synthesis of 2'-O-alkylnucleosides is performed using two ideologically different approaches. One of them entails the maximum protection of all reactive centres of the molecule and, as a consequence, involves many steps. The other, in contrast, is aimed at the reduction of steps, which inevitably results in side reactions and, correspondingly, complicates the chromatographic separation of the reaction mixture. It should be noted that the total yield of the target product in the former approach is higher, as a rule. The advantage of the latter approach consists in the reduction of the time and cost of the synthesis.

Currently, the methods of nucleoside alkylation with diazomethane and trimethylsulfonium hydroxide, as well as with dialkyl sulfates in aqueous media, have only a historical significance. The most efficient procedure for the preparation of pyrimidine 2'-O-alkylnucleosides is the synthesis via O²,2'-anhydronucleosides and treatment with alkyl iodides in the presence of silver(I) oxide.⁴³ The alkylation of pyrimidine nucleosides with alkyl halides in the presence of transition metal derivatives can be recommended only for those cases where the reactants contain groups sensitive to strong bases, since this procedure yields a large amount of the 3'-isomer.

Alkylation in the presence of alkali metal hydrides is the method of choice for adenosine and its derivatives. It is of note that this method excludes the protection of 3'- and 5'-hydroxy groups as well as the functional groups of the heterocyclic base.

The use of cyclic sulfates as alkylating reagents is especially attractive, since the alkylation product can be subjected to further nucleophilic substitution.^{91, 92}

The alkylation of uridine and thymidine in the presence of alkali metal hydrides affords considerable amounts of the 3'-isomers. Therefore, the 3'- and 5'-hydroxy groups as well as the heterocyclic base should be protected. If this approach is chosen, 2'-O-alkylcytidine is prepared preferably by transamination of 2'-O-alkyluridine.

The optimum procedure for the synthesis of 2'-O-alkylguanosine and its derivatives proposed by Sproat *et al.*⁶⁴ is rather costly and cost reduction is hardly possible. The alkylation of 9-(β-D-ribofuranosyl)-6-chloro-2-aminopurine and subsequent conversion of the reaction product into guanosine derivatives is a promising alternative to this method.⁹¹ However, the conditions of this reaction were not optimised and the possibility of its

application in large-scale syntheses was not investigated. The use of transglycosylation is another promising approach;⁹¹ however, this reaction is extremely sensitive to both the structure of the aglycon and the substituent at the C(2') atom of the carbohydrate fragment and will hardly ever be used as a versatile procedure.

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Endohedral metal derivatives and exohedral fluorine derivatives of fullerenes

L N Sidorov, O V Boltalina

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Abstract. The thermodynamic studies of fullerenes and their stable derivatives, namely, endohedral metallofullerenes and exohedral fullerene fluorides, are generalised. The methods of synthesis and purification of fullerene fluorides are considered and the structures of these compounds are characterised. The thermodynamic properties of fullerenes and fullerene fluorides are discussed. The bibliography includes 150 references.

I. Introduction

In 1985, it was established experimentally that carbon, one of the most abundant elements in the Earth, can form stable cage structures consisting of 60 or more atoms.¹ This new allotropic form of carbon was termed 'fullerene.' The discovery of fullerenes was recognised as a remarkable and one of the most important events in science of the XX Century. In 1990, methods for the preparation of macroscopic quantities of fullerenes were developed² and methods for their isolation and purification were found.³ In addition, important structural and physicochemical characteristics of C₆₀ fullerene, which is the most frequently encountered representative of this class of compound, were determined. Currently, the total number of publications dealing with fullerenes exceeds 10 000, and the 'fullerene rush' has embraced fields of knowledge that seem to be far from one another such as astronomy and organic chemistry, solid-state physics and medical biology, inorganic chemistry and geology. Fullerenes can be classified as both inorganic materials (a new allotropic modification of carbon) and organic compounds because they exhibit many properties of unsaturated hydrocarbons in chemical transformations. More recently, unique possibilities of chemical modification of fullerenes have been found, including the addition of various functional groups at the double bonds to give exo derivatives, in particular, complexes with transition metals; insertion of atoms and whole clusters inside the carbon sphere (endo

derivatives) and replacement of some carbon atoms by heteroatoms (heterofullerenes).

It is impossible to cover all the results obtained during the last 10 years within the framework of one review. The purpose of this review is to shed light on some lines of research that have developed successfully in the chemistry of fullerenes and their endo metal and fluoro derivatives. The structure of this review corresponds to the chronological sequence of investigations. For example, in the early stages, especially in the experiments leading to the discovery of fullerenes, the crucial role was played by mass spectrometry. Therefore, the review begins with a description of mass-spectrometric studies dealing with determination of the fundamental characteristics of higher fullerenes and endohedral metal fullerenes such as ionisation energy and electron affinity.

The next important stage — fullerene functionalisation — is reflected by a series of works dealing with the synthesis of fluorinated derivatives. Primary attention is devoted to selective synthesis of individual compounds, which has required modification of traditional or development of new methods. The use of HPLC for separation and purification of fullerenes is described. Chromatographic studies in which the authors succeeded in isolating geometric isomers of individual fluorofullerenes are specially noted.

Systematic research into the physicochemical properties of fullerenes and their derivatives became possible only after thorough development of methods for the synthesis and purification of macroscopic quantities of these compounds. Study of fluorofullerenes by NMR spectroscopy and X-ray diffraction analysis revealed that the addition of fluorine atoms to the fullerene carbon atoms with formation of strong valence bonds results in a pronounced deformation of the carbon cage. This is illustrated taking the structures of flattened, squashed and indented fluorofullerenes as examples. The thermodynamic properties of fullerenes and their fluoro derivatives are discussed and the possible applications of fluorofullerenes are considered.

II. Ions and molecules of fullerenes and their derivatives in the gas phase

Electron affinity (*EA*) and ionisation energy (*IE*) are fundamental characteristics of molecules. For C₆₀ ([60]fullerene), the *EA* and *IE* values are equal to 2.667 ± 0.001 eV (see Ref. 4) and 7.57 ± 0.01 eV (see Ref. 5), respectively. This *EA* value is substantially higher than these values for most aromatic compounds, indicating a fairly high electron-withdrawing capacity of fullerene molecules.

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The combination of rather high electron affinity with low ionisation energy (for comparison, for the benzene molecule, IE is 9.24 eV and EA is negative), which is seldom encountered in chemistry, indicates that fullerene molecules can act as both electron donors and electron acceptors in chemical processes. The data concerning other representatives of this class of compound, so-called higher fullerenes, C_{2n} ($n > 30$), some of which can also be prepared in macroquantities, showed that they differ substantially in their properties from [60]fullerene. These differences are manifested, first of all, in fundamental characteristics such as ionisation energy and electron affinity.

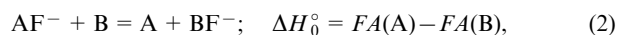
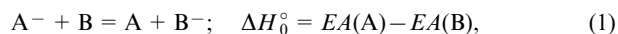
Experimental research of negative ions in the gas phase has been actively carried out since the 1970s. One experimental method used successfully to determine ions of non-volatile inorganic compounds was called 'the method of ion-molecular equilibria' (IME).⁶ This method is based on either the classical effusion technique with mass-spectroscopic detection of vaporisation products or high-temperature mass-spectrometry (Knudsen Cell Mass Spectrometry, KCMS), which is used to assess the contents of neutral species. The improved KCMS–IME procedure allows one to detect charged species present in the saturated vapour of inorganic compounds. To obtain measurable concentrations of ions in the vapours of inorganic compounds, salts such as $KAlF_4$ characterised by a low energy of heterolytic dissociation into ions, are added. Even at 1000 K, the vapours of these salts contain such high amounts of cations and anions that the Debye shielding radius becomes smaller than the effusion cell dimensions and, consequently, electron-free plasma is formed. The pressure of neutral species remains 5 to 7 orders of magnitude higher than the ion pressure.⁶ The addition of these salts to other inorganic compounds whose vapours do not contain measurable concentrations of ions results in systems with large amounts of ion-molecular associates. In particular, the addition of KF to the $Pt-MnF_3$ system gave rise to a set of negative ions including PtF_4^- and PtF_6^- and enabled the first direct experimental measurements of the EA values of platinum tetra- and hexafluorides.⁷ Subsequently, a series of studies dealing with the determination of the electron affinities of transition metal oxides and fluorides have been carried out.⁸ For several years, the authors of the review⁸ attempted to extend this method to organic compounds (in particular, compounds containing electronegative substituents and having high thermal stability, for example, perfluorinated derivatives) but were unable even to detect thermal anions (*i.e.*, those resulting from thermal ionisation). Therefore, when publications appeared pointing to unique properties of fullerenes⁹ and data on their thermal stability were obtained,^{10,11} it became clear that the use of the IME method to study compounds of this class may prove successful. The first publication opening a series of IME experiments aimed at determining the electron affinity and ionisation energy of fullerenes appeared in 1993.¹² The description of the IME method as applied to fullerenes has been reported in detail.¹² Here, we shall only consider several key procedural points and the most important results.

1. Procedure for the measurement of equilibrium constants of ion–molecule reactions and the proof of thermodynamic equilibration

The first task to be accomplished by experimentalists was to generate thermal negative ions in the fullerene vapour under equilibrium conditions and within temperature limits where fullerenes are still thermally stable. Of numerous experimental parameters, the electron work function of the metal surface is the most significant, because the efficiency of thermal ionisation resulting in the generation of ions largely depends on the properties of the surface where thermal ionisation takes place. In the IME method, this is the internal surface of the Knudsen effusion cell the work function for which can vary over a broad range. For example, the addition of alkali metals and their compounds to the cell decreases, while fluorination of the walls increases the electron work function for the internal surface of the effusion cell. Practi-

cally, it was possible to control the work function in the 4–6.5 eV range.^{13,14} The EA and IE values of fullerenes were found to be at the boundaries of this range. This opened up broad and unique opportunities for the generation of both positive and negative thermal ions of fullerenes and initiated an extensive series of studies involving fullerene gas-phase ions.

In the KCMS–IME analysis of charged species, the technique of relative measurements is widely used; this implies measurement of the equilibrium constants of isomolecular reactions with participation of a reference species (B), whose thermochemical characteristics have been reliably established



where ΔH_0° is the standard enthalpy of the reaction at 0 K, and EA and FA are the electron and fluoride-ion affinities, respectively.

The reference should have a volatility close to that of the specimen under study, and the absolute magnitude of the enthalpy of reactions (1) and (2) should not exceed 100 kJ mol⁻¹. Thus, the thermochemical characteristics of the reference should be similar to those of compound A under study determined in the reaction. When investigating the negative ions of fullerenes, the addition of alkali metal compounds was used to lower the work function. When working with cations, iron trifluoride was added to increase the electron work function of the internal surface of the nickel effusion cell.¹⁴

Yet another difficulty arising in the production of measurable concentrations of ions in fullerene vapours lies in the fact that the temperature of thermal ionisation of fullerenes does not coincide with their sublimation point. To attain the required degree of ionisation, the vapour should, most often, be superheated. It was proposed to use double effusion cells of 'Russian matreshka' type (Fig. 1). The more volatile substance (fullerene) was placed in the smaller cell and an inorganic fluoride was put in the larger one. By controlling the relative sizes of the effusion orifices in the internal and external cells, it was possible to desaturate the vapour of the volatile component by a factor of 7–10, so it became possible to raise the temperature without violating the conditions of molecular effusion from the orifice of the external cell.¹³ The experimental setup permitted the ratios of the partial pressures of both neutral and charged components of the vapour to be measured consecutively within one experiment. The neutral species were measured by recording the ion currents resulting from the electron impact on the molecular beam coming from the effusion cell. Then the ratio of partial pressures (p) was calculated using the equation relating the ion currents to the partial pressures of neutral species

$$\frac{p_A}{p_B} = \frac{I_A}{I_B} \frac{\sigma_B}{\sigma_A},$$

where I is the ion current intensity; σ the full ionisation section of the molecule.

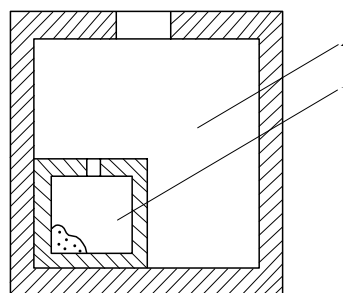


Figure 1. Effusion cell of the 'Russian matreshka' type: (1) internal cell with the fullerene; (2) external cell with the metal fluoride.¹³

The partial pressures of charged species were measured by recording the ion currents generated upon direct drawing of thermal ions out of the effusion cell by an electric field. The ratios of the pressures of thermal anions were calculated from the equation

$$\frac{p_{A^-}}{p_{B^-}} = \frac{I_{A^-}}{I_{B^-}} \frac{\sqrt{M_{A^-}}}{\sqrt{M_{B^-}}},$$

where M is the molecular mass. This gave the equilibrium constants of the ion–molecule reactions.

Particular attention was devoted to verification of the thermodynamic equilibration. For this purpose, the composition of the gas phase was varied over a broad range and the equilibrium constants were measured. At equilibrium, the constants determined for the same temperature should remain invariable, no matter how the partial pressures of the reactants (or products) may change.

The experimental data^{12,15} obtained for the reaction



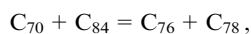
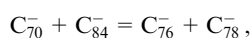
indicate that even upon a change in the $C_{60}:C_{70}$ ratio by two orders of magnitude, the equilibrium constant remains invariant to within the experimental error (Table 1). Similar verifications of

Table 1. Experimental values of the ion current intensity (I), the equilibrium constant (K_p) and the Gibbs energy ($\Delta_r G_T^\circ$) for reaction (3).¹⁵

System ^a	T/K	N^b	$I(C_{70}^+):I(C_{60}^+)$	$I(C_{60}^-):I(C_{70}^-)$	K_p	$\Delta_r G_T^\circ$ (see c)
1	810	1	1.52	0.33	0.36	6.83
	936	4	0.50	0.90	0.33	8.81
1 + 2	957	4	0.42	1.12	0.35	8.46
	966	2	0.67	0.76	0.37	7.90
	1019	3	0.60	0.87	0.38	8.13
	820	2	0.267	1.768	0.35	7.16
2	846	3	0.280	1.478	0.30	8.37
	865	2	0.310	1.222	0.27	9.22
	877	3	0.125	4.456	0.41	6.52
	887	2	0.195	1.844	0.32	8.48
	815	4	71.62	0.0073	0.38	6.49
3	826	5	60.56	0.0095	0.42	5.92
	836	4	80.26	0.0076	0.45	5.55
	854	3	56.58	0.0094	0.39	6.69
	872	3	13.02	0.0500	0.48	5.35

^a Composition of specimens: **1**, 50% C_{60} , 50% C_{70} ; **2**, 75% C_{60} , 24% C_{70} , 1% C_n ($n > 70$); **3**, 1.5% C_{60} , 98.5% C_{70} . ^b The number of measurements. ^c The $\Delta_r G_T^\circ$ value is expressed in kJ mol^{-1} ; the average $\Delta_r G_T^\circ$ is $7.77 \pm 1.43 \text{ kJ mol}^{-1}$.

the thermodynamic equilibration by varying the composition of the reaction mixtures have also been carried out for other reactions, in particular, for electron exchange in the vapours of higher fullerenes and for fluorine exchange. Conversely, it was found that in ionic and molecular reactions involving rearrangement of the fullerene carbon skeleton



no equilibrium is established, and the number of components in a mixture of higher fullerenes is determined as the number of substances.

2. Electron affinity, ionisation energy and electronegativity of higher fullerenes

Owing to the use of the KCMS–IME procedure, in addition to the frequently encountered C_{70} , C_{76} , C_{78} and C_{84} fullerenes, it was also possible to study other fullerenes¹⁵ present in the specimens in minor amounts (the dynamic range of measurable concentrations reaches eight orders of magnitude), up to C_{106} fullerene, which have not been isolated in a pure state. Due to the high sensitivity together with the capacity of mass-spectrometric analysis of the components, the KCMS–IME procedure is superior over traditional spectroscopic methods used to determine the EA and IE values, although the latter are, in principle, more accurate. An EA value for C_{60} fullerene found by the photodetachment method has been reported.⁹ The first experimental EA value for C_{70} fullerene was reported by Boltalina *et al.*;¹² later, this value was estimated from the photodetachment threshold of an electron from the C_{70}^- anions, which were preliminarily cooled upon collisions with helium atoms in an ASTRID storage ring.⁴ The resulting vertical electron affinity of C_{70} fullerene (2.68 eV) proved to be somewhat lower than the value (2.73 eV) determined from the KCMS–IME measurement of the electron exchange enthalpy, which is the adiabatic EA value.¹⁵ Note that the last-mentioned result is in good agreement with the results of measurements of the relative ion mobility of C_{60} and C_{70} in non-polar solvents¹⁶ and also with the EA estimates from the reduction electrochemical potentials of C_{60} and C_{70} , which also refer to the adiabatic electron affinity.¹⁷ Experimental data on the EA of higher fullerenes have been obtained only using the KCMS–IME procedure.¹⁵ Theoretical calculations^{18,19} have been carried out only for C_{74} – C_{84} molecules.

Particular attention should be paid to studies devoted to determination of isomer compositions of mixtures of higher fullerenes and to assignment of the experimental ionisation characteristics to the molecules of particular geometric isomers. According to published data, only for several fullerenes (C_{78} – C_{92}), was the isomer composition determined sufficiently reliably by analysing the structures of individual compounds obtained by chromatographic separation and by using NMR spectroscopy. Thus it was found that C_{76} fullerene forms only one isomer, C_{78} has two major isomers, and for C_{84} , seven geometric isomers have been found, the isomers with D_{2d} and D_2 symmetry being the most widespread;²⁰ the calculated EA values for these two isomers virtually coincide.

Curious observations have been made for C_{72} and C_{74} fullerenes, which fall out of the general series of C_{2n} fullerene homologues, first of all, due to the fact that they have not yet been isolated as individual compounds from typical fullerene extracts. It can be seen from the dependence of the EA on the fullerene size (Fig. 2, curve 2) that the values for the C_{72} and C_{74} molecules are abnormally high, which violates the monotonic pattern of EA variation. The diagram of the energy levels of molecular orbitals (MO) of C_{74} fullerene (Fig. 3)²¹ indicates that the energy difference between the highest occupied molecular orbital (HOMO) and the lowest unoccupied molecular orbital (LUMO), which allows one to judge the relative kinetic stability of a molecule, is very small and equals only 0.05 eV, whereas for C_{60} , this difference is 1.6 eV. This finding is in line with the fact that C_{74} fullerene, which is present in perceptible amounts in soot, is lost almost entirely during subsequent extraction with organic solvents (apparently, due to degradation or polymerisation and transition into an insoluble form). Only recently, two research groups in the USA²¹ and China²² proposed procedures for the synthesis and isolation of C_{74} fullerene; however, this compound has not yet been isolated in a pure state or characterised by spectroscopic methods.

Comparison of the experimental EA values for C_{72} fullerene with the theoretical values for the single isomer that obeys the rule of isolated pentagons and for isomers in which this rule is violated

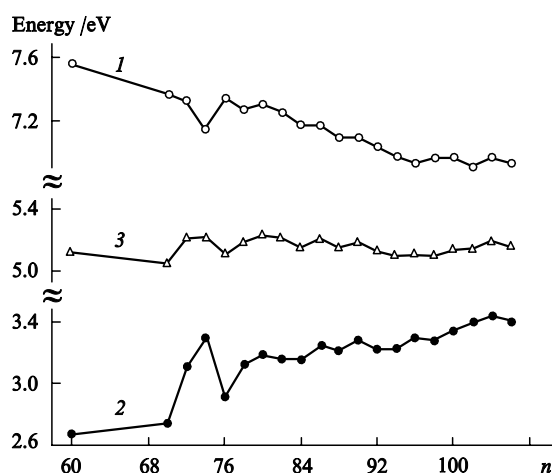


Figure 2. Ionisation energy (1), electron affinity (2) and their half-sum (Mulliken electronegativity) (3) vs. the number of carbon atoms (n) in the fullerene molecule.¹⁴

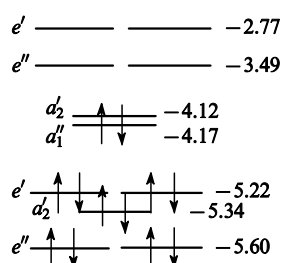
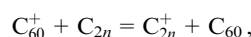


Figure 3. Diagram of the MO energy levels for the C_{74} molecule (the D_{3h} group of symmetry) calculated by the BLYP/6-31G*/3-21G* procedure. The numerals at the energy levels are energies (in eV).²¹

showed that the best agreement between the experimental and theoretical results is attained for the molecule with C_{2v} symmetry, which contains both isolated and conjugated five-membered rings.²³

Later, thermal cations in the vapours of higher fullerenes have been studied,¹⁴ and for a series of C_{2n} molecules, the equilibrium constants for the reaction



where $n = 35-53$, were measured. The resulting EA and IE values for the higher fullerenes and the corresponding electronegativity values are shown in Fig. 2.

The simple physical model in which fullerene is considered as a rigid conducting sphere¹⁴ makes it possible to derive an equation that relates the electron affinity and the ionisation energy to the radius of a sphere (R_N)

$$EA = \varphi_\infty - 0.5R_N^{-1},$$

$$IE = \varphi_\infty + 0.5R_N^{-1},$$

where φ_∞ is the electron work function of a graphite monolayer, which is the limiting value for both the EA and the IE as the size of the fullerene molecule tends to infinity; a theoretical estimate of this value gives 5.37 eV. The effective sphere radius R_N is proportional to the square root of its mass, because the surface area of the molecule is proportional to the number of carbon atoms located on it. The appropriate proportionality coefficients can be found using the known geometric parameters and the known EA and IE values for [60]fullerene. However, in reality, the shapes of many fullerene molecules deviate from a sphere, which may result in deviations of experimental data from theoretical predictions

concerning the pattern of the dependence of the EA on the fullerene size. Nevertheless, this simple model generally provides a satisfactory description of experimental data — both the monotonic increase in the electron affinity and the decrease in the ionisation energy following an increase in the size of the molecule. The rate of variation of both parameters markedly decreases on passing to heavy fullerenes with about 100 carbon atoms in the molecule. Noteworthy are clearly mirror patterns of variation of the EA and IE curves, which shows itself as a rather narrow energy range fitting the electronegativity values $(EA + IE)/2$ for the whole series of fullerenes studied, 5.2 ± 0.2 eV (see Fig. 2); the above-mentioned theoretical estimate of the electron work function for a graphite monolayer also falls in this range.

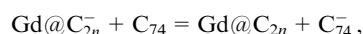
3. Ion-molecular equilibria in the vapours of fullerene derivatives

Fullerene derivatives can be classified into two main groups, namely, exo- and endohedral fullerenes. Exohedral fullerenes are those compounds in which functional groups add on the outside of the fullerene cage; as a rule, the species add in pairs with rupture of the double bonds. The term ‘endohedral’ means ‘enclosed inside’. These derivatives have been obtained by admixing oxides of some metals (mainly, lanthanides) to the graphite rods used in fullerene synthesis in the discharge arc. The space inside the fullerene cage suffices to accommodate one, two and, according to the latest data, even three or four metal atoms, some of these compounds being characterised by high thermal stability. Endohedral compounds of noble gases are also known.

In studies of ion–molecule equilibria involving fullerene derivatives, the researchers meant to find out how these two types of functionalisation influence the electron-withdrawing properties of fullerenes. Whereas in the case of fluorofullerenes, one could expect an increase in the EA compared to that for the initial C_{60} due to the high electronegativity of fluorine, it was difficult to predict the effect of the intra-sphere metal on the electron-withdrawing properties of fullerene. This problem could not be solved until experimental results were obtained.

a. Endohedral metallofullerenes

The equilibrium constants for the ion–molecule reactions of the type



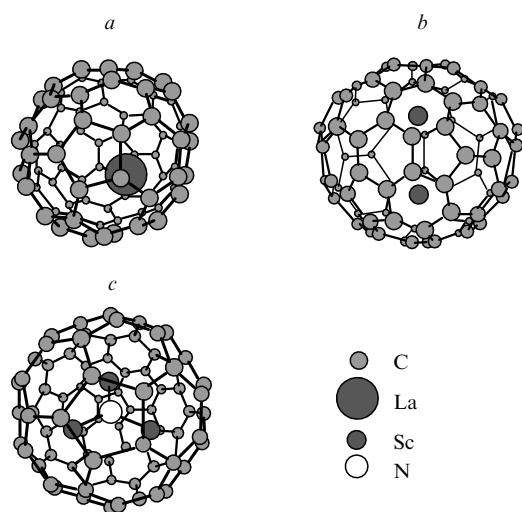
where $n = 37-41$, were measured using specimens manufactured by the ‘TDA Research’ company by evaporation of graphite rods in the discharge arc, followed by sublimation of fullerenes and metallofullerenes from the soot accumulated on the cold walls of the reactor. These specimens were free from soot; hence, there was no need to carry out extraction in a Soxhlet apparatus, which may be accompanied by solvent-induced destruction of metallofullerenes. Although the content of endohedral compounds in the mixtures did not exceed several percent, $Gd@C_{2n}$ ions were detected in the mass spectra recorded at 900–960 K. The ratio of the partial pressures of endohedral and empty fullerenes proved to be higher for negative ions than for neutral molecules, which points to more pronounced electron-withdrawing properties of endohedral fullerenes compared to the analogues containing no metal atoms. The calculations of the EA values for $Gd@C_{2n}$ showed that all values are fitted into a narrow range (3.2–3.3 eV, Table 2) and, on average, they are higher than the EA of the corresponding hollow fullerenes. Thus, it was found that accommodation of a rare earth metal (gadolinium) inside the fullerene cage results in an increase, although slight, in the EA with respect to that of the hollow fullerene molecule; the only exception is $Gd@C_{74}$, which shows an opposite effect. In addition, it was found that for fullerenes containing the same metal atom inside the cage, an increase in the size of the C_{2n} molecule in the series $C_{74}-C_{84}$ has no substantial influence on the electron affinity. This result differs from the pattern of EA variation established for

Table 2. Electron affinity of endohedral fullerene compounds.

Compound	EA /eV	Ref.
La@C ₇₄	> 2.9	24
La@C ₈₀	3.32	see ^a
Gd@C ₆₀	2.85	24
Gd@C ₇₄	3.2 ± 0.1	24
Gd@C ₇₆	3.22 ± 0.02	24
Gd@C ₇₈	3.41 ± 0.09	24
Gd@C ₈₀	3.37 ± 0.05	24
Gd@C ₈₂	3.38 ± 0.06	24
Sc ₂ @C ₈₀	3.20 ± 0.04	25
Sc ₂ @C ₈₂	3.21 ± 0.04	25
Sc ₂ @C ₈₄	3.10 ± 0.04	25
Sc ₃ N@C ₈₀	2.81 ± 0.05	25

^a Author's unpublished results.

hollow fullerenes, where C₇₄ fullerene exhibits an abnormally high EA value. These data suggest that in the case of endohedral compounds, the electron-withdrawing properties of the molecule are dictated by the charge on the intra-sphere metal atom. This hypothesis is supported by theoretical calculations. We were also able to determine the EA for some endohedral metallofullerenes with two scandium atoms inside the sphere and for a new type of endo compound with a trimetallic nitride cluster, Sc₃N@C₈₀ (Fig. 4, see Table 2).

**Figure 4.** Structures of the compounds La@C₈₂ (a), Sc₂@C₈₂ (b) and Sc₃N@C₈₀ (c). [The structure of Sc₃N@C₈₀ is published by authority of the journal Nature (www.nature.com)].

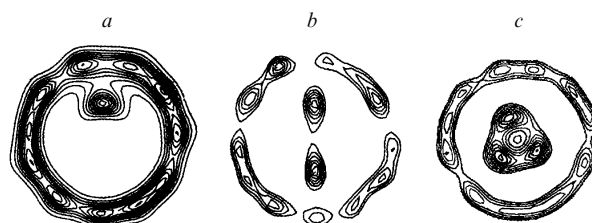
Endohedral metallofullerenes had attracted the attention of theoretical chemists even before they were prepared in macro-quantities. The first quantum-chemical study of the model La@C₆₀ molecule with the lanthanum atom located at the centre of gravity was reported by Rosen and Wastberg.²⁶ The calculations showed strong interaction between the 5*d* orbitals of the lanthanum atom and the π -system of the carbon cage, which results, in particular, in an increase in the electron affinity of the endohedral molecule relative to that of the hollow C₆₀ molecule by several tenths of electron-volt. Subsequently, the theoretical studies devoted to the structure of endohedral metallofullerenes have also been ahead of experiments and usually gave correct predictions.

In a series of quantum-chemical works performed by Japanese researchers^{27–29} and devoted to endohedral metallofullerenes

containing Group III metal atoms (Sc, Y) and lanthanide atoms, it was shown, first, that the metal atom is markedly shifted out of the centre of the molecule, and, second, that substantial charge transfer from the metal atom to the carbon cage takes place; as a consequence, the former acquires a charge of 2+ to 3+ (this is true for both mono- and di- or trimetallofullerenes). The ionisation potential of the endohedral metallofullerene is markedly lower, while the electron affinity is somewhat higher, despite the negative charge on the carbon cage, compared to that of the corresponding metal-free fullerene.^{27–29}

Evidence supporting these theoretical conclusions was first obtained in electrochemical investigations of endohedral metallofullerenes.³⁰ The oxidation and reduction potentials of these compounds demonstrated that they give off or accept an electron more easily than fullerenes themselves. This was also confirmed by the results of mass-spectrometric studies (see above). The presence of a charge on metal atoms was confirmed indirectly by EPR data,³¹ according to which the putative terms of electron states corresponded to metal ions rather than to atoms. Later, it was found by photoelectron spectroscopy^{32,33} that the HOMO in the molecules of endohedral metallofullerenes have higher energies than similar orbitals of hollow fullerenes.

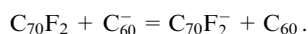
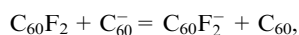
With progress in developing methods of isolation and purification of endohedral molecules, direct evidence confirming the theoretical predictions also appeared. An important role was played by powder X-ray diffraction studies of the polycrystalline specimens of endohedral metallofullerenes, Y@C₈₂, Sc₂@C₈₄, Sc@C₈₂ and Sc₃@C₈₂ with utilisation of the Rietveld method and the maximum entropy method.^{34–37} The maps of electron density distribution in these molecules constructed on the basis of these results clearly demonstrated the displacement of metal atoms from the centre of the molecule and the presence of a charge of ~2+ on these atoms. The cross-sections of the electron density maps for scandium endohedral fullerenes are shown in Fig. 5. Similar data on the distances between the metal atom and the nearest carbon atoms in an endohedral fullerene have been obtained for some molecules by EXAFS.³⁸

**Figure 5.** Cross-sections of the electron density maps for the molecules of Sc@C₈₂ (a), Sc₂@C₈₄ (b) and Sc₃@C₈₂ (c).^{34–37} Level lines for bulk charge density from 0.3 (1.0 for Sc₂@C₈₄) to 6.0 e Å^{–3} with a step of 0.3 e Å^{–3} are shown. (Published by authority of the American Physical Society and Elsevier publishing house).

Since the distribution of the products of synthesis of endohedral fullerenes over the number of carbon atoms in the molecule differed appreciably from that for hollow fullerenes, the question arose as to whether the carbon cage topology is the same for the major isomers of hollow and endohedral fullerenes for a given number of carbon atoms. An answer to this question was provided, first of all, by X-ray diffraction results. It was found that the symmetry of the carbon cage in Sc@C₈₂ differs from that in C₈₂ fullerene, while the Sc₂@C₈₄ molecule has the same carbon cage as one of the major isomers of C₈₄. It is noteworthy that these results were also first predicted by a group of Japanese theoretical chemists,^{27–29} who thus demonstrated high efficiency of quantum-chemical techniques for the study of fullerenes and their derivatives.

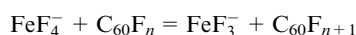
b. Fluorofullerenes

The electron affinity of fullerene difluorides was determined using the reactions

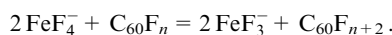


The *EA* values of C_{60}F_2 and C_{70}F_2 fluorofullerenes found in this way are equal to 2.73 and 2.82 eV, respectively.³⁹ These data indicate that upon the addition of two fluorine atoms to C_{60} and C_{70} fullerenes, the *EA* increases, although insignificantly. Naturally, a higher electron affinity is expected of a molecule with a higher content of fluorine atoms. Evidence supporting this assumption was gained from measurements of the reduction electrochemical potentials of $\text{C}_{60}\text{F}_{36}$ fluorofullerene and by comparison of the results with the data for C_{60} . On the basis of a known correlation between the electrochemical potential and the electron affinity, the *EA* for $\text{C}_{60}\text{F}_{36}$ was estimated to be 3.48 eV.⁴⁰ In a study by the 'brackets' method in terms of the ion cyclotron resonance mass spectrometry of the electron exchange between $\text{C}_{60}\text{F}_{44}$ – $\text{C}_{60}\text{F}_{48}$ fluorofullerenes and various standards, a substantial increase in the *EA* (4.05 ± 0.5 eV)⁴¹ with an increase in the number of fluorine atoms added was found.

Experiments on the determination of the dissociation energy of the C–F bond in fluorofullerene molecules and anions were carried out using the same equipment as was used for *EA* measurements; however, this time fluorine exchange between fullerenes and fullerene anions was the object of investigation. The compounds FeF_3 , UF_4 , UO_2F_2 and $\text{C}_{60}\text{F}_{48}$ were used as mild fluorinating agents. In these systems, fullerene mono- and difluoride anions were detected at 800–1000 K (Fig. 6).^{42,43} This allowed the researchers to calculate the absolute magnitudes of the C–F bond energy for C_{60}F_n fluorofullerenes from the reaction



or



It was found that the C–F bond energy in the fullerene difluorides under study and their anions is 370–400 kJ mol^{−1}, *i.e.*, this bond is much stronger than was predicted by theoretical calculations (Tables 3, 4). A similar value was found, for example, for the C–F bond energy in the difluoroethane molecule. It is of interest to compare these results with the data on the thermodynamic stability of highly fluorinated fullerenes. The measurements of the combustion energies for C_{60} ,⁴⁶ $\text{C}_{60}\text{F}_{36}$ ⁴⁷ and $\text{C}_{60}\text{F}_{48}$ ⁴⁸ and

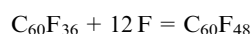
Table 3. Energies of C–F bond rupture [*D*(C–F)] in mono- and difluorides of C_{60} and C_{70} fullerenes and their anions.

Compound	<i>D</i> (C–F) /kJ mol ^{−1}	Ref.
C_{60}F	≥ 362	42, 43
	403	44
C_{60}F^-	388	42, 43
C_{60}F_2	369	42, 43
	365	44
	306	45
$\text{C}_{60}\text{F}_2^-$	372	42, 43
C_{70}F_2	366	42, 43
$\text{C}_{70}\text{F}_2^-$	370	42, 43

Table 4. Thermodynamic parameters (ΔH_0° and ΔG_7°) and energies of C–F bond rupture for higher fullerenes.^{39,42,43}

Reaction	ΔG_7° kJ mol ^{−1}	ΔH_0° kJ mol ^{−1}	<i>D</i> (C–F) kJ mol ^{−1}
$\text{C}_{60}^- + 2\text{F} = \text{C}_{60}\text{F}_2^-$	−496	−744	372
$\text{C}_{70}^- + 2\text{F} = \text{C}_{70}\text{F}_2^-$	−492	−740	370
$\text{C}_{72}^- + 2\text{F} = \text{C}_{72}\text{F}_2^-$	−527	−774	387
$\text{C}_{74}^- + 2\text{F} = \text{C}_{74}\text{F}_2^-$	−548	−796	398
$\text{C}_{76}^- + 2\text{F} = \text{C}_{76}\text{F}_2^-$	−519	−767	384
$\text{C}_{78}^- + 2\text{F} = \text{C}_{78}\text{F}_2^-$	−523	−770	385
$\text{C}_{80}^- + 2\text{F} = \text{C}_{80}\text{F}_2^-$	−546	−793	397
$\text{C}_{82}^- + 2\text{F} = \text{C}_{82}\text{F}_2^-$	−541	−788	394
$\text{C}_{84}^- + 2\text{F} = \text{C}_{84}\text{F}_2^-$	−535	−782	391
$\text{C}_{60}^- + \text{F} = \text{C}_{60}\text{F}^-$	−267	−388	388
$\text{C}_{70}^- + \text{F} = \text{C}_{70}\text{F}^-$	−274	−395	395
$\text{C}_{60}\text{F}^- + \text{F} = \text{C}_{60}\text{F}_2^-$	−237	−361	361
$\text{C}_{60}\text{F}_2^- + 2\text{F} = \text{C}_{60}\text{F}_4^-$	−412	−665	332
$\text{C}_{60} + \text{F} = \text{C}_{60}\text{F}$	≥ −242	≥ −363	≤ 363
$\text{C}_{70} + \text{F} = \text{C}_{70}\text{F}$	≥ −253	≥ −374	≤ 374

the enthalpies of sublimation of these compounds gave average values for the C–F bond energy in $\text{C}_{60}\text{F}_{36}$ and $\text{C}_{60}\text{F}_{48}$ fluorofullerenes equal to 295.0 ± 5.6 and 287.5 ± 3.5 kJ mol^{−1}, respectively. These data also made it possible to estimate the enthalpy of the reaction



per fluorine atom; the result was 265 kJ mol^{−1}.⁴⁷ This value can be regarded as being approximately equal to the average C–F bond energy for the formation of $\text{C}_{60}\text{F}_{48}$ from $\text{C}_{60}\text{F}_{36}$. It follows from these results that the bond energy decreases, although slightly, with an increase in the number of fluorine atoms attached. This is apparently due to the enhancement of the steric strain in the molecules of highly fluorinated fullerenes. Presumably, the decrease in the bond energy would not be monotonic: the most pronounced changes in the *D*(C–F) value would be expected for the formation of energetically and kinetically favourable compounds, namely, $\text{C}_{60}\text{F}_{18}$, $\text{C}_{60}\text{F}_{36}$ and $\text{C}_{60}\text{F}_{48}$. Although no quantitative data confirming this hypothesis have been obtained yet, the assumption is supported by the highly selective formation of compounds of exactly this composition observed experimentally.

III. Synthesis of fluorofullerenes

1. Mass-spectrometric studies of reactions of fullerenes with transition metal fluorides

The idea of using a mass-spectrometric setup as a chemical reactor is not new; it is widely employed in investigations of the reactivity of gaseous species (neutral molecules and ions). An attractive feature of these investigations is that they provide information about the reaction 'just as it is', *i.e.*, not complicated by processes

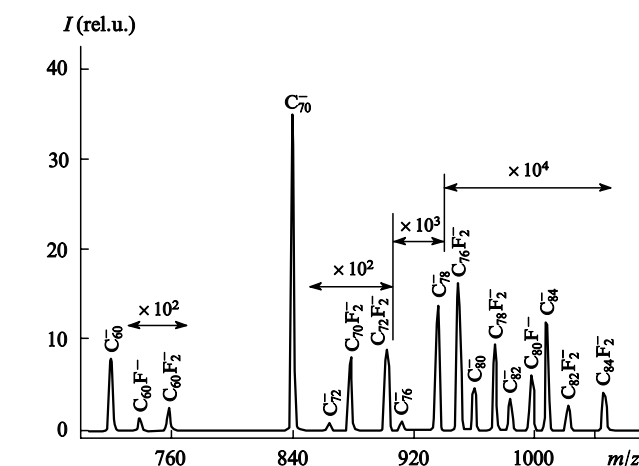


Figure 6. Electron impact (EI) mass spectrum of thermal anions in the vapour of the C_{60} – $\text{C}_{60}\text{F}_{46}$ system.^{42,43}

I is relative intensity.

of solvation (if the reaction takes place in solution) or by the state of reactants in heterogeneous processes. A typical scheme of these experiments is as follows. Gaseous species of a reactant are generated by vaporisation of appropriate chemical compounds and are let into a cell in which they are mixed with the other reactant. By recording the mass spectrum of the gas phase formed in the cell, one can gain information about the reactivity of the species and about the reaction products. More complex cases include the study of reactions as functions of temperature, reactant pressure or the charge of the reacting species.

The use of a mass-spectrometric setup as the main tool in the investigation of fullerene fluorination was started, as a matter of fact, due to a fortuitous discovery. As noted in the previous Section, the preparation of $C_{60}F_n$ in the gas phase and the determination of the energies of addition of fluorine atoms and fluoride ions to fullerene molecules was associated with the use of transition metal fluorides. The ion–molecule equilibria in the vapours of these compounds have been studied in detail previously and, what is especially important, the energies of addition of F atoms and F^- ions to transition metal difluorides and trifluorides have been determined.⁴⁹ Therefore, these compounds served not only as good fluorinating agents in the synthesis of fluorofullerenes but also as standards in the calculation of thermochemical characteristics from the equilibrium constants of fluorine exchange.

In one experiment, manganese trifluoride was used to generate fluorinated species in the gas phase.⁵⁰ When this compound was heated as a mixture with fullerene, it was noted that in a narrow temperature range, the vapour consisted mainly of $C_{60}F_{36}$ molecules. The condensate formed on the cold parts of the ion source was subjected to mass-spectrometric analysis, which confirmed that the fullerene reaction with manganese trifluoride occurs selectively, *i.e.*, $C_{60}F_{36}$ is formed as the predominant product.⁵⁰ This finding, fortuitous in a certain sense, gave impetus to the development of a new method of solid-phase selective synthesis of fluorofullerenes accompanied by evaporation of volatile products. The last-mentioned circumstance, *i.e.*, the removal of the target products from the reaction area, is a crucial factor, because the attempts to perform a similar synthesis in a closed reactor failed. They resulted in fullerene destruction to give thermodynamically the most stable compound — tetrafluoromethane.

The subsequent studies included the search for new fluorinating agents having different fluorinating capacities, which would enable the preparation of products with fluorine contents varying over a broad range. In the study,⁵¹ researchers' attention was focused on the fluorides of transition and rare earth metals in higher oxidation states.

All fluorination experiments were carried out in two stages. The first stage included *in situ* experiments in a mass spectrometer with continuous monitoring of gaseous reaction products. The reaction mixture consisting of thoroughly blended fullerene and fluorinating agent taken in definite mass ratios was charged to the effusion cell of the high-temperature evaporating chamber of the ion source of a mass spectrometer and heated under a high vacuum over a broad temperature range. The gaseous products of fluorination were detected as positive (electron impact) or negative (thermal ionisation) ions by the output recording unit of the mass spectrometer.

The use of this approach, which included a preliminary stage of synthesis inside the mass spectrometer, provided obvious advantages over the traditional one-step synthesis⁵⁰ carried out in a chemical reactor. First, it was possible to gain information on the product distribution as a function of time and temperature directly during the reaction. Second, the number of experiments needed to select the optimal conditions for the preparation of compounds of particular stoichiometric composition markedly diminished.

Thus it was found that fluorination of [60]fullerene by MnF_3 at 615 K gives virtually a single compound, $C_{60}F_{36}$, whereas the reaction of C_{60} with K_2PtF_6 at 730 K gives mainly $C_{60}F_{18}$.⁵² In

addition, experiments in the Knudsen cell require much less reactants and minimise the loss of products, which is especially important for expensive fullerenes C_n ($n > 70$) or derivatives such as bisazafullerene $(C_{59}N)_2$ (see Ref. 53).

The second stage included preparation of macroquantities of compounds in a setup representing a vacuum reactor with a cooling area for collection of volatile products. A detailed description of these experiments has been published.⁵⁴ This procedure was used to prepare gramme amounts of $C_{60}F_{36}$ and $C_{60}F_{18}$ fluorofullerenes, which were used for physicochemical investigations, in particular, for determination of the enthalpies of their formation by combustion (bomb) calorimetry.

2. Solid-phase topochemical reactions with evaporation of the volatile products $C_{60}F_{18}$ and $C_{60}F_{36}$

Heterogeneous solid-phase fluorination reactions proceed in mechanical mixtures of fullerenes with higher metal fluorides, which can give off fluorine on heating, thus being converted into fluorides with a lower oxidation state of the metal. The temperatures at which fluorofullerenes are formed (350–400 °C) are sufficiently high for these products to be removed from the reaction mixture *via* the gas phase and to condense on cooler surfaces of the reactor. Meanwhile, the temperatures are insufficient for evaporation of the reactants and decomposition products formed from metal fluorides; this allows one to avoid contamination of the resulting fluorofullerenes by the initial compounds or side products. By selecting an appropriate solid fluorinating agent (SFA) and reaction conditions, the researchers accomplished a selective process and prepared for the first time virtually pure $C_{60}F_{18}$ (see Ref. 51) and $C_{60}F_{36}$ (see Ref. 50).

It should be noted that selective solid-phase synthesis of fluorofullerenes normally gives, along with the major $C_{60}F_{2m}$ product, side products with similar chemical compositions. Thus in the case of a $C_{60}-MF_n$ reaction mixture ($M = Mn, Co$) in a dynamic vacuum at temperatures of 330–380 °C, apart from $C_{60}F_{36}$ fluorofullerene formed predominantly, its close analogues $C_{60}F_{34}$ and $C_{60}F_{38}$ also pass to the gas phase.^{50, 51} The contents of the side products, as shown by experiments, depend somewhat on both the degree of dispersion of the initial materials and the procedure used for mixing them, in particular, on how thorough the mixture components have been blended or on the degree of pressing. The latter circumstance is illustrated in Table 5 in relation to the reaction of C_{60} with CeF_4 . The compaction of the

Table 5. Effect of the method of preparation of specimens on the product yield in the reaction of C_{60} with CeF_4 (data of mass spectrometry).⁵⁴

Reactants	$C_{60} : CeF_4$ (mol : mol)	T / K	Relative intensities of ion signals		
			$C_{60}F_{34}^+$	$C_{60}F_{36}^+$	$C_{60}F_{38}^+$
CeF_4 (cryst.) + + C_{60} (cryst.)	1 : 15	515	25.0	100	—
		549	8.9	100	—
		553	18.6	100	—
		640	35.7	100	—
CeF_4 (cryst.) + + C_{60} (cryst.)	1 : 36	500	7.4	100	—
		560	7.6	100	—
		640	8.4	100	—
CeF_4 (cryst.) + + C_{60} (ground)	1 : 18	535	26.1	100	1.3
		683	32.1	100	0.7
		701	39.4	100	0.9
CeF_4 (cryst.) + + C_{60} (ground), compression, 100 atm	1 : 18	563	8.5	100	—
		613	6.5	100	—
		641	12.4	100	—
		673	1.3	100	—
		708	0.1	100	—
		793	0.2	100	—

mixture under pressure decreases the content of $C_{60}F_{34}$ in the reaction products and, at a definite temperature, this allows one to attain an almost 100% yield of the major product, $C_{60}F_{36}$. The influence of the reactant ratio on the product yield is shown in Table 6, which presents the data for reactions of C_{60} with MnF_3 carried out over a broad range of initial concentrations. It can be seen from Table 5 that the dependence of the product composition on the procedure of sample preparation is rather weak and has no substantial influence on the qualitative pattern of fluorination. It is also noteworthy that the reaction rate (monitored based on the intensity of product vaporisation) remains nearly constant throughout almost the whole process (except for the initial section where the temperature approaches the specified one and for the final stage), although the composition of the reaction mixture constantly changes during fluorination because of gradual accumulation of the decomposition products of the SFA, which are lower metal fluorides (see Table 6).

Table 6. Mass spectrum of volatile products formed in the C_{60} – MnF_3 system at different component ratios.⁵⁵

$C_{60} : MnF_3$ (mol : mol)	T/K	Relative intensities of ion signals		
		$C_{60}F_{34}^+$	$C_{60}F_{36}^+$	$C_{60}F_{38}^+$
1 : 1	603	11.5	100	—
	644	18.1	100	—
	664	18.9	100	—
1 : 18	572	6.6	100	8.1
	631	7.5	100	—
	648	7.3	100	—
	675	18.4	100	—
1 : 36	704	37.7	100	—
	592	1.3	100	2.9
	648	3.2	100	—
	729	13.1	100	—

Thus, the qualitative outcome of reactions, including the selectivity with respect to a particular compound or the absence of selectivity, is determined by the nature of the SFA used. It was found that the reactions of C_{60} with MnF_3 , CoF_3 or CeF_4 give $C_{60}F_{36}$ as the major product.^{50, 51, 54, 56} Potassium hexafluoroplatinate ensures the selective synthesis of $C_{60}F_{18}$.⁵² Iron trifluoride does not react with C_{60} to give highly fluorinated derivatives, whereas TbF_4 (the strongest SFA) yields a rather broad spectrum of $C_{60}F_{2m}$ fluorofullerenes including those with the number of fluorine atoms $m > 24$ and even slight amounts of hyperfluorinated molecules ($m > 30$).⁵⁶

In view of the constant accumulation of the SFA decomposition products, *i.e.*, lower metal fluorides, it would be reasonable to expect that the reaction rate would decrease with time; however, this is at variance with experimental results. Evidently, heterogeneous solid-phase reactions take place only in limited areas where the solid reactants are in direct contact with each other. In particular, it can be assumed that the MnF_2 formed in the area where C_{60} reacts with MnF_3 would hamper the contact between grains of the reactants. Thus, there must exist an effective mechanism to compensate for the deficiency of fluorine and to maintain a steady-state reaction course. It is rather unlikely that the gas phase plays any significant role in the transfer of fluorine from SFA to C_{60} , as the equilibrium partial pressures of both molecular and atomic fluorine above the metal fluorides used are too low at given temperatures to ensure the observed concentrations of the fluorination products, which correspond to pressures of about 0.1 Pa. Perhaps, atomic fluorine, which is rather mobile, enters the reaction area through surface diffusion. Note that the high mobility of F atoms in systems based on inorganic metal fluorides has been confirmed experimentally.⁵⁷ Finally, it was found⁵⁵ that evaporation of fluorofullerenes is not only a

convenient way to accumulate the products of synthesis as a condensate but it is also a necessary condition for fluorination to take place. The attempts to obtain a fluorofullerene in the reaction between C_{60} and MnF_3 in a sealed tube kept in a furnace at 330 °C for several hours have not met with success. Mass-spectrometric analysis did not reveal any traces of fluorinated fullerene. Evidently, the presence of even microscopic amounts of these compounds between the surfaces of the reactant grains results in the cessation of fluorination.

3. Selectivity of fluorination

The question naturally arises of why the solid-phase reactions of C_{60} with SFA, unlike those with molecular fluorine, can proceed as selective fluorination to give $C_{60}F_{18}$ and $C_{60}F_{36}$ fluorofullerenes. To answer this question, a number of experiments have been conducted on fluorination of [60]fullerene by molecular fluorine with evaporation of volatile reaction products and continuous monitoring by mass spectrometry (see Fig. 7).⁵⁸ To this end, a mass-spectroscopic setup equipped by a Knudsen effusion cell and a system for the inlet of molecular fluorine was used. A [60]full-

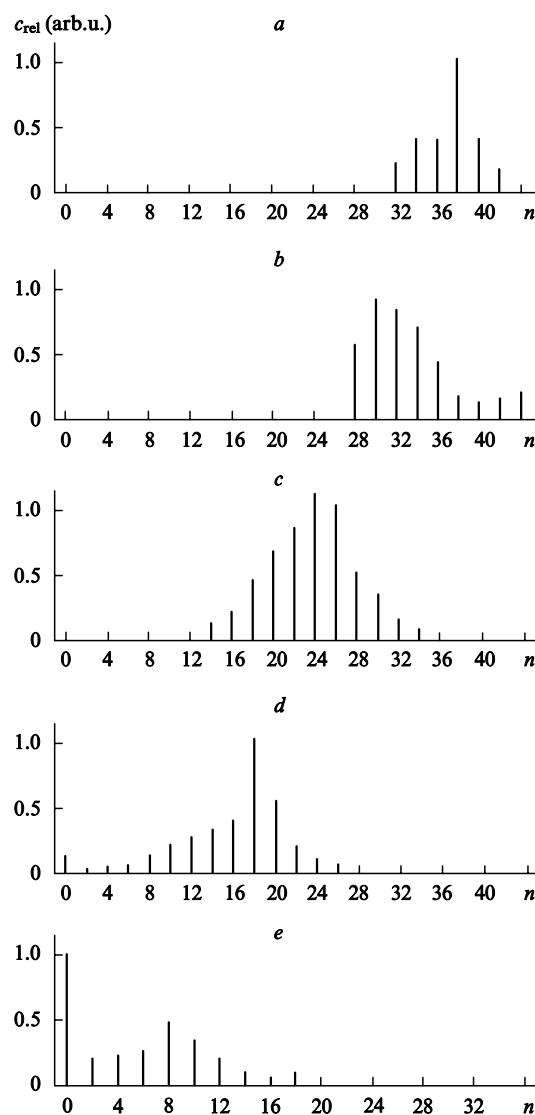


Figure 7. Composition of the gas phase vs. temperature for similar fluorination times and a constant fluorine flow rate in the $C_{60}(\text{solid})$ – F_2 system.⁵⁸

$T = 510$ (a), 615 (b), 670 (c), 720 (d) and 760 K (e).

Here and in Figs 9 and 10, the following designations are used: c_{rel} is the relative concentration of $C_{60}F_n$, n is the number of fluorine atoms.

erene powder was placed in the cell. Fluorination was studied in the temperature range of 500–800 K with fluorine delivered to the reaction area at two flow rates which differed by an order of magnitude and created fluorine pressures of 10^{-4} and 10^{-5} atm, respectively, in an empty reactor. The volatile products of the reaction, fluorofullerenes, came out of the reactor through the effusion orifice and entered the ionisation area where they were subjected to the impact of the electron beam with an energy of 60–100 eV. The positive ions thus formed were analysed on a mass spectrometer and the results of analysis were used to determine the molecular composition of the reaction products (Fig. 7). It can be seen from Fig. 7 that the gaseous products are characterised by a broad distribution over the number of fluorine atoms: they contain almost all $C_{60}F_n$ molecules with even n values up to 44. This distribution depends on the temperature, fluorination time and the flow rate of fluorine entering the reaction area. For constant flow rates and fluorination times, raising the reaction temperature results in displacement of the distribution maximum towards smaller n values, which is illustrated in Fig. 7.

No signs of selectivity are observed in the fluorination in this case. In particular, at 615 K (which is the optimal temperature for selective solid-phase fluorination of [60]fullerene by manganese trifluoride), the electron impact mass spectrum of the $C_{60}-F_2$ system exhibits a series of peaks for $C_{60}F_{28}^+$ – $C_{60}F_{44}^+$ with a feebly defined maximum at about $n = 30$. Conversely, in the mass spectrum of the $C_{60}-MnF_3$ system, the signal for $C_{60}F_{36}^+$ clearly stands out against the background of the closest homologues; the reaction products do not contain measurable amounts of the $C_{60}F_{32}^+$ ion or ions with lower contents of fluorine (Fig. 8).

The partial pressures of the products of fullerene fluorination in the experiments described were 0.1–1.0 Pa. The distribution of the products of direct fluorination of [60]fullerene over the number of F atoms starts to change when manganese difluoride is added to the mixture. These changes become visible in the mass spectrum when the mole fraction of manganese difluoride is $\sim 50\%$. If the fluorination system contains C_{60} and 97 mol.% of MnF_2 , selective formation of $C_{60}F_{18}$ can be observed at 720 K, and $C_{60}F_{36}$ is formed selectively at 615 K. This is illustrated in Figs 9 and 10.⁵⁹

Thus, it can be concluded that direct fluorination with molecular fluorine of a mechanical mixture $C_{60}-MnF_2$ (97 mol.%) provides the possibility of selective preparation of both $C_{60}F_{18}$ and $C_{60}F_{36}$ in the gas phase. If fluorination is carried out at 615 K, the major volatile reaction product is $C_{60}F_{36}$.⁵⁹ This result coincides with the results of experiments on solid-phase fluorination of C_{60} with manganese trifluoride, which also gives predominantly $C_{60}F_{36}$. If fluorination is carried out at 720 K, the major volatile product formed is $C_{60}F_{18}$,⁵⁹ which is in line with the results of experiments on solid-phase fluorination of [60]fullerene with potassium hexafluoroplatinate (K_2PtF_6).

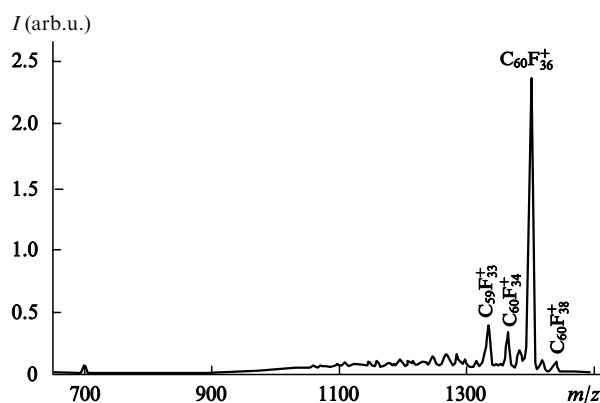


Figure 8. Electron impact mass spectrum of the volatile products of the solid-phase reaction between C_{60} fullerene and MnF_3 .

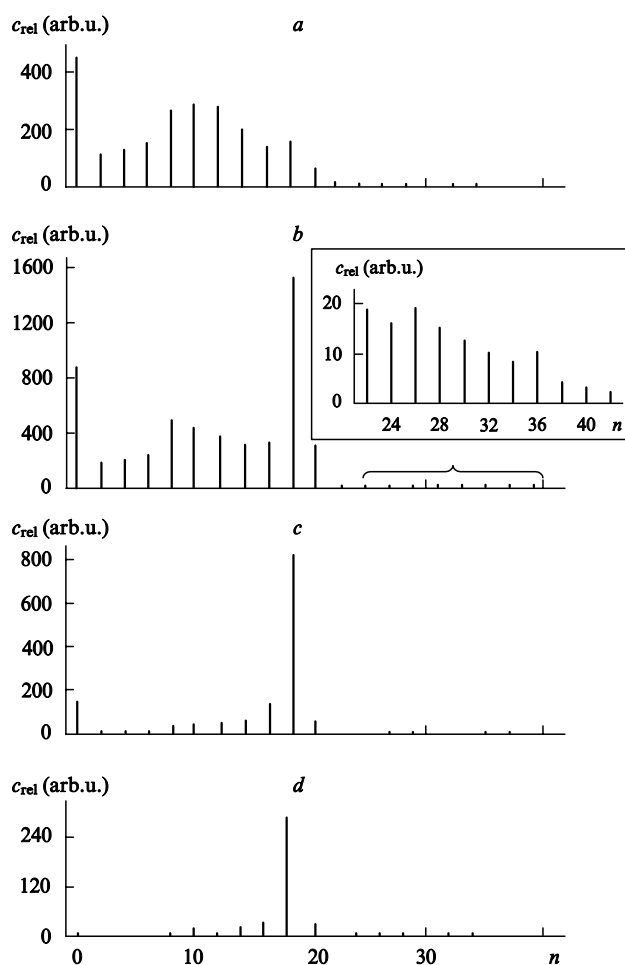


Figure 9. Composition of the gas phase after fluorination with molecular fluorine of a mixture of solid C_{60} with MnF_2 at approximately equal time intervals (2.5 h, initial stage) at $T = 720$ K.⁵⁹ (a) pure C_{60} ; (b) $C_{60} + MnF_2$ (50%); (c) $C_{60} + MnF_2$ (90%); (d) $C_{60} + MnF_2$ (97%).

At present, we have data at our disposal on the saturated vapour pressures of $C_{60}F_{18}$ and $C_{60}F_{36}$ fluorofullerenes (see Section VI), which can be used to explain the results obtained. At 720 K (see Fig. 9), the $C_{60}F_{18}$ fluoride is sublimed and fluorination stops at this stage. When the process is carried out

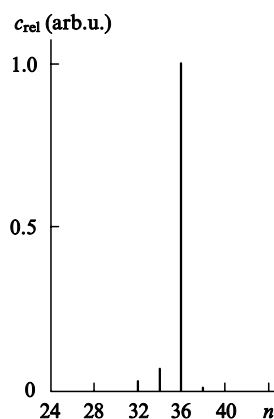


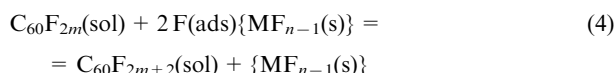
Figure 10. Composition of the volatile products of fluorination with molecular fluorine of a mixture of solid C_{60} and MnF_2 (97%) for 4.68 h at $T = 615$ K.⁵⁹

at 615 K (see Fig. 10), the $C_{60}F_{18}$ fluoride remains in the reaction mixture and fluorination goes on up to the formation of $C_{60}F_{36}$, which is sublimed at this temperature. The formation of the same product, $C_{60}F_{36}$, in the direct fluorination of a C_{60} – MnF_2 mixture by molecular fluorine and in the solid-phase reaction of C_{60} with MnF_3 indicates that these two processes include a common step responsible for selectivity. Apparently, this is the transition of F atoms from the chemisorbed state to the chemically bound state in the fluorofullerene molecule. The fluorination process can be represented as a sequence of three steps: (1) surface diffusion of fluorine to the reaction area; (2) transition of the F atoms adsorbed on the surface of the lower metal fluoride to the chemically bound (C–F) state in the fluorofullerene molecule; (3) transfer of the resulting fluorinated molecules to the gas phase. In the case of heterogeneous fluorination, the first step is preceded by adsorption of molecular fluorine from the gas phase on the surface of metal fluoride.

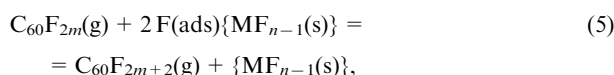
The surface diffusion is involved both in the direct fluorination by molecular fluorine and in the solid-state synthesis. Indeed, in the former case, selectivity is attained only after fluorine has passed through the layer of manganese difluoride and occurs in the chemisorbed state. The same is true for the solid-state synthesis because MnF_3 and C_{60} are separated by a layer of manganese difluoride formed during the reaction. Note that in both cases, the deficiency of fluorine in the reaction area at the boundary between the reactants is made up by the ‘flow’ of fluorine over the manganese difluoride surface, and the reactions proceed at a constant rate.

In the final step, evaporation of the reaction products takes place, which prevents them from accumulating in the reaction mixture. Apparently, due to this fact and to the relatively high rate of fluorine diffusion over the difluoride surface, the observed pattern of time variation of the reaction rate is atypical of topochemical reactions, *i.e.*, the rate remains constant and shows no significant attenuation caused by accumulation of the reaction products.

The key step can be represented as the following equation:



or



where ads is adsorbate and s is solid, and the fullerene-containing components are either taken as solid solutions (sol) [reaction (4)] or (with allowance for the final step) occur as gases (g) [reaction (5)].

The question arises as to why this manner of fluorine transfer easily ensures predominant formation of a particular single product, whereas the use of F_2 or some other gaseous fluorinating agents affords, as a rule, mixtures of fluorofullerenes of different compositions.

A correlation is known to exist between the reaction rate and enthalpy. Highly exothermal reactions usually proceed faster. This implies that the activation energy of the reaction (E_a) decreases as the enthalpy (ΔH) becomes more negative. If a quantitative relationship between these values is established, thermodynamic characteristics of reactions, in particular, the enthalpy, can be used to estimate the relative reaction rates. Usually, a set of reactions is chosen for this purpose in which the reactants differ from one another only by the functional group involved in the reaction. (This is called a one-parameter sequence. An example is the empirical correlation established by Brønsted between the reaction rates and the strength of acids or bases that catalyse these reactions.)

The reactions (4) and (5) considered here are members of such a one-parameter sequence in which the parameter is represented by the number of fluorine atoms ($2m$) in the reacting fluorofuller-

ene molecule. This gives grounds for using the correlation approach similar to the so-called Bell–Evans–Polanyi (BEP) model, well-known in organic chemistry.⁶⁰

The BEP model is based on consideration of rather large numbers of reactions as processes of independent rupture and formation of chemical bonds in ensembles of isomeric molecular species which yield the same products. According to this model, the energy characteristics of reactions are described using two potential curves dependent on the same reaction coordinate. The first (descending) curve corresponds to the formation of a chemical bond between two species of the ensemble, while the second (ascending) curve describes the energy variation in the rupture of the same bond in one of the isomeric species. The point of intersection of these curves corresponds to the transition state; its y -coordinate determines the activation energy of the reaction (E_a).

The groups of reactions that obey the BEP principles are characterised by a nearly linear relationship between the activation energy and the reaction enthalpy; the latter should vary insignificantly within this group

$$E_{ai} = a + b\Delta H_i. \quad (6)$$

The proportionality factor b tends to decrease as $|\Delta H|$ increases, therefore, in comparison of two groups of reactions with markedly different enthalpies, the most pronounced dependence of E_{ai} on ΔH_i is expected for the group where the enthalpies are close to zero, because even a slight shift of ΔH_i would ensure a considerable change in the E_{ai} value. The described concept forms the basis of the Brown selectivity rule for aromatic substitution.

Figure 11 shows the possible pattern of the Evans–Polanyi curves for a pair of neighbouring homologues of fluorofullerenes ($\Delta m = 1$), each reacting with two SFA ($M^I F_n$ and $M^{II} F_n$) which differ appreciably in fluorinating capacity.⁵⁵ Due to this difference, if the ΔH_i^I values for the reactions of fluorofullerenes with the first SFA (group I) are small, their reactions with the second SFA (group II) are highly exothermal. Correspondingly, in the case of the ‘weaker’ $M^I F_n$ reagent, the $a_1(I)$ and $a_2(I)$ curves for the formation of bonds in fluorofullerene molecules intersect the $b(I)$ curve for the abstraction of fluorine from SFA in the region where the slope of this curve is much greater than that in the case of the ‘stronger’ $M^{II} F_n$ reagent. As a consequence, the change in the activation energy for the first reaction (δE_a^I) is much greater than that for the second reaction (δE_a^{II}), although the enthalpy jumps ($\delta \Delta H_i^I$) are equal in both cases.

The relationship between the reaction rate constant and the activation energy is described by the equation

$$K = A \exp\left(\frac{E_a}{RT}\right).$$

By substituting into this expression [see Eqn (6)] the E_a values determined for two successive steps with the rate constants k and K and by taking their ratio, we obtain the key condition of selectivity

$$\frac{k}{K} = \exp \frac{b\delta\Delta H}{RT} \ll 1, \quad (7)$$

where k and K are the rate constants for the slow and fast steps, respectively, in the sequence of successive reactions. We neglected the difference between the pre-exponential factors, *i.e.*, we assumed that $A(k) = A(K)$.

Thus, if the BEP principles are applicable to solid-phase reactions of the given type, we can conclude that in the optimal case, the selective formation of a particular product requires transition from a slightly exothermal to slightly endothermal reaction to take place for the sequence member that corresponds to the fluorination of the given compound. However, this is not an obligatory condition. It is only necessary that the jump in enthalpy should ensure a sufficient change in the activation energy. Recall

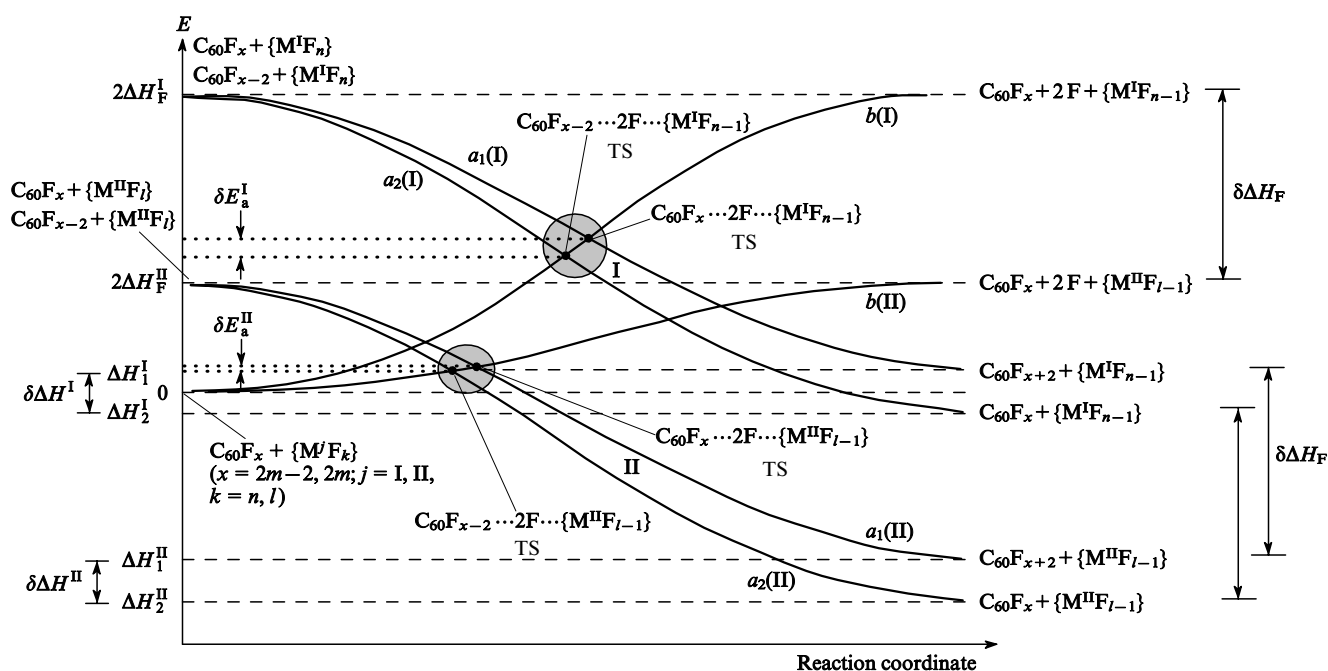


Figure 11. Evans–Polanyi curves for an elementary step of the solid-state reaction $C_{60}F_x + M^IF_k$ (TS is the transition state).⁵⁵ For explanations, see the text.

also that we are dealing with the enthalpies of reactions (4) determined by the difference between the C–F bond energies in fluorofullerene molecules and in the SFA.

A specific feature of fluorofullerenes hampering the selective synthesis of these compounds is, apparently, the fact that the reactivity with respect to fluorine changes only slightly over the $C_{60}F_{2m}$ series ($m = 1–24$). The difference between the energies of successive cleavage of the C–F bonds for this series is also relatively small. The success in the synthesis of individual $C_{60}F_{18}$ and $C_{60}F_{36}$ is attributable to the appearance of slow steps at $m = 9$ and 18 in the sequence of reactions of successive addition of fluorine atoms to [60]fullerene. These steps are due to the decrease in the exothermal effect of fluorination and the corresponding increase in the activation energies of each individual reaction.

It follows from the foregoing that, according to the approach proposed by Borcshevsky *et al.*,⁵⁵ the energy characteristics of one elementary step of solid-phase fluorination, namely, the step of fluorine transfer from the SFA to fullerene, is the criterion for the selection of reagents for preparation of individual fluorofullerenes. As noted above, by selecting the SFA in such a way that ΔH of the step responsible for the selectivity of the whole process is close to zero, we ensure the jump in the activation energy for two consecutive reactions, needed for the selectivity, and thus trigger the whole set of transformations along the chosen pathway.

Analysis of the experimental results from the standpoint of this approach provides an explanation for the non-selective pattern of direct fluorination. The enthalpy of dissociation of the F_2 molecule is $\sim 150 \text{ kJ mol}^{-1}$. The average C–F bond energies in the $C_{60}F_{48}(g)$ and $C_{60}F_{36}(g)$ molecules are 287.5 and 295 kJ mol^{-1} , respectively.^{47,48} This allows one to calculate the average C–F bond energy for the addition of 12 fluorine atoms to the $C_{60}F_{36}$ molecule, which equals 265 kJ mol^{-1} (see Section VI.3.b). On the basis of these data, the jump in the C–F bond energy on passing from $n < 36$ to $n > 36$ in the series of $C_{60}F_n$ is estimated as 30 kJ mol^{-1} . These values imply that the direct fluorination by molecular fluorine is a highly exothermal reaction. As compared with the enthalpy of this reaction, the difference between the enthalpies of two successive steps involving $C_{60}F_{34}$ and $C_{60}F_{36}$ (30 kJ mol^{-1}) is too small, and, hence, the change in the sign of ΔH is by no means expected. However, when MnF_2 is added, the crystals of [60]fullerene become mainly isolated from

direct contact with gaseous fluorine. As a consequence, the vast majority of fluorine atoms get into the reaction area (near the contact between C_{60} and MnF_2 grains) through surface diffusion over the crystals of manganese difluoride on which they are adsorbed. This reproduces the conditions inherent in the solid-phase fluorination by manganese trifluoride, and, hence, the selectivity is ensured. If the enthalpy of fluorine desorption is taken to be equal to the enthalpy of the reaction $MnF_3(s) = MnF_2(s) + F(g)$ (244 kJ mol^{-1}),⁶¹ the exothermal effect of the reaction of [60]fullerene with the fluorine attached to the surface of manganese difluoride sharply decreases, giving rise to conditions under which the difference between the properties of individual representatives of the $C_{60}F_{2m}$ series becomes observable. In particular, slow steps appear and the key condition of selectivity holds [see Eqn (7)].

Yet another important feature of solid-phase fluorination with evaporation of volatile products is that the reaction takes place in the fullerene–SFA contact area without accumulation of products in the solid phase. In this case, in the sequence of fluorination processes, sublimation proceeds as a side reaction having a lower order and independent of the fluorine concentration. As a result, fulfillment of the key condition of selectivity [see Eqn (7)] does not suffice for the preparation of the target product, and additional conditions taking into account the ratios between the rates of fluorination and the rates of sublimation of fluorination products need to be satisfied. This has been reported in more detail.⁵⁵

4. Preparation of the $C_{60}F_{48}$ fluorofullerene

The reaction of [60]fullerene with molecular fluorine proceeds even at room temperature; the products are normally mixtures of highly fluorinated $C_{60}F_n$ compounds ($n = 36–48$). Gakh *et al.*⁶² passed a stream of molecular fluorine above a mixture of C_{60} fullerene with NaF at 250 °C and, after 20 h, they obtained a product, which was extracted with $CFCl_3$, dried, and treated again with an F_2 stream for 30 h at 275 °C with the addition of a fresh portion of NaF. After extraction and drying, the sample composition was estimated by mass-spectrometric analysis. The content of $C_{60}F_{48}$ was $\sim 70\%$. The NMR spectrum of this compound was recorded, which exhibited eight equal-intensity lines.

Table 7. Experimental data on fluorination of [60]fullerene with molecular fluorine.⁶³

Regime	<i>T</i> / °C	<i>t</i> / h	Element composition (C : F)	<i>I</i> _{rel} (%) (see a)		
				C ₆₀ F ₄₄ ⁺	C ₆₀ F ₄₆ ⁺	C ₆₀ F ₄₈ ⁺
Static	315	2.3	60 : (44 ± 1) ^b	41	100	22
	315	10		19	91	100
Quasi-static	313	2.5		82	100	63
	315	5.5	60 : (48 ± 1) ^b	13	33	100
	315	10.5	60 : (48 ± 1) ^b	—	5	100
			60 : (46 ± 2) ^c			
Dynamic (flow)	315	10.5	60 : (49 ± 1) ^b	5	51	100
	350	2	60 : (48.0 ± 0.5) ^b	—	16	100
	345	3		—	5	100

^a The relative intensity of the ion signal in the mass spectrum. ^b Elemental analysis data. ^c ESCA data.

Somewhat later, one-step synthesis of C₆₀F₄₈ was performed.⁶³ In order to find the optimal conditions for fluorination, a number of experiments have been carried out with variation of the conditions, duration and temperature of the reaction of C₆₀ fullerene with molecular fluorine. Series of specimens were synthesised in three regimes, namely, static, quasi-static and dynamic ones (Table 7). In the static regime, C₆₀ fullerene powder was kept at a temperature of 315 °C and at a fluorine pressure of 50–300 Torr in a closed cell for 2.3 and 10 h. Under these conditions, the highest degree of fluorination, estimated conventionally as the ratio of the intensity of the signal of the C₆₀F₄₈⁺ ion to the total intensity of ion signals in the mass spectrum, was 63%. The quasi-static reaction conditions, embodied as the periodical renewal of fluorine portions in the reactor at 315 °C, resulted in a higher degree of fluorination of fullerene (68%). In the dynamic regime of fluorination where a fluorine flow (1 atm) was passed at 315 °C over powdered C₆₀ fullerene at a constant rate, the proportion of C₆₀F₄₈ in the resulting mixture of fluorofullerenes increased with an increase in the reaction time. As a result, fluorination for 10.5 h at 315 °C yielded a sample, whose elemental analysis corresponded to the ratio C : F ≈ 60 : 48 (see Table 7). The mass spectrum of this product contains only C₆₀F₄₈⁺ and C₆₀F₄₆⁺ molecular ions, the other peaks correspond to fragment ions (Fig. 12).

Meanwhile, at these high temperatures, the loss of fluorofullerenes due to destruction induced by fluorine becomes noticeable. This is indicated by analysis of a sample of the gas phase taken directly from the reaction area. According to mass-spectrometry

data, CF₄ and C_{*n*}F_{2*n*+2} perfluorocarbons (*n* = 2–4) were the major combustion products.

5. 'Hyperfluorination' of C₆₀ fullerene

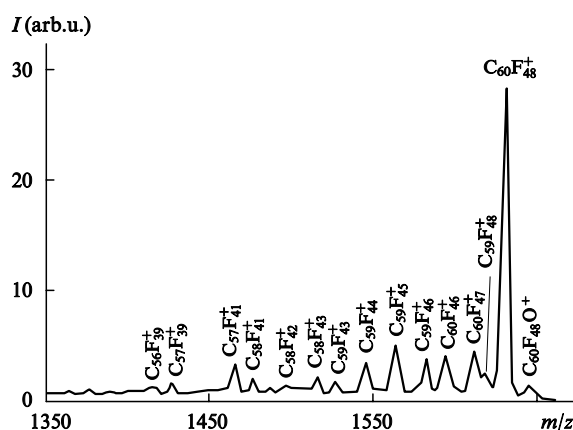
The interest in C₆₀F₆₀ perfluorofullerene, in which the double bonds have been fully utilised for the addition of fluorine was triggered by the publication in 1991 of a study by Kroto and coworkers,⁶⁴ who suggested that the perfluorinated fullerene can prove to be an analogue of Teflon and possess unique properties (for example, it could be suitable as a lubricant). Theoretical calculations⁴⁵ showed that this molecule can, in principle, exist; however, its structure should be distorted due to steric crowding. Moreover, the formation of structures with cleavage of several C–C bonds and arrangement of fluorine atoms inside the fullerene carbon cage has been suggested.

The phenomenon of fullerene 'hyperfluorination' was discovered in a study of the fluorination products obtained under more rigorous conditions such as UV irradiation of a mixture of C₆₀ with molecular fluorine,⁶⁵ or the use of powerful fluorinating oxidants (KrF₂).⁶⁶ These experiments were aimed at the attainment of the highest degree of fluorination and, finally, preparation of the perfluorinated fullerene (C₆₀F₆₀).

Later, the formation of [60]fullerene hyperfluorides was observed in the reaction of C₆₀ with terbium tetrafluoride.⁵⁶ In the reaction of [60]fullerene with terbium tetrafluoride, when a temperature of 350 °C has been attained, an explosion-like blow-out of the reaction mixture from the hot zone of the reactor takes place, and the fluorination products are found to contain C₆₀F_{*n*} (*n* > 60) fluorides. This reaction carried out below 350 °C also gives fluorofullerenes but no hyperfluorinated species are detected in the mass spectrum of the products. Apparently, in the explosion mode, the C–C bonds of the fullerene carbon skeleton are partially cleaved and excess fluorine atoms are added. Although this has not been confirmed by structural experiments due to the too small content of these species in the synthesised samples. Nevertheless, as noted above, species corresponding to C₆₀F_{*n*} hyperfluorides (*n* > 60) were still detected in the mass-spectrometric investigation of the products obtained in the reaction of C₆₀ with KrF₂⁶⁶ or TbF₄⁵⁶ (Fig. 13).

It is notable that these structures are not destroyed under the action of high temperatures (300 °C) or electron impact ionisation (70 eV), although the content of these species is relatively low and equals 0.01%–0.10% relative to the content of major components, C₆₀F₄₂–C₆₀F₄₆. Analysis of the mass spectra shows that hyperfluoride molecules undergo more extensive fragmentation than C₆₀F_{*n*} molecules with lower contents of fluorine (*n* < 48); the intensity of signals corresponding to fragment ions formed upon abstraction of the CF₃ group reaches 50%–60%, whereas for species containing less than 48 fluorine atoms fragmentation is insignificant under the same ionisation conditions and equals 5%–10%. This suggests that further progress in the study of fullerene hyperfluorides would depend on the choice of investigation techniques. In particular, 'mild' methods of ionisation such as electrospray and field desorption may prove rather promising. Note that the use of laser ionisation (which is a harsher method than electron impact), even in the matrix isolation variant, did not show the presence of any hyperfluorides in the mass spectra of the same specimens.

The phenomenon of hyperfluorination is still to be studied, in particular, in the context of possible applications of these compounds. Thus it is necessary to develop methods of analysis and techniques for the synthesis of macroquantities of fullerene hyperfluorides in the condensed phase. Nevertheless, even at the current stage, one can understand the fundamental significance of this type of transformation in which 'windows' with sizes exceeding those of five- or six-membered rings are formed with retention of the basic cage as a whole. Hypothetically, these 'windows' could be used to insert atoms and molecules into the fullerene cavity, which would result finally in the preparation of endohedral compounds of a new type.

**Figure 12.** Electron impact mass spectrum (70 eV) of C₆₀F₄₈ vapour (*I* is the ion current intensity).⁶³

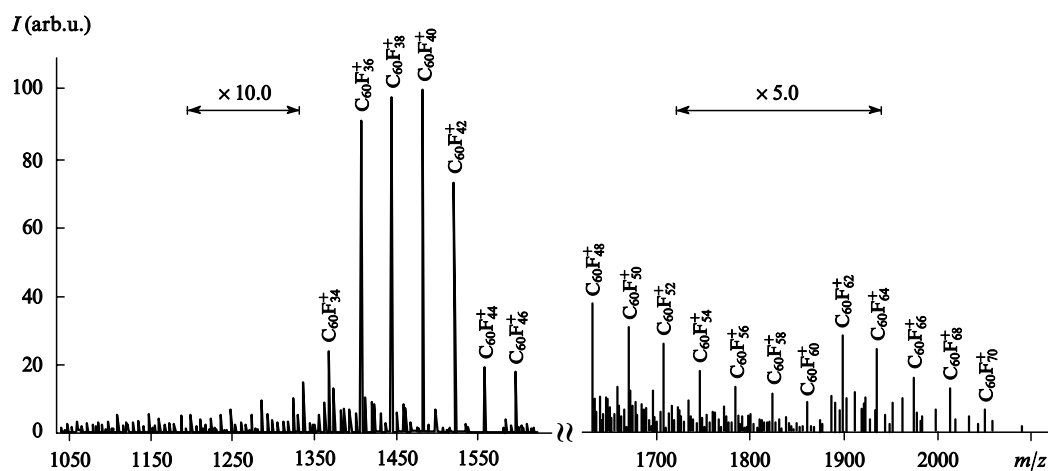


Figure 13. Electron impact mass spectrum of the products of fluorination of C_{60} fullerene with terbium tetrafluoride ($T = 350\text{ }^{\circ}\text{C}$).⁵⁶ The left-hand and right-hand parts of the spectra are given with different magnifications.

6. Fluorination of C_{70} and higher fullerenes

Functionalisation of higher fullerenes has scarcely been studied. Only several works have been reported dealing with the preparation of hydrides of a number of higher fullerenes.⁶⁷ In experiments on hydrogenation of C_{76} and C_{84} fullerenes, it was found that 40–50 hydrogen atoms can add to the former molecule and 54 hydrogen atoms can be attached to the latter one.⁶⁸ Heating of these compounds in an effusion cell entails thermal degradation of hydrides of higher fullerenes. This is accompanied by not only partial loss of the hydrogen atoms but also destruction of the carbon cage itself to give C_{60} and C_{70} hydrides containing 36 and 38–40 hydrogen atoms, respectively.⁶⁹

The theoretical studies dealing with functionalisation of higher fullerenes have not progressed significantly either. Higher fullerenes are characterised by a lower symmetry than C_{60} , and large numbers of isomers are possible for them, which greatly complicates the calculations.

Experiments on fluorination of higher fullerenes have been reported.⁷⁰ It was found that, as in the case of [60]fullerene, reactions with transition metal fluorides proceed selectively, the ‘magic numbers’ of the fluorine atoms added being different for different fullerenes. Fluorination of C_{84} on treatment with K_2PtF_6 , which is a milder fluorinating agent, gives mainly $C_{84}F_{40}$, while C_{76} adds only 26 fluorine atoms. Surprisingly, the reaction of C_{70} fullerene with K_2PtF_6 does not yield fluorinated products at all, no matter how the experimental conditions (temperature, composition of the reaction mixture) are varied. The $C_{70}F_{36}$ – $C_{70}F_{40}$ fluorofullerenes can be readily obtained by the reaction of C_{70} with MnF_3 , while the fluorinating capacity of K_2PtF_6 does not suffice for the formation of these products. Apparently, due to specific features of the structure of the C_{70} molecule, the first step of fluorination gives $C_{70}F_{36}$ – $C_{70}F_{40}$, while a stable intermediate structure similar to $C_{60}F_{18}$ simply does not exist.

In the case of higher fullerenes C_{76} and C_{84} , both reactions proceed to give similar degrees of fluorination, although the products prepared on treatment with MnF_3 contained slight amounts of more extensively fluorinated compounds, which, in principle, corresponds to the difference between the fluorinating capacities of these reagents.

Thus, the stability regions for functionalisation of higher fullerenes have been established:⁷⁰ for $C_{84}F_m$ and $C_{76}F_m$, the m values are 40 and 26, respectively. The results are presented in Table 8 and in Fig. 14. Detailed reviews of the studies on direct fluorination of fullerenes by molecular fluorine⁷¹ and transition metal fluorides⁵⁴ have been published.

Table 8. Fluorination products of higher fullerenes.⁷⁰

Fullerene	Fluorinating agent	T/K	$m_{\max}$ in $C_{2n}F_m$	Major products
C_{70}	K_2PtF_6	670	—	—
	MnF_3	660	40	$C_{70}F_{38}$
	F_2	590	56	$C_{70}F_{54}$
C_{76}	K_2PtF_6	711	30	$C_{76}F_{26}$
	MnF_3	660	30	$C_{76}F_{26}$
C_{78}	MnF_3	660	36	$C_{78}F_{32}$ – $C_{78}F_{36}$
	F_2	590	54	$C_{78}F_{54}$
C_{84}	K_2PtF_6	711	40	$C_{84}F_{40}$
	MnF_3	660	44	$C_{84}F_{40}$
	F_2	590	62	$C_{84}F_{56}$, $C_{84}F_{58}$, $C_{84}F_{60}$

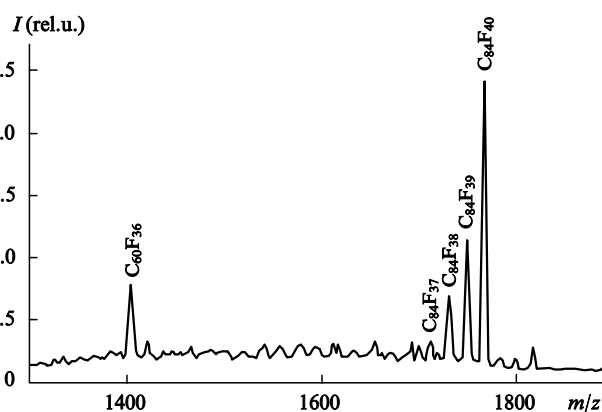


Figure 14. Electron impact mass spectrum of the product of fluorination of C_{84} fullerene.⁷⁰

IV. The use of HPLC for the separation of fluorofullerenes

Chromatography is used successfully to separate the product mixtures resulting from the synthesis of fullerenes in a discharge arc followed by extraction with organic solvents from soot in the Soxhlet apparatus.³ The use of chromatography for the separation of endohedral metallofullerenes⁷² and numerous exohedral derivatives⁷³ is documented. Nevertheless, this method was considered to be inapplicable to mixtures of fluorinated fullerenes

because their properties are virtually identical. The attempts to separate mixtures of highly fluorinated fullerenes by fractional sublimation were unsuccessful.⁷⁴ Experiments on sublimation of fluorofullerene mixtures have shown that the sublimate becomes depleted in more extensively fluorinated components compared to the initial specimen, apparently, due to their predominant thermal degradation, but separation of the mixture into individual components does not take place.

The first publication on the use of HPLC for the separation of fluorofullerenes, devoted to the preparation of $C_{60}F_{18}$ in a pure state, appeared in 1996.⁵² Since $C_{60}F_{18}$ is much more polar than the unreacted C_{60} or the side product impurities present in the specimen after the synthesis, the retention times of these compounds were found to be markedly different. This stipulated the successful use of chromatography for the isolation of the pure product. For key fluorofullerenes, a correlation has been established between the number of fluorine atoms in the molecule and the retention time: the higher the degree of fluorination, the shorter the retention time ($C_{60}F_{18} > C_{60}F_{36} > C_{60}F_{48}$). However, the compound $C_{60}F_2$ is eluted far ahead of the $C_{60}F_{18}$ fluoride, which is due to the high polarity of the latter.

Subsequently, it was shown⁷⁵ that HPLC is suitable for the separation of not only compounds with substantially different compositions and molecular structures but also fluorofullerenes with rather similar structures, for example, two $C_{60}F_{36}$ isomers. An even more vivid example should be mentioned, namely, the isolation and spectroscopic characterisation (IR spectroscopy, mass spectrometry and, in some cases, NMR spectroscopy) of 49 isomers of C_{70} fluorides.⁷⁶ In the two last-mentioned cases, the composition of the eluent had to be changed stepwise during the separation, ranging from pure toluene through toluene–hexane mixtures of various compositions to pure hexane. Thus, in the early stages, the most polar fractions with long retention times were separated and, after that, fractions with short retention times were subjected to separation in mixed eluents.

In addition to the $C_{60}F_{36}$ and $C_{70}F_{2m}$ isomers mentioned above, a series of low-fluorinated oxides of C_{60} fullerene were isolated from a sample synthesised by the reaction of C_{60} with potassium hexafluoroplatinate.⁷⁷ Note that according to mass-spectra, the fluorination products did not contain any noticeable amounts of fluorofullerene oxides, while the corresponding $C_{60}F_2$, $C_{60}F_4$, $C_{60}F_6$ and $C_{60}F_8$ fluorides were present in concentrations of the order of several percent of the concentration of the major component, $C_{60}F_{18}$. Nevertheless, the cycles of chromatographic purification and separation into fractions gave the $C_{60}F_4O$, $C_{60}F_6O$ and $C_{60}F_8O$ oxyfluorides in amounts sufficient for spectroscopic characterisation. Presumably, these oxyfluorides were not formed during the synthesis but appeared as a result of interaction of the corresponding fluorides with traces of water, present inevitably in the solvents used in chromatographic experiments. Thus, the above examples of using HPLC for the separation and purification of some fullerenes convincingly demonstrate that virtually any mixtures of fluorinated fullerenes can be separated by chromatography into individual compounds. However, when performing these works, special precautions are required because even traces of water present in the solvent can destroy fluorofullerenes.

V. Characterisation of the structure of fluorofullerenes by NMR spectroscopy and X-ray diffraction analysis

The most interesting feature of fullerenes is that they combine the properties of dienes and aromatic compounds. This can be clearly seen upon comparison of the C–C bond lengths in benzene (1.40 Å), butadiene (1.35 and 1.47 Å for the double and single bonds, respectively)⁷⁸ and [60]fullerene in which the distances between the carbon atoms at double and single bonds are 1.40 and 1.46 Å, respectively.⁷⁹ It is clear that the addition of functional

groups to the fullerene double bonds giving rise to isolated aromatic rings, diene chains, or isolated double bonds on the carbon sphere changes the π -electron system of the molecule. These aspects were discussed back in 1991–1993,^{80,81} when the first fullerene derivatives were prepared and characterised. Naturally, the mutual arrangement of functional groups on the carbon cage depends on their size. It is known that the addition of several bulky functional groups results in adducts with a uniform distribution of these groups over the carbon sphere. For example, in the hexaadduct of [60]fullerene with diethyl malonate, the functional groups are symmetrically distributed over the surface of the sphere.⁸² This gives rise to eight aromatic rings, which contribute to the stabilisation of the molecular system formed. A large number of other cycloaddition products have been described. The most frequently encountered situation is the formation of a bridging bond with addends at the 6–6 bond between two neighbouring hexagonal rings. A large variety of products is observed in the synthesis of fullerene derivatives with small functional groups or halogen or hydrogen atoms. Oxygen derivatives of fullerene can contain not more than three O atoms; therefore, they are not of special interest.

Two fundamental problems are to be solved in considering polyaddition reactions to fullerene double bonds. The first one is to elucidate the pathway along which the carbon sphere is covered successively by X atoms added in pairs and to understand the factors that dictate this pathway. The other task concerns the determination of the most preferable geometric isomers of the many thousands of isomers theoretically possible. Below, we present the numbers of theoretically possible positional isomers for the addition of X atoms to [60]fullerene.⁸³

n in $C_{60}X_n$	The number of isomers	n in $C_{60}X_n$	The number of isomers
2	23	10	628 330 629
4	4 190	12	11 661 527 055
6	418 470	20	34 932 048 763 560
8	21 330 558	30	985 538 239 868 528

It can be seen that even for $n = 8$, the number of possible $C_{60}X_8$ isomers is an astronomical value which is beyond the potential of theoretical calculations. Therefore, various approaches are used to restrict the number of probable structures. It is clear that much fewer isomers can really be synthesised. The researchers need to find out what factors favour stabilisation of particular structures and also to elucidate the cases where either kinetic or thermodynamic factors play crucial role.

It may seem that the C_{60} –hydrogen system is the most natural model system for these studies. Indeed, several hydrides of [60]fullerene have been described: $C_{60}H_2$, $C_{60}H_4$ and $C_{60}H_6$; the molecular structure of $C_{60}H_{18}$ has been determined; the compound $C_{60}H_{36}$ has been obtained in macroscopic quantities.⁶⁸ However, the structural characterisation of hydrides is far from being complete due to the low stability of these species in solutions. In particular, the isomeric composition of $C_{60}H_{36}$, which is prepared most easily, is still unknown. No successful X-ray diffraction studies have been carried out for this class of compound.

The number of fullerene halides characterised to date increases in the series: $C_{60}I_x$, $C_{60}Cl_x$, $C_{60}Br_x$, $C_{60}F_x$. Whereas for iodinated derivatives, only the formation of an unstable molecular complex $C_{60} \cdot I_2$ has been described,⁸⁴ the chloride $C_{60}Cl_6$ has been fully characterised,⁸⁵ and unconfirmed data on the existence of $C_{60}Cl_{24}$ and $C_{60}Cl_{40}$ have been reported.^{86,87} Three bromofullerenes are known, $C_{60}Br_6$, $C_{60}Br_8$ and $C_{60}Br_{24}$; for each of them, X-ray diffraction data have been reported.^{88,89} The C_{60} –fluorine system clearly stands out in this series of halogenated derivatives. First, the existence of the whole series of $C_{60}F_{2x}$ fluorofullerenes, from $C_{60}F_2$ to $C_{60}F_{60}$ has been proven experimentally.⁵³ Second, the three most stable compounds,

$C_{60}F_{18}$, $C_{60}F_{36}$ and $C_{60}F_{48}$, have been obtained in macroscopic amounts and their structures have been determined. Third, the chemical structures of a series of fluorofullerenes with low fluorine contents, including $C_{60}F_2$, have been determined. Thus fluorinated fullerenes can serve as a 'training ground' for working-out the main approaches to the preparation of fullerene derivatives with small functional groups. First of all, this is associated with the fact that, due to the exceptional strength of the C–F bond, fluorofullerenes are stable in air, rather thermally stable and can be subjected to virtually any type of physicochemical investigations. The good solubility of these compounds in many organic solvents has played an important role in the development of methods for chromatographic separation of fluorofullerenes according to the number of added groups or into individual geometric isomers. After the first successful experiments on chromatographic isolation of individual $C_{60}F_{18}$ fluoride and separation of the two major isomers of $C_{60}F_{36}$, it became clear that it is possible to prepare pure products of C_{60} fluorination over a broad range of fluorine contents. Although not all fluorinated fullerenes have been isolated and characterised, the spectroscopic and X-ray diffraction data concerning their structures make it possible to establish some important features of successive addition of fluorine atoms to the fullerene double bonds.

1. [60]Fullerene difluoride

The difluoride of [60]fullerene and difluorides of higher fullerenes have been detected^{13,39} during mass-spectrometric analysis of fluorofullerene vapours (the results of experiments on determination of the electron affinity and the C–F bond energies of these molecules are described in Section II). However, it was not until the year 2000 that [60]fullerene difluoride was prepared in macroscopic amounts.⁹⁰ The ^{19}F NMR spectrum of the $C_{60}F_2$ fluorofullerene exhibits a singlet at 148.3 ppm. The 1,2- and 1,4-isomers have been considered as possible alternatives, because, according to theoretical calculations, they are much more stable than the other formally conceivable isomers and also because of the fact that the first fluorine atom added polarises most of all the nearest region of the π -system of the molecule.⁹⁰ The 1,2-isomer of $C_{60}F_2$ is more stable than the 1,4-isomer, as the latter contains a double bond in a five-membered ring, which destabilises the compound. This compound is formed only with relatively large substituents. For example, methylation of [60]fullerene gives a mixture of 1,2- and 1,4-methyl derivatives, whereas benzylation results in the formation of the 1,4-benzyl derivative.⁹¹ Since the fluorine atom is smaller than the carbon atom, there are no pre-requisites for the formation of the 1,4-derivative.

The position of the peak in the ^{19}F NMR spectrum of $C_{60}F_2$ fluorofullerene is more consistent with the 1,2-isomer rather than with the 1,4-isomer. In the latter compound, each sp^3 -hybridised carbon atom bearing a fluorine atom is surrounded by three sp^2 -hybridised carbon atoms, whereas in the 1,2-isomer, only by two

sp^2 carbon atoms. Therefore, in the case of the 1,4-isomer, it would be reasonable to expect a peak in the region of 120–130 ppm.

Additional information on the structure of $C_{60}F_2$ was gained from its ^{13}C NMR spectrum. The 1,4-isomer of $C_{60}F_2$ (C_s symmetry) should account for $27 \times 2C + 4 \times 1C = 31$ lines in the spectral region corresponding to sp^2 atoms, while the 1,2-isomer (C_{2v} symmetry) should give rise to $3 \times 2C + 13 \times 4C = 16$ lines. The spectrum of the $C_{60}F_2$ fluorofullerene displays less than 28 peaks. This confirms once again that the 1,2-isomer of $C_{60}F_2$ was isolated.

2. Oxyfluoride $C_{60}F_4O$

The ^{19}F NMR spectrum of the $C_{60}F_4O$ oxyfluoride consists of two lines of equal intensity. The structure proposed for this compound⁷⁷ is presented in Fig. 15a. As can be seen from the Figure, the fluorine atoms added occur in positions 1, 2, 3 and 4, and the oxygen atom is, apparently, attached to the carbon atoms of the 6–5 bond, *i.e.*, this compound is an intramolecular ether.

3. Oxyfluoride $C_{60}F_6O$

The ^{19}F NMR spectrum of $C_{60}F_6O$ reported by Boltalina *et al.*⁷⁷ consists of six lines of equal intensity. The positions of lines lead to the conclusion that the fluorine atoms in $C_{60}F_6O$ fall into two groups, one comprising two F atoms and one comprising four F atoms. The chemical shifts of the first-group fluorine atoms are much smaller. This suggests that they are attached to the same carbon atoms as oxygen. In addition, two fluorine atoms of the second group are characterised by similar chemical shifts, which may attest to their similar positions with respect to the oxygen bridge. On the basis of these data, a structure was proposed for this compound (Fig. 15b).

4. Oxyfluoride $C_{60}F_8O$

The ^{19}F NMR spectrum of $C_{60}F_8O$ consists of four lines of equal intensity.⁷⁷ It was concluded that the $C_{60}F_8O$ molecule has, most probably, C_s symmetry. A structure consistent with these conditions was proposed (Fig. 15c).

5. Fluorofullerene $C_{60}F_{16}$

The ^{19}F NMR spectrum of $C_{60}F_{16}$ fluorofullerene consists of eight lines of equal intensity.⁹² The fluorine atoms attached to the carbon atoms that are surrounded by three sp^3 -hybridised C atoms are responsible, in most cases, for a signal at about –150 to –160 ppm. The $C_{60}F_{16}$ molecule contains two fluorine atoms of this type (B). The signals of fluorine atoms attached to the carbon atoms whose environment comprises one sp^3 and two sp^2 carbon atoms are usually displayed in the region of –120 to –130 ppm. Two pairs of these fluorine atoms (A and H) are present in the $C_{60}F_{16}$ molecule. The positions of other fluorine atoms were established using 2D COSY ^{19}F NMR spectra. On the basis of the results obtained, a structure for $C_{60}F_{16}$ was proposed

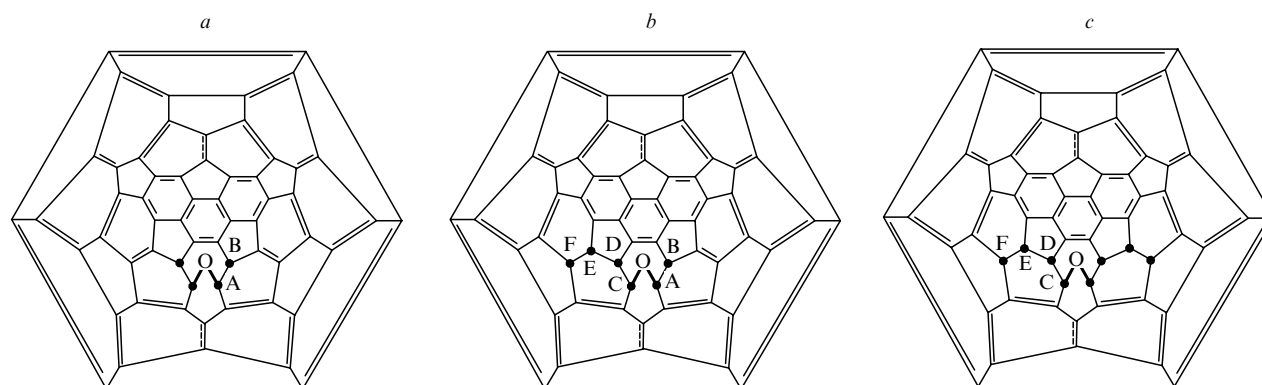


Figure 15. Schlegel diagrams of $C_{60}F_4O$ (a), $C_{60}F_6O$ (b) and $C_{60}F_8O$ (c).⁷⁷ The dark circles show the positions of fluorine atoms.

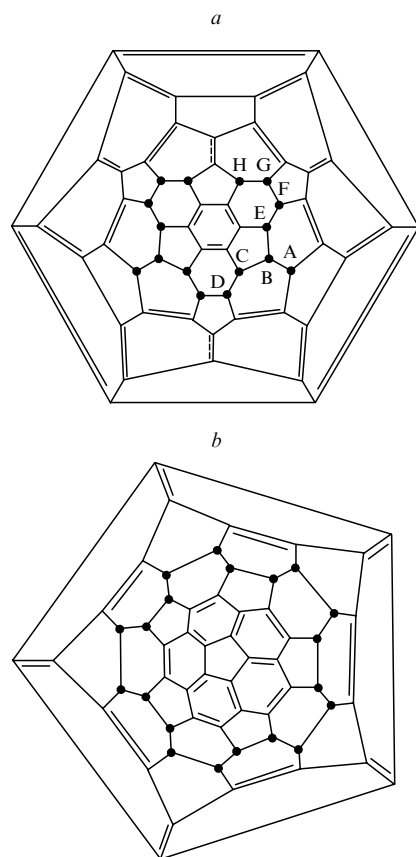


Figure 16. Schlegel diagrams of C₆₀F₁₆ (a)⁹² and C₆₀F₂₀ (b)⁹³. The dark circles show the positions of fluorine atoms.

(Fig. 16 a). Researchers were able to prove convincingly that this structure differs from the structure established for the C₆₀F₁₈ fluorofullerene (see below) only by the absence of the two fluorine atoms attached to the 6–6 bond.

6. Fluorofullerene C₆₀F₂₀

The ¹⁹F NMR spectrum of C₆₀F₂₀ fluorofullerene contains only one line at –138.8 ppm (see Ref. 93). The structure proposed in the study cited is shown in Fig. 16 b. A specific feature of the structure is that all 20 fluorine atoms are arranged along the equator, while the poles are occupied by five-membered rings surrounded by five six-membered aromatic rings. This molecule, the carbon cage of which is ‘squashed’ along a fivefold axis and is surrounded by an annulus made of fluorine atoms along the equator, has been called ‘saturnene.’

7. Compounds C₆₀F₁₈ and C₆₀F₁₈O

These two compounds are remarkable due to the fact that single crystals suitable for X-ray diffraction analysis were grown for them and the full set of interatomic distances was obtained. Therefore, we shall discuss these compounds in more detail.

The ¹⁹F NMR spectrum of C₆₀F₁₈ fluorofullerene (376.14 MHz, CDCl₃) was first recorded in 1996.⁵² The spectrum consists of four lines with $\delta = -131.6$ (d); –136.0 (dd); –143.4 (d) and –158.1 ppm (dt) with an intensity ratio of 1:2:2:1 (Fig. 17).

Of all kinds of structures, the isomer with C_{3v} symmetry complies best with this spectrum; the Schlegel diagram for this molecule is presented in Fig. 18. This structure was confirmed by ¹³C NMR spectroscopy. As can be seen from Fig. 18, all the fluorine atoms are located in one hemisphere. The six-membered ring consisting of *sp*²-hybridised carbon atoms is entirely sur-

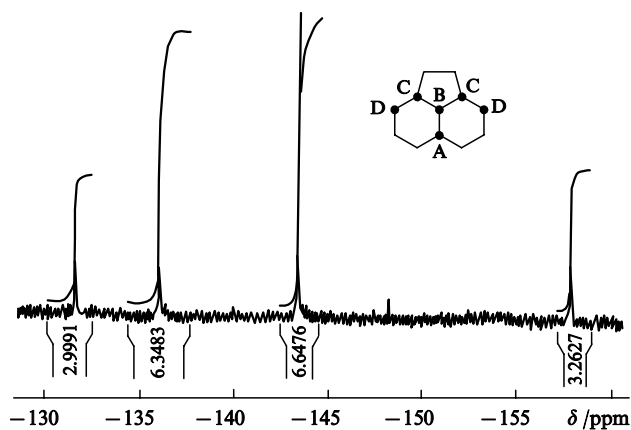


Figure 17. ¹⁹F NMR spectrum of C₆₀F₁₈ fluorofullerene.⁵²

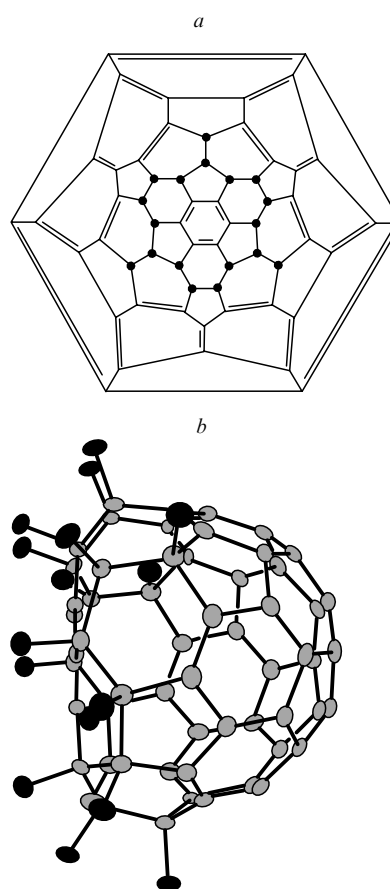


Figure 18. Schlegel diagram (a) and the structure (b) of the C₆₀F₁₈ molecule.⁹⁵ The dark circles show the positions of fluorine atoms.

rounded by the *sp*³-hybridised carbon atoms that bear fluorine atoms.

The C₆₀F₁₈O oxyfluoride was first isolated by HPLC in 1998 as a side product of the reaction between C₆₀ fullerene and K₂PtF₆; the ¹⁹F NMR spectrum of this compound was recorded.⁹⁴ The fluorine atoms are arranged in the same way as in the C₆₀F₁₈ molecule. Elucidation of the position of oxygen appears to be a key point because the character of the C–O bond in this compound is of prime importance for the understanding of the structure of other fullerene oxyfluorides. If oxygen is incorporated either along or across the plane of symmetry (three options), the ¹⁹F NMR spectrum should consist of ten lines, 8 × 2F and 2 × 1F. For other variants of oxygen addition, the number of lines

in the spectrum should increase to eighteen due to the loss of symmetry. Analysis of the ^{19}F NMR spectrum (10 lines) and 2D COSY ^{19}F NMR spectrum showed that this isomer has C_s symmetry. The positions of three peaks are characteristic, namely, at -94.60 (K), -161.27 (B) and -168.81 ppm (G). The peak of atoms K occurs in the spectral region typical of fluorine atoms located in the close vicinity of the oxygen atom. The positions of peaks of atoms B and G are similar to the peaks in the spectra of fullerene fluorides for the fluorine atoms attached to carbon atoms surrounded by three sp^3 -hybridised C atoms.

The structure of $\text{C}_{60}\text{F}_{18}\text{O}$ will have C_s symmetry in the case where oxygen adds either at the cleaved 6–5 bond forming an ether bridge (to the fullerene cage) or at the 6–6 bond to give an epoxide. In one publication,⁹⁴ preference was given to the epoxide structure on the basis of NMR data. In 2000, we succeeded in growing single crystals and performing full X-ray diffraction analysis of the molecular complexes of $\text{C}_{60}\text{F}_{18}$ and $\text{C}_{60}\text{F}_{18}\text{O}$ with toluene and the complexes of $\text{C}_{60}\text{F}_{18}$ with *m*- and *p*-xylenes. These were the first crystallographic data for fluorinated fullerenes.^{95–97} The resulting structures of the $\text{C}_{60}\text{F}_{18}$ and $\text{C}_{60}\text{F}_{18}\text{O}$ molecules are presented in Fig. 19. First of all, note that $\text{C}_{60}\text{F}_{18}\text{O}$ is an ether in which the ether bridge is located in place of the 6–5 bond (see Fig. 19a). The oxygen atom is inserted into the weakest (longest) C–C bond to give the so-called intra-ether derivative. This is the first structure of this type among fullerene compounds. Relying on the results obtained for $\text{C}_{60}\text{F}_{18}\text{O}$,⁹⁵ structures with ether bridges were ascribed to all oxyfluorides considered. The X-ray diffraction analysis of molecular complexes formed by $\text{C}_{60}\text{F}_{18}$ confirmed the NMR data pointing to the location of the 18 fluorine atoms on one half of the carbon sphere. Moreover, it was shown that this accumulation of fluorine around one six-membered ring results in a substantial change in the C–C bond lengths, in particular, the bond lengths in this six-membered fragment become equal, and it becomes a fully aromatic (benzene-like) ring. Global changes in the fluorinated hemisphere itself have also been noted: in particular, the curvature radius of the benzene-like fragment substantially increases, the fragment is flattened, whereas the second half not occupied by fluorine largely retains its size and shape, as in the initial fullerene molecule.^{95–97} The carbon cage of this molecule has been termed ‘flattened’.

8. Fluorofullerene $\text{C}_{60}\text{F}_{36}$

The first fullerene derivative, obtained in 1991,⁶⁸ was the $\text{C}_{60}\text{H}_{36}$ hydride. Since then, attempts at determining the structure of this compound were repeatedly undertaken; however, no apparent progress was made. A large number of theoretical studies have been devoted to calculations of the molecular structure of $\text{C}_{60}\text{X}_{36}$ ($\text{X} = \text{H}, \text{F}$). The isomer with T symmetry containing four isolated benzene-like rings was found to be the most stable.⁹⁸

It was natural to suggest that the products of hydrogenation and fluorination of [60]fullerene (C_{60}H_x and C_{60}F_x) would be isostructural at identical x . An important factor is the similarity of steric effects; the fluorine and hydrogen atoms are smaller than the carbon atom, and similar radical mechanisms have been suggested for both reactions.

Initially, it was found that the first stages of both fluorination and hydrogenation give compounds with 18 addends, which are characterised by a highly symmetric structure (C_{3v} symmetry), and the X atoms are arranged on the carbon cage like a crown framing a six-membered ring.⁵²

The second stage of both hydrogenation and fluorination is the formation of the $\text{C}_{60}\text{X}_{36}$ structure. In the fluorination of C_{60} on treatment with MnF_3 , $\text{C}_{60}\text{F}_{36}$ is the major product.

Nevertheless, the ^{19}F NMR spectrum of the resulting material displayed up to 30 lines; this can indicate either low symmetry of the $\text{C}_{60}\text{X}_{36}$ molecule or the presence of a mixture of positional isomers.

After purification of the sample by sublimation, the number of lines decreased to 12, and analysis of the 2D COSY spectrum pointed to the presence of several positional isomers. It was

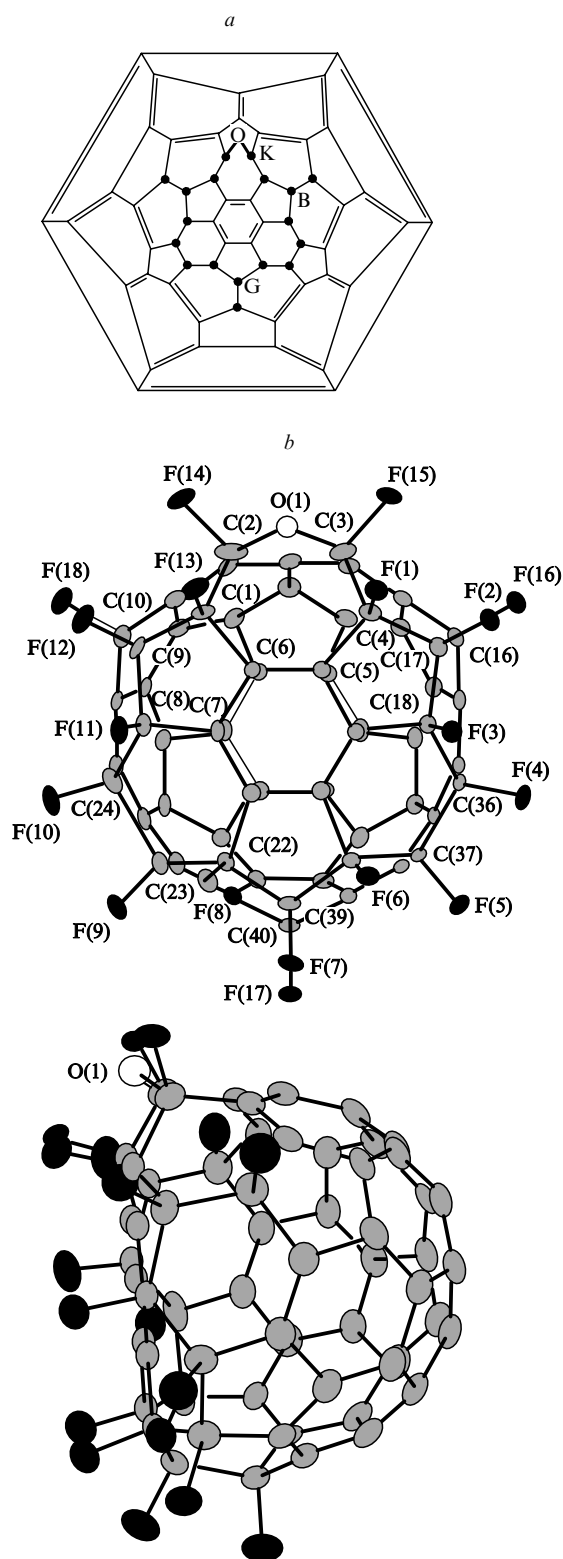


Figure 19. Schlegel diagram (a) and the structure (b, two projections are given) of the $\text{C}_{60}\text{F}_{18}\text{O}$ molecule.⁹⁵ The dark circles show the positions of fluorine atoms.

assumed that one isomer responsible for only three lines with equal intensity had T symmetry. Chromatography gave two major fractions exhibiting virtually identical mass spectra. The ^{19}F NMR spectrum of the first fraction that had a shorter retention time contained 12 equally intense lines. Theoretical

analysis indicated that this spectrum could correspond to a structure with C_3 symmetry.

The ^{19}F NMR spectrum of the second fraction exhibited only three lines with an intensity ratio of 1 : 1 : 1, as was to be expected for a structure with T symmetry. However, three isomers with D_{3d} symmetry also comply theoretically with the observed spectrum. The final decision in favour of the T structure was based on the ^{13}C NMR spectrum of the second fraction, which contained two equally intense lines at 136.6 and 137.5 ppm (the region corresponding to sp^2 -hybridised carbon atoms). Meanwhile, the D_{3d} isomers would require the presence of three lines with a 1 : 1 : 2 intensity ratio. The Schlegel diagram for the $\text{C}_{60}\text{F}_{36}$ fluorofullerene with T symmetry⁷⁵ is shown in Fig. 20a.

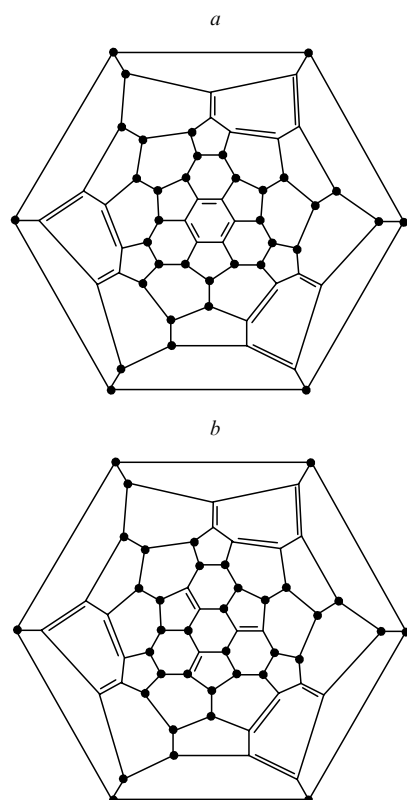


Figure 20. Schlegel diagrams of T (a)⁷⁵ and C_3 isomers (b)¹⁰⁰ of $\text{C}_{60}\text{F}_{36}$ fluorofullerene. The dark circles show the positions of fluorine atoms.

The isomer with C_3 symmetry was suggested initially to contain three benzene-like rings of the four rings present in the T isomer and three isolated double bonds of the 6–6 type.⁹⁹ This conclusion was based on kinetic reasoning according to which pairs of fluorine atoms are added successively to 6–6 double bonds; therefore, the double bonds of the same type remaining in the molecule should not change positions. Boltalina *et al.*⁹⁹ have found evidence for this assumptions in a study of $\text{C}_{60}\text{F}_{36}$ by 2D COSY ^{19}F NMR spectroscopy. However, according to the data of quantum-chemical calculations, the proposed isomer was markedly less stable than the isomer with T symmetry. Conversely, a recent NMR study of the C_3 isomer of $\text{C}_{60}\text{F}_{36}$ attests in favour of a structure that also contains three benzene-like rings and three isolated double bonds but the latter occupy 6–5 positions.¹⁰⁰ The Schlegel diagram of this isomer is shown in Fig. 20b. According to theoretical calculations, it is comparable in stability with the isomer having T symmetry, which suggests thermodynamic control in the formation of $\text{C}_{60}\text{F}_{36}$. This might imply the possibility of rearrangements of fluorine atoms on the carbon cage during fluorination.

9. Fluorofullerene $\text{C}_{60}\text{F}_{48}$

The first experimental data on the structure of $\text{C}_{60}\text{F}_{48}$ were obtained by Gakh *et al.*⁶² Later, these data were confirmed using more pure specimens.¹⁰¹ The ^{19}F NMR spectrum of the $\text{C}_{60}\text{F}_{48}$ fluorofullerene was found to display eight equally intense lines corresponding to eight nonequivalent fluorine atoms. According to theoretical data, this spectrum is consistent with nine possible structures, namely, five enantiomer pairs with D_3 symmetry and four S_6 isomers. The Schlegel diagrams for the $\text{C}_{60}\text{F}_{48}$ molecule with D_3 symmetry⁶² and for the molecule with S_6 symmetry, which are the most stable according to calculations,¹⁰² are shown in Fig. 21.

It should be noted that analysis of 2D COSY spectra recorded in the study cited⁶² showed the presence of 1,2-interactions (A–E, A–G, B–F, B–G, C–H, D–F, D–H, E–F), which corresponded to the theoretical structure with D_3 symmetry; however, of the set of predicted 1,3-interactions (A–B, A–D, A–F, B–C, B–D, B–E, C–D, D–E, E–G, F–G, F–H), only the first, the second, the fourth and the seventh ones were detected. Later,¹⁰¹ a 2D COSY spectrum was recorded pointing to the existence of the A–F, D–E, E–G and F–G interactions. This confirms the D_3 structure proposed by Gakh *et al.*,⁶² but does not rule out the molecule with S_6 symmetry. The final decision concerning the structure of this fluorofullerene was based on the results of X-ray diffraction analysis of a $\text{C}_{60}\text{F}_{48}$ single crystal grown from a mesitylene solution,¹⁰³ which showed that the reaction of C_{60}

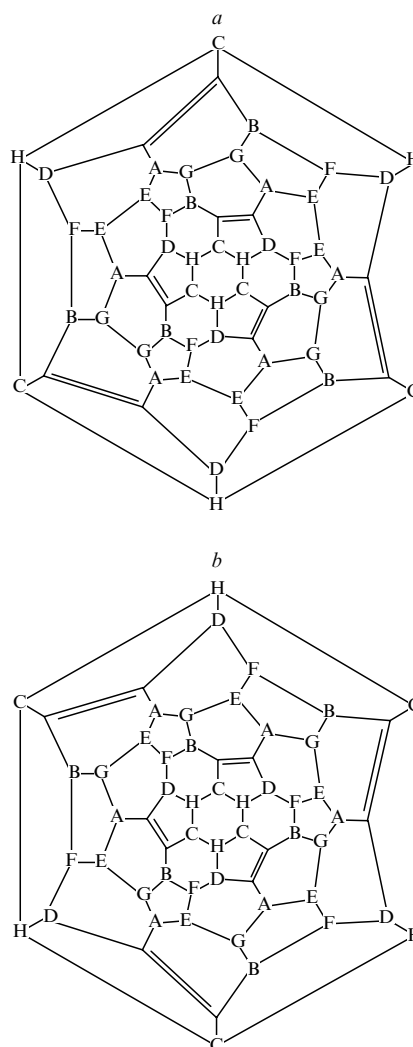


Figure 21. Schlegel diagrams of D_3 (a) and S_6 isomers (b) of $\text{C}_{60}\text{F}_{48}$ fluorofullerene.⁶²

with gaseous fluorine gives comparable amounts of both isomers. Note that the carbon cage regions near the double bonds in these molecules are characterised by a slight negative curvature; therefore, they are called 'indented'. It is remarkable that of the many millions of $C_{60}F_{48}$ isomers possible theoretically, the reaction with gaseous fluorine gives only two isomers. According to the results of MNDO¹⁰⁴ and AM1¹⁰⁵ semiempirical calculations, these molecules are thermodynamically much more stable than the other possible isomers with exohedral addition of fluorine atoms. Our calculations by the density functional method predict that the isomer with D_3 symmetry is 15 kJ mol^{-1} more stable than that with S_6 symmetry. Note that according to AM1 calculations,¹⁰⁵ an isomer in which six fluorine atoms are attached to the inside of the carbon cage is expected to be even more stable. However, the formation of such a compound should be kinetically hampered, and no experimental data confirming its existence have been obtained.

Thus, the amount of experimental data accumulated to date is sufficient for evaluating its correspondence to the theoretical descriptions of such systems. The good coincidence of the theoretical estimates for the thermodynamically stable $C_{60}F_{48}$ isomers with the experimental data on the enthalpies of formation and the molecular structures of the isomers having S_6 and D_3 symmetry can be taken as the starting point.

The NMR spectra of solid samples usually do not provide enough information to draw conclusions about the molecular structure of the compound, due to the strong interactions between the nuclei in the solid. The fine spectral structure is observed rather rarely in these cases. Nevertheless, having prepared reasonable ($> 1 \text{ g}$) amounts of the $C_{60}F_{48}$ fluorofullerene, Boltalina *et al.*¹⁰¹ attempted to study the crystalline specimen by ^{19}F NMR spectroscopy.

The high-resolution MAS ^{19}F NMR spectrum of crystalline $C_{60}F_{48}$ recorded at 340 K consists of eight principal lines with equal intensity (Fig. 22) corresponding to eight non-equivalent fluorine atoms attached to positions A–H in the $C_{60}F_{48}$ molecule (see Fig. 21). Note that the chemical shifts in the ^{19}F NMR spectrum recorded in solution virtually coincide with those for the solid specimen, indicating the absence of an appreciable influence of the solvent. Apart from the eight principal lines, the spectrum contains four groups of low-intensity lines (10% of the total intensity), which refer apparently to $C_{60}F_{2n}$ ($2n < 48$) impurities or to $C_{60}F_{48}$ with a different symmetry.

The data on the molecular structures of compounds $C_{60}F_4O$, $C_{60}F_6O$, $C_{60}F_8O$, $C_{60}F_{16}$, $C_{60}F_{18}$ and $C_{60}F_{20}$ derived from NMR

spectra and presented as Schlegel diagrams (see Figs 15, 16, 18), allow one to consider the possible mechanism of successive addition of small functional groups to C_{60} fullerene. After addition of the first two fluorine atoms, the localised double bonds in the two conjugated six-membered rings that have lost the common double bond and contain two sp^3 carbon atoms become the reaction centres of choice. Further addition of atoms is directed at these particular bonds and partial or complete aromatisation of the six-membered rings which have retained three double bonds takes place at certain degrees of saturation. Yet another specific feature of the mechanism of fullerene fluorination is that fluorine atoms are able to migrate over the surface of the carbon cage. This results in the formation of thermodynamically the most stable isomers. As a consequence, each subsequent fluorofullerene in the series $C_{60}F_{18}$, $C_{60}F_{36}$, $C_{60}F_{48}$ does not contain the substructure of the preceding one, *i.e.*, it cannot be prepared from the preceding isomer by mere addition of more fluorine atoms. These aspects have been considered in detail.¹⁰⁶

To date, only three compounds of the $C_{60}F_{2n}$ series have been synthesised in macroscopic quantities and comprehensively characterised. These are $C_{60}F_{48}$, $C_{60}F_{36}$ (two isomers with T and C_3 symmetry) and $C_{60}F_{18}$. The stability of two isomers of $C_{60}F_{36}$ and $C_{60}F_{18}$ is due to delocalisation of π -electrons in six-membered rings, *i.e.*, to the formation of aromatic substructures. In addition, one hemisphere of the carbon cage of the $C_{60}F_{18}$ fluorofullerene inherits the π -system of [60]fullerene. However, the existence of the C_3 isomer of the $C_{60}F_{36}$ fluorofullerene indicates that in the presence of 36 attached fluorine atoms, steric factors, namely, deformation of the carbon cage upon transition of some carbon atoms to the sp^3 state and repulsion of substituents, already play an important role. The bond angles typical of both sp^3 - and sp^2 -hybridised carbon atoms cannot be attained simultaneously for all of the atoms due to geometric restrictions, which results in a rather strained structure. In addition, the proximity of the fluorine atoms (in fluorofullerene molecules, especially in $C_{60}F_{48}$, the distances between neighbouring fluorine atoms are often several tenths of an angstrom smaller than twice the van der Waals radius of fluorine¹⁰³) leads to their repulsion and, as a consequence, weaken the σ -bonds in the carbon cage; in some cases, these bonds become $1.63\text{--}1.67 \text{ \AA}$ long. Stabilisation of the carbon cage could, apparently, be expected for a more uniform distribution of the carbon–carbon double bonds, although this results in separation of the bonds from one another and, hence, a decrease in the π – π conjugation. This might account for the formation of an isomer with C_3 symmetry with three isolated carbon–carbon double bonds, apart from the T isomer in which all double bonds are combined in benzene-like aromatic rings. In the case of $C_{60}F_{48}$ fluorofullerene, the steric factor predominates. Note that the remaining six double bonds are practically difficult to access and attempts at further fluorination under more drastic conditions lead to the partial destruction of the carbon cage. It is of interest that according to some theoretical calculations,¹⁰⁵ stabilisation of fullerene fluorides containing ~ 48 fluorine atoms could be attained by repudiating the convexity of the carbon cage, assuming that some fluorine atoms are attached on the inside. In this type of structure containing both *exo*- and *endo*-fluorine atoms, the bond angle could be more consistent with hybridisation states of the carbon atoms, *i.e.*, strain relaxation in the carbon cage could take place. At present, it is difficult to verify this hypothesis because the pathway to these isomers should face, in any case, substantial kinetic impediments.

Full sets of structural parameters have been obtained only for the $C_{60}F_{18}$, $C_{60}F_{48}$, $C_{60}F_{18}O$ and $C_{60}F_{17}CF_3$ fluorinated fullerenes, which crystallise as molecular complexes with various aromatic compounds. The study of $C_{60}F_{36}$ fluorofullerene is appreciably hampered by two factors. These are, first, rotation of molecules and, second, the presence of structural isomers. For other fluorofullerenes, the task is reduced to the preparation of compounds in macroscopic quantities sufficient for growing single crystals. Studies along this line are in progress.

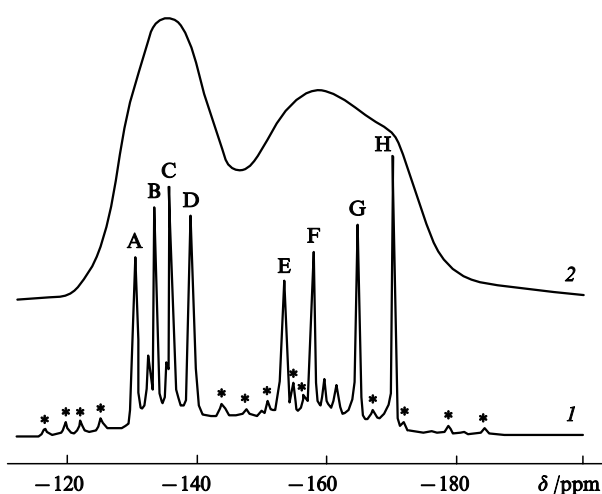


Figure 22. High-resolution MAS ^{19}F NMR spectrum of crystalline $C_{60}F_{48}$.¹⁰¹

(1) MAS/ $\Omega = 4050 \text{ Hz}$; (2) $\Omega = 0 \text{ Hz}$.

The asterisks show the satellites caused by rotation.

VI. Thermodynamic properties

1. Heat capacity and orientational phase transitions

Low-temperature heat capacities of $C_{60}F_{48}$ and $C_{60}F_{36}$ were determined in 1999¹⁰⁷ (no other data have appeared thereafter). The heat capacity was measured in a fully automated vacuum adiabatic calorimeter described in the literature.^{108, 109}

The temperature dependence of the heat capacity of $C_{60}F_{48}$ (Fig. 23) exhibits a thermal anomaly represented by a reversible order–disorder phase transition in the temperature range of 315–345 K. To establish the nature of the anomaly, the substance was studied by NMR spectroscopy and powder X-ray diffraction analysis.¹⁰⁷ According to calorimetric measurements,¹⁰⁷ NMR spectroscopy and X-ray diffraction data, the $C_{60}F_{48}$ fluorofullerene undergoes a reversible non-isothermal phase transition ‘ordered crystal II $\rightarrow$ plastic crystal I’ accompanied by rearrangement of the body-centered tetragonal (BCT) crystal structure into a face-centred cubic (FCC) structure.¹¹⁰ The phase transition temperature in $C_{60}F_{48}$ was taken to be 329.6 ± 0.4 K. At this temperature, the apparent heat capacity is a maximum. The thermodynamic parameters of the ‘order–disorder’ transitions for $C_{60}F_{48}$ fluorofullerene and C_{60} fullerene¹¹¹ are listed in Table 9. The enthalpies of the transitions ($\Delta_{\text{trs}}H^\circ$) were determined by calorimetry¹⁰⁸ on the basis of the total amount of energy required for the phase transition. The $\Delta_{\text{trs}}H^\circ$ value is lower for

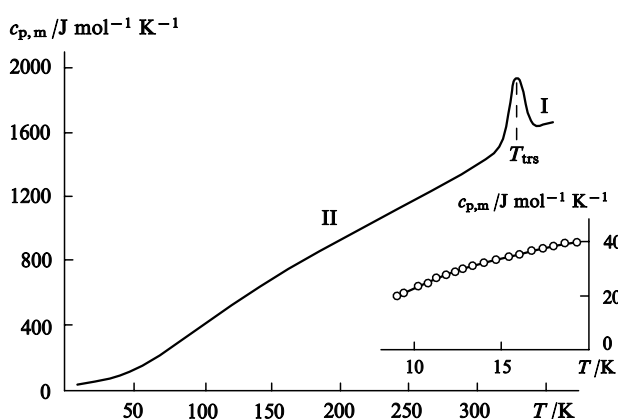


Figure 23. Temperature dependence of the heat capacity of $C_{60}F_{48}$ fluorofullerene.

Here and in the inset in Fig. 24, the initial pattern of the dependence is shown.

Table 9. Thermodynamic parameters of ‘order–disorder’ phase transitions for $C_{60}F_{36}$, $C_{60}F_{48}$ and C_{60} and absolute entropies and entropies of formation of these fluorofullerenes at 298.15 K.

Parameter	Compound		
	C_{60}	$C_{60}F_{48}$	$C_{60}F_{36}$
$\Delta_{\text{trs}}T$ / K	185–275	315–345	
T_{trs} / K	260.7	329.6 ± 0.4	370
$\Delta_{\text{trs}}H^\circ$ / kJ mol ^{−1}	7.46 ± 0.15	7.0 ± 0.7	
$\Delta_{\text{trs}}H^\circ$ / J g ^{−1}	10.4 ± 0.2	4.8 ± 0.4	
$\Delta_{\text{trs}}S^\circ$ / J mol ^{−1} K ^{−1}	28.6 ± 0.6	21.2 ± 2.4	
S_m° / J mol ^{−1} K ^{−1}	426.5	1137.2 ± 6	1014.5 ± 5
$\Delta_f S_m^\circ$ / J mol ^{−1} K ^{−1}	84.5	-4071.6 ± 6	-2978.2 ± 5

Note. ΔT_{trs} , T_{trs} , $\Delta_{\text{trs}}H^\circ$ and $\Delta_{\text{trs}}S^\circ$ are the temperature range, the temperature, and the enthalpy and entropy of the phase transition, respectively; S_m° and $\Delta_f S_m^\circ$ are the absolute entropy and the entropy of formation of fluorofullerene, respectively.

$C_{60}F_{48}$ fluorofullerene than for C_{60} fullerene. The resulting temperature dependences of the heat capacities, enthalpy, and entropy of phase transitions were used to calculate the thermodynamic functions at 298.15 K¹¹² (see Table 9).

It can be seen from Fig. 24 that the temperature dependence of the heat capacity of $C_{60}F_{36}$ plotted using the data of adiabatic calorimetry displays no anomalies in the range of 8–356 K. A phase transition was discovered by differential scanning calorimetry (DSC) at a higher temperature, namely, at 370 K.¹¹³ The high-temperature phase of $C_{60}F_{36}$ existing at $T > 370$ K has a FCC lattice, which passes to a simple cubic (SC) lattice as the temperature decreases.¹¹⁴ According to NMR and powder X-ray diffraction data, this is also an orientational transition. The orientational transitions discovered in fluorofullerenes are similar to the well-known phase transition in [60]fullerene. The molecules of C_{60} are known to form a FCC lattice at temperatures $T > 260$ K and an SC lattice at $T < 260$ K.¹¹⁵ It was found that at 260 K, a first-order phase transition takes place caused by transformation of a high-temperature orientationally ordered phase into a low-temperature orientationally ordered one. As this takes place, the centres of gravity of the molecules virtually do not shift, and the C_{60} molecules assume a quite definite orientation, thus changing the translational symmetry of the crystal. A specific feature of the orientational phase transition is that the C_{60} molecules execute re-orientations, fast on the ¹³C NMR time scale ($\nu \approx 10^{-13}$ s^{−1}). At high temperatures ($T > 260$ K), these are chaotic isotropic re-orientations, while at $T < 260$ K, correlated group re-orientations take place.¹¹⁵

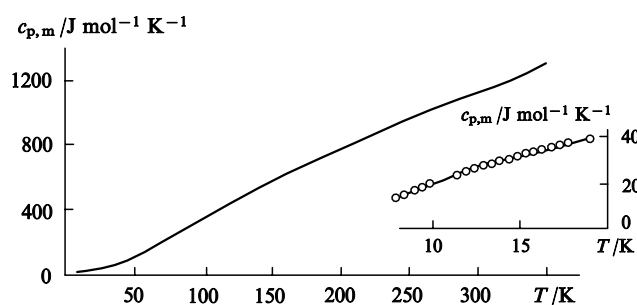


Figure 24. Temperature dependence of the heat capacity of $C_{60}F_{36}$ fluorofullerene.

During calorimetric measurements of the characteristics of the orientational phase transition (enthalpy and temperature) in a C_{60} fullerene crystal, an interesting feature was discovered: after mechanical grinding in a mortar, the temperature and the enthalpy of phase transition of the C_{60} specimen decreased down to the complete disappearance of the maximum in the temperature dependence of heat capacity, the fullerene crystallinity being retained.^{116–119} Meanwhile, the NMR study of the temperature dependence of the spin–lattice relaxation time of ¹³C nuclei showed that at 260 K, this value changes jumpwise for both the initial and ground C_{60} specimens, although the jump is less pronounced in the latter case.^{119, 120} These results were interpreted¹²¹ in the following way. The spatial defects that originated upon the mechanical treatment of a [60]fullerene specimen break the crystalline phase of C_{60} into a great number of regions in which the orientational ordering of the C_{60} molecules occurs independently. In other words, local transitions take place instead of a collective effect throughout the whole phase (specimen). Finally, the orientational phase transition in a calorimetric experiment becomes smeared, but the low-temperature phase is still formed (as indicated by the step in the temperature dependence of the spin–lattice relaxation time of ¹³C nuclei). It should also be noted that the presence of impurities (solvent molecules) barely influences the parameters of the orientational phase transition,¹¹⁸ but it

does influence the ^{13}C spin – lattice relaxation time, although only in the high-temperature phase,¹²⁰ in which the C_{60} molecules execute orientationally disordered motion.

The influence of an increase in the rate of crystallisation (from solutions) or vacuum sublimation is similar to mechanical grinding: both processes increase the degree of defectiveness of crystals, which results in smearing of the orientational phase transition. Unfortunately, no theoretical description of these phenomena is available to date. The works that can be regarded as the latest achievements along this line include the development of theoretical approaches to the description of the orientational phase transition in the C_{60} crystal, namely, the model of thermal behaviour of a thermoelastic medium with internal orientation based on the Landau theory and the model of anisotropic reorientations of the C_{60} molecules for the description of the spin – lattice relaxation time.^{122, 123}

The characteristic features of phase transformations in $\text{C}_{60}\text{F}_{36}$ or $\text{C}_{60}\text{F}_{48}$ fluorofullerenes, which are molecular crystals, are probably similar to those in crystalline C_{60} fullerene. In any case, mechanical grinding of both C_{60} and $\text{C}_{60}\text{F}_{36}$ and $\text{C}_{60}\text{F}_{48}$ specimens brings about the same effect, namely, disappearance of the phase transitions from the temperature dependences of heat capacity.¹¹³ No data on the heat capacity of $\text{C}_{60}\text{F}_{18}$ fluorofullerene have been obtained yet, although works along this line are in progress. Apparently, the presence of a dipole moment in $\text{C}_{60}\text{F}_{18}$ would also influence the heat capacity curves and would stipulate substantial differences between the behaviours of $\text{C}_{60}\text{F}_{18}$, on the one hand, and $\text{C}_{60}\text{F}_{36}$ or $\text{C}_{60}\text{F}_{48}$, on the other hand, during heating. The heat capacities of higher and endohedral fullerenes have not yet been determined.

2. Enthalpy of sublimation

a. Fullerenes C_{60} , C_{70} , C_{78} and C_{84}

After crystalline [60]fullerene had been obtained in macroscopic quantities at the end of 1990,² vigorous studies into the physico-chemical properties of this compound were started. Later, studies of higher fullerenes also began (as these compounds have been isolated in a pure state). As soon as 1991, it was found¹²⁴ that C_{60} fullerene is sublimed *in vacuo* (1 Pa) without decomposition even at temperatures of about ~ 1000 K. This result is a sort of sensation if one recalls that graphite is sublimed at this pressure at temperatures of about 3000 K. Thus, there appeared the possibility of producing pure carbon in the gas phase at temperatures of ~ 1000 K. Later, this property of fullerene has been used in diamond synthesis from the gas phase.¹²⁵

The high thermal stability of fullerenes and the possibility of transferring them to the gas phase allowed determination of the characteristics of their free molecules. The electron affinity and ionisation energy of C_{60} , the electron capture and light absorption energies, and cross-sections of various chemical reactions of fullerenes have been determined. For these measurements and for film deposition experiments or growth of single crystals from the vapour phase, data on the saturated vapour pressure of fullerene are needed. The saturated vapour pressure and the enthalpy of sublimation have been measured repeatedly (see, for example, the review¹²⁶). Virtually all measurements were carried out by the Knudsen effusion method implemented either in the classical version or with mass-spectrometric analysis of the vaporisation products. Since the experiments were carried out by research groups from different countries (Germany, India, Italy, Russia, Slovenia, and the USA), naturally, some scatter of the results can be noted.

Analysis of the data on the saturated vapour pressure of fullerene shows that the scatter in the obtained values goes far beyond the inaccuracy inherent in the effusion method. At present, the reasons for the substantial discrepancies are more or less clear. First, this is the quality of specimens. Preparation of sufficiently pure and thoroughly characterised specimens is a fairly difficult task. The second, more specific reason for the discrepancies is related to the fact that fullerene represents a

metastable phase and transition to more stable phases (amorphous carbon) might take place, and this transition can often be catalysed by an impurity or the surface of the container. Finally, the most significant point responsible for the differences between the data on the saturated vapour pressure is the fact that experiments were carried out in different temperature regimes. Elevated temperatures required for the generation of measurable saturated vapour pressures accelerate the thermal degradation of fullerenes, giving rise to noticeable amounts of the amorphous carbon phase. The accumulation of this non-volatile form results in underestimated saturated vapour pressures. This destruction of fullerene is markedly facilitated by an organic solvent contained in fullerene specimens. However, it has been reported¹²⁷ that fullerene specimens containing no solvent also undergo this transformation but to a substantially lesser extent. It was shown that the time of storage has a more pronounced influence on the degree of conversion than temperature.¹²⁷ This, apparently, accounts for the fact that the non-fullerene carbon forms are sometimes present even in the initial specimens not subjected to high temperatures.¹²⁸

The effusion experiments on fullerene sublimation were normally carried out after prolonged many-hour storage of specimens at 400–500 K in a dynamic vacuum. Under these conditions, the solvent should have been completely removed. However, it is still retained in the samples in concentrations of 0.01%–1.0% and occurs in the adsorbed state in closed space dislocations.¹²¹ These minor amounts of the solvent barely influence the weight loss of the specimen but they accelerate the transformation of fullerene into non-fullerene carbon. As a consequence, the saturated vapour pressure decreases in the course of measurements, giving rise to substantial scatter of the thermodynamic data obtained. As noted above, the destruction rate depends on many factors but the presence of solvents is normally the most significant among them. The saturated vapour pressures for the number of fullerenes recommended in a study by Markov *et al.*¹²⁶ are shown in the logarithmic form in Fig. 25, and the parameters of the corresponding equations are given in Table 10. It can be seen that the enthalpy of sublimation increases rather smoothly with an increase in the size of the fullerene molecule, *i.e.*, heavier fullerenes are less volatile. Apparently, this trend should be retained throughout the whole series of higher fullerenes. At present, more precise determination of the saturated vapour pressures of C_{76} (see Refs 129, 130) and C_{84} (see Ref. 128, 131) using repeatedly sublimed samples and the study of the sublimation of other higher fullerenes as they are prepared in macroscopic quantities remain topical tasks. Indirect experimental data attest that endohedral metallofullerenes exhibit lower volatilities than the corresponding hollow fullerenes. However, no quantitative data have been obtained so far.

In conclusion, we would like to mention the problem of interpretation of thermodynamic data obtained for higher full-

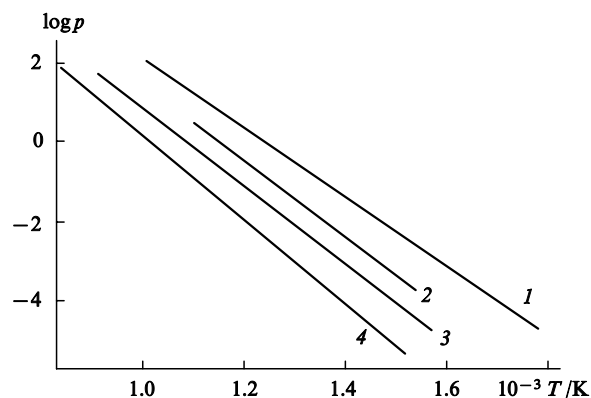


Figure 25. Logarithmic dependence of the saturated vapour pressure of fullerenes C_{60} (1), C_{70} (2), C_{76} (3) and C_{84} (4) on temperature.¹²⁶

Table 10. Equations for the temperature dependence of the saturated vapour pressure and recommended values for the sublimation enthalpy.¹²⁶

Fullerene	Temperature range	$\log p = -BT^{-1} + A^a$		T/K (see ^b)	$\Delta_{\text{sub}}H_T^\circ$ /kJ mol ⁻¹
		B/K	A		
C ₆₀	560–990	8738 ± 472	10.85 ± 0.76	750	167 ± 9
C ₇₀	650–904	9768 ± 774	11.23 ± 1.49	773	187 ± 15
C ₇₆	637–1069	10027 ± 253	10.94 ± 0.33	831	192 ± 6
C ₈₄	658–1190	10760 ± 267	10.92 ± 0.29	899	206 ± 5

^a The pressure in this equation (p) is expressed in Pascals. ^b The temperature to which the $\Delta_{\text{sub}}H_T^\circ$ value should be referred.

erenes, which is related to the existence of various geometric isomers. For fullerenes containing 78 or more carbon atoms, two or more isomers which obey the rules of isolated pentagons have been obtained;¹³² however, thermodynamic measurements were carried out only for isomer mixtures. Quantum-mechanical estimates show that the difference between the energies of stable isomers, for example of C₈₄ fullerene, can reach 100–120 kJ mol⁻¹ (see Ref. 133). Hence, the enthalpies of sublimation of these isomers may also be appreciably different. It is clear that the data advised in a study by Markov *et al.*¹²⁶ for C₈₄ refer to a mixture of isomers (according to an original publication,¹³⁴ a C₈₄ specimen isolated by chromatography consists of at least seven isomers). The success of further work on the determination of the saturated vapour pressures of higher fullerenes will be directly related to the progress in the elaboration of effective and economical techniques both for isolation and collection of individual fullerenes and for separation of them into pure isomers.

b. Fluorofullerenes C₆₀F₁₈, C₆₀F₃₆, C₆₀F₄₈

Two experimental methods were used for the measurements, namely, the classical Knudsen effusion method (KEM) combined with the mass analyser (KCMS)^{135, 136} or with effusion-torsional (ET) technique.¹³⁷

Fluorofullerene C₆₀F₃₆. The recommended¹³⁷ value for the enthalpy of sublimation $\Delta_{\text{sub}}H_T^\circ(\text{C}_{60}\text{F}_{36})$ was calculated by least-squares processing of experimental data obtained by both the KEM and KCMS methods. The values obtained by different methods were averaged with weight factors inversely proportional to their variances; and the resulting recommended value is $\Delta_{\text{sub}}H_{466}^\circ(\text{C}_{60}\text{F}_{36}) = 135 \pm 8$ kJ mol⁻¹.

Combination of the above value of the sublimation enthalpy and the absolute pressure measured by the Knudsen effusion method gave the following equation for the temperature dependence of the saturated vapour pressure of C₆₀F₃₆ in the temperature range of 408–539 K:¹³⁷

$$\ln p(\text{C}_{60}\text{F}_{36}) = (-16292 \pm 939)T^{-1} + (30.90 \pm 1.97).$$

Here and in the subsequent equations, pressure is expressed in Pascals and the temperature is in Kelvins

Fluorofullerene C₆₀F₄₈. The saturated vapour pressure above C₆₀F₄₈ in the temperature range of 473–527 K was determined by the Knudsen effusion method (KEM) and, in parallel, by the effusion-torsional measurements.¹³⁷ On the basis of these measurements, the average molecular masses at temperatures of 499, 508 and 530 K were calculated; the resulting values were 1616, 1660 and 1620 amu, respectively. The average value, 1633 amu, is in good agreement with the molecular mass of C₆₀F₄₈ (1632 amu). This proves convincingly that C₆₀F₄₈ is sublimed without decomposition. This result is confirmed by mass spectra, in which C₆₀F₄₈⁺ was identified as the predominant fullerene-containing ion. The overall pressures measured by the effusion-torsional method at the temperatures mentioned above were 0.10, 0.13 and 0.56 Pa, respectively, which is in good agreement with the KEM results.¹³⁷

The enthalpy of sublimation of C₆₀F₄₈ is 108 ± 7 (KEM) or 111 ± 7 kJ mol⁻¹ (KCMS). In order to compare the partial pressures of C₆₀F₃₆ and C₆₀F₄₈, an additional KCMS experiment was carried out.¹³⁷ Fluorofullerene specimens were placed in two separate compartments of a double Knudsen cell. On the basis of direct measurements of the C₆₀F₄₈⁺:C₆₀F₃₆⁺ ratio of ion currents, the ratio of partial pressures was calculated. The ratio of ionisation cross-sections $\sigma(\text{C}_{60}\text{F}_{36}):\sigma(\text{C}_{60}\text{F}_{48}) = 0.93$ found using the additivity rule, was utilised in the calculations.¹³⁸ The ratios of the partial pressures of C₆₀F₃₆ and C₆₀F₄₈ at 481 and 528 K were 0.37 and 0.54, respectively.

The recommended¹³⁷ enthalpy of sublimation is $\Delta_{\text{sub}}H_{476}^\circ(\text{C}_{60}\text{F}_{48}) = 109 \pm 7$ kJ mol⁻¹. The temperature dependence of the saturated vapour pressure in the temperature range of 395–528 K is described by the following equation:¹³⁷

$$\ln p(\text{C}_{60}\text{F}_{48}) = (-13146 \pm 827)T^{-1} + (24.34 \pm 1.71).$$

Fluorofullerene C₆₀F₁₈. The saturated vapour pressure was measured by the effusion method.¹³⁹ The recommended¹³⁹ equation for the temperature dependence of the saturated vapour pressure in the temperature range of 591–671 K has the form

$$\ln p(\text{C}_{60}\text{F}_{18}) = (-23739 \pm 1234)T^{-1} + (33.23 \pm 1.97).$$

The enthalpy of sublimation $\Delta_{\text{sub}}H_{627}^\circ(\text{C}_{60}\text{F}_{18})$ determined by the classical effusion method equals 197 ± 10 kJ mol⁻¹. According to KCMS data, $\Delta_{\text{sub}}H_{585}^\circ(\text{C}_{60}\text{F}_{18}) = 186 \pm 9$ kJ mol⁻¹.

Comparison of the data on the vapour pressure of C₆₀F₁₈, C₆₀F₃₆ and C₆₀F₄₈. In the temperature range studied by Boltalina *et al.*,¹³⁷ the saturated vapour pressures of C₆₀F₃₆ and C₆₀F₄₈ are rather similar to each other. This can be easily explained in terms of the structures of these molecules. Both molecules can be represented as spheres whose radius is equal to the sum of the radius of the fullerene cage (3.5 Å) and the C–F bond length (1.29 Å). The enthalpy of sublimation of C₆₀F₃₆ (135 ± 8 kJ mol⁻¹) is markedly higher than that for C₆₀F₄₈ (109 ± 7 kJ mol⁻¹). This difference indicates that the enthalpy of sublimation of fluorinated fullerenes tends to decrease with an increase in the total number of fluorine atoms on the carbon cage. {For comparison, the enthalpy of sublimation of [60]fullerene¹²⁶ is $\Delta_{\text{sub}}H_{298}^\circ(\text{C}_{60}) = 172 \pm 11$ kJ mol⁻¹.} The entropies of sublimation of C₆₀F₃₆ and C₆₀F₄₈ (see Ref. 137) are also substantially different

$$\Delta_{\text{sub}}S_{466}^\circ(\text{C}_{60}\text{F}_{36}) = 161 \pm 16 \text{ J mol}^{-1} \text{ K}^{-1},$$

$$\Delta_{\text{sub}}S_{476}^\circ(\text{C}_{60}\text{F}_{48}) = 107 \pm 14 \text{ J mol}^{-1} \text{ K}^{-1}.$$

The value for the enthalpy of sublimation obtained for C₆₀F₁₈ was much higher than those for C₆₀F₃₆ and C₆₀F₄₈. Even pure C₆₀ fullerene has a lower enthalpy of sublimation. Thus, C₆₀F₁₈ clearly does not comply with the general trend of the enthalpy to decrease in the series C₆₀, C₆₀F₃₆, C₆₀F₄₈. This anomaly in the thermal properties of C₆₀F₁₈ can be easily explained by specific features of its molecular structure. All the 18 fluorine atoms are located in one hemisphere of the carbon cage, and the C₆₀F₁₈ molecule (C_{3v} symmetry) has a dipole moment of 6.3 or 6.9 D according to MNDO or density functional theory (DFT) calculations. The C₆₀ and C₆₀F₄₈ molecules have no dipole moment and in the case of C₆₀F₃₆, the dipole moment is also absent for the *T* isomer. The dipole moment of the C₃ isomer of C₆₀F₃₆ (2.3 D, according to our estimates done by MNDO) is much lower than that of C₆₀F₁₈ (7–9 D).¹³⁹ The presence of a dipole moment results in a stronger interaction between the C₆₀F₁₈ molecules in the crystal compared to the dispersion interactions in the crystals of C₆₀, C₆₀F₃₆ or C₆₀F₄₈. As a consequence, more energy is required to transfer C₆₀F₁₈ molecules from the solid state to the vapour. The relatively long retention time of the C₆₀F₁₈ fluorofullerene in the HPLC separation (~40 min vs. 2.9 min for C₆₀F₃₆)¹³⁹ also points to the polar structure of this molecule.

3. The enthalpies of formation

a. Fullerenes C₆₀ and C₇₀

The thermal properties of [60]- and [70]fullerenes are surveyed in detail in a review by Dikii and Kabo.¹⁴⁰ Here we shall consider only the most recent studies devoted to this topic.^{46, 141}

Fullerene C₆₀. An *et al.*¹⁴¹ measured the energy of combustion of [60]fullerene using a liquid calorimeter with an isothermal shell. The average energy of combustion of C₆₀ fullerene found from five experiments was $-36036.06 \pm 6.04 \text{ J g}^{-1}$, and the enthalpy of formation of solid C₆₀ was $2359.47 \pm 9.72 \text{ kJ mol}^{-1}$. A significant difference between the study cited¹⁴¹ and the preceding works is that the authors¹⁴¹ had a substantial amount of [60]fullerene at their disposal. In combustion experiments, 0.5 g weighed portions of fullerene were used, and the energy of combustion of C₆₀ accounted for up to 70% of the total energy evolved in the experiment. This increases the reliability of the values presented above compared to other data on the energy of combustion. In 1997, An *et al.*¹⁴² determined once again the enthalpies of combustion and formation of C₆₀ fullerene using a microcalorimeter. The researchers did not analyse the gaseous products of combustion for carbon dioxide. The energy of combustion of [60]fullerene they found ($-36004.6 \pm 11.8 \text{ J g}^{-1}$) was close to the value determined previously.¹⁴¹

Kolesov *et al.*⁴⁶ were the first to pay attention to the dependence of the enthalpies of combustion and formation of [60]fullerene on the crystal size. They studied two specimens of C₆₀. One specimen prepared by a standard procedure (fast crystallisation of fullerene from a solution and removal of the solvent *in vacuo*) was a brown-coloured finely crystalline powder. The other specimen was prepared using a special procedure: small crystals (0.1–0.2 mm) were grown by slow crystallisation of C₆₀ from a solution in toluene. This material was coloured black and had a characteristic metallic lustre. HPLC analysis showed that the former specimen contained 0.4 mol.% of C₇₀, and the second one was found to contain neither C₇₀, nor C₆₀O.

To determine the energy of combustion of C₆₀ fullerene, Kolesov *et al.*⁴⁶ used a liquid calorimeter with an isothermal shell and a stationary bomb. The energy of combustion of the first specimen found in a series of three experiments was -35896 J g^{-1} , and that for the second specimen found in eight experiments was $-36030 \pm 16 \text{ J g}^{-1}$.

In the study in question,⁴⁶ the gaseous products of combustion were analysed for carbon dioxide. For the first material, the amount of CO₂ found experimentally was markedly lower than the value calculated theoretically, the average content of CO₂ being 99.80%. In the second specimen, the content of CO₂ in the combustion products virtually coincided with the calculated value ($99.99 \pm 0.02\%$). These results of the analysis for the second C₆₀ specimen point to complete burning of the substance and confirm additionally the material purity.

Proceeding from this fact, the researchers⁴⁶ chose as reliable the standard energy of combustion determined for the second C₆₀ specimen with a well-developed crystal structure. The standard enthalpy of formation of crystalline C₆₀ fullerene is equal to $2355 \pm 15 \text{ kJ mol}^{-1}$ (see Ref. 46); this is the most reliable value. The results of An's and Kolesov's studies described above are in good agreement with each other.

Fullerene C₇₀. In 1997, An *et al.*¹⁴² also determined the energy of combustion of [70]fullerene. The energy of combustion of C₇₀ calculated based on the sample weight was $-35629.4 \pm 10.6 \text{ J g}^{-1}$ and the enthalpy of formation was $2410.4 \pm 8.9 \text{ kJ mol}^{-1}$, which did not coincide with earlier data (see the review¹⁴⁰).

The same year Kolesov *et al.*¹⁴³ determined the energy of combustion of C₇₀ fullerene using a liquid calorimeter with an isothermal shell. According to HPLC, the C₇₀ specimen contained an impurity of C₆₀ fullerene (2.0 mass %). Five experiments were carried out, each being accompanied by analysis of the gaseous products of C₇₀ combustion for carbon dioxide; the average result was $99.81\% \pm 0.02\%$. The energy of combustion of C₇₀ fullerene (specimen 1) calculated from the sample weight with correction

for the energy of combustion of the C₆₀ impurity amounts to $-35664 \pm 44 \text{ J g}^{-1}$. The same procedure was also used to burn the coarsely crystalline C₇₀ fullerene (specimen 2), which contained 0.23 mass % of C₆₀ and 0.40 mass % of C₈₄. Nine experiments were carried out for specimen 2; in all experiments, the gaseous products did not contain carbon monoxide. In seven experiments, the gaseous products were analysed for carbon dioxide. The amount of CO₂ determined experimentally (on average, $99.95\% \pm 0.05\%$) coincided, to within the accuracy of analysis, with the theoretical value. The average energy of combustion of C₇₀ for specimen 2 amounted to $-35679 \pm 38 \text{ J g}^{-1}$ (see Ref. 144), which is very close to the value obtained previously for specimen 1. The enthalpies of formation of crystalline C₇₀ reported in two publications^{143, 144} are 2439 ± 38 and $2452 \pm 33 \text{ kJ mol}^{-1}$, respectively. As in the case of [60]fullerene, the data of the two last-mentioned works coincide within experimental error with the results obtained by An *et al.*¹⁴²

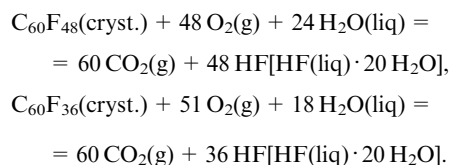
b. Fluorofullerenes C₆₀F₄₈ and C₆₀F₃₆

The enthalpies of formation of C₆₀F₄₈ (see Ref. 48) and C₆₀F₃₆ (see Ref. 47) fluorofullerenes were first determined experimentally at the laboratory of thermochemistry of the Moscow State University.

The energies of combustion of fluorofullerenes were found using a calorimeter with an isothermal shell and with a rotating bomb platinum-lined from the inside. The rise of temperature was recorded by a copper resistance thermometer included in a bridge circuit. The sensitivity of the temperature measurement was $5 \times 10^{-5} \text{ K}$.

Each of the two fluorofullerenes was pressed to form a pellet, which was then crushed into pieces. Several pieces with a total weight of 60–70 mg were placed into a terylene-film bag (produced and weighed beforehand), the bag was hermetically sealed, weighed, and heated in a platinum crucible together with a weighed pellet of benzoic acid. Benzoic acid served as the auxiliary material that ensured virtually complete combustion of fluorofullerenes to give only a small amount of soot in the crucible. The correction for this non-burnt residue was only 0.6–2.3 J, while the total amount of heat evolved in the experiment was $\sim 13\,000 \text{ J}$. The heat of combustion of the auxiliary substances, benzoic acid and the terylene film, accounted for 92%–93% of the whole measured heat in the case of C₆₀F₄₈ and 90%–92% for C₆₀F₃₆. After the calorimetric experiments, the combustion products were analysed for the contents of CO₂, HF and HNO₃. The results of the analysis were used to calculate the amount of tetrafluoromethane formed upon combustion, and appropriate corrections were applied (2–10 and 0–4 J for C₆₀F₄₈ and C₆₀F₃₆, respectively).

After all the corrections were applied (including those for impurities contained in the specimens and those for adjustment to the standard conditions), the standard energies of combustion were found in relation to the reactions



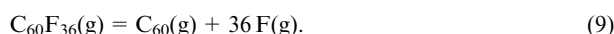
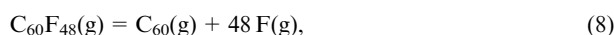
Five experiments were carried out for each substance. The average standard energies of combustion thus obtained and the standard enthalpies of combustion and formation calculated from these values are presented in Table 11. The errors were determined for a 95% significance level. The same Table presents the enthalpies of sublimation of fluorofullerenes¹³⁷ and the standard entropies measured by Druzhinina *et al.*¹⁰⁷ Proceeding from these values, the standard enthalpies of formation of fluorofullerenes in the gaseous state and the Gibbs energies of formation of these compounds in the crystalline state were calculated.

Table 11. Thermodynamic characteristics of C₆₀F₄₈ and C₆₀F₃₆ fluorofullerenes at 298.15 K.^{47, 48, 107, 137}

Parameter	C ₆₀ F ₄₈	C ₆₀ F ₃₆
–Δ _c U _m ^o (cr)/kJ mol ^{–1}	24668 ± 163	24714 ± 199
–Δ _c H _m ^o (cr)/kJ mol ^{–1}	24638 ± 163	24692 ± 199
–Δ _f H _m ^o (cr)/kJ mol ^{–1}	7563 ± 166	5362 ± 201
Δ _{sub} H _m ^o /kJ mol ^{–1}	109 ± 7	139 ± 8
–Δ _f H _m ^o (g)/kJ mol ^{–1}	7454 ± 166	5223 ± 201
S ^o /J mol ^{–1} K ^{–1}	1137.2 ± 5.7	1014.5 ± 5.1
–Δ _f G _m ^o (cr)/kJ mol ^{–1}	6349 ± 166	4474 ± 201

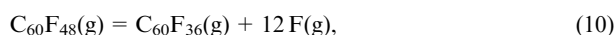
Note. Δ_cU_m^o is the standard combustion energy, Δ_cH_m^o, Δ_fH_m^o and Δ_{sub}H_m^o are the standard enthalpies of combustion, formation and sublimation, respectively, S^o is the standard entropy, and Δ_fG_m^o is the Gibbs energy of formation of fluorofullerenes.

The resulting Δ_fH_m^o(g) values for C₆₀F₄₈ and C₆₀F₃₆, the enthalpy of formation of crystalline C₆₀ recommended above (2355 ± 15 kJ mol^{–1}), the enthalpy of sublimation of C₆₀ (181 ± 2 kJ mol^{–1})¹⁴⁵ and the enthalpy of formation of gaseous molecular fluorine (79.38 ± 0.30 kJ mol^{–1})¹¹² were used to calculate the enthalpies of gas-phase decomposition of the fluorofullerenes into fullerene and gaseous fluorine



This gave Δ_rH(8) = 13800 ± 167 kJ mol^{–1} (or 287.5 ± 3.5 kJ per C–F bond) and Δ_rH(9) = 10617 ± 202 kJ mol^{–1} (or 294.9 ± 5.6 kJ per C–F bond).

For the reaction



the calculations gave Δ_rH(10) = 3184 ± 261 kJ mol^{–1} (or 265 ± 22 kJ for each of the twelve C–F bonds that are cleaved on passing from C₆₀F₄₈ to C₆₀F₃₆). Thus, the first experimental data on the energy characteristics of the C–F bonds in fluorofullerenes with high fluorine contents were obtained.

VII. Conclusion

We shall consider some promising lines of research related to fullerenes and their derivatives. A necessary condition for further advancement of thermochemical studies, *i.e.*, accumulation of fundamental thermochemical characteristics of individual fullerene compounds, is the preparation of these compounds in macroscopic amounts (about hundreds of milligrammes) and with satisfactory purity. One may expect that the progress along this line would depend, among other factors, on the practical interest in useful properties of fullerene derivatives. From a fundamental standpoint, it would be of interest to obtain data on the enthalpies of formation and heat capacities of a number of simple fullerene halides (for example, C₆₀Br₂₄, C₆₀Cl₆), the synthesis of which is documented. In combination with the currently available data on C₆₀, C₇₀ and [60]fullerene fluorides and hydrides (C₆₀X₃₆), this would provide a more comprehensive picture of the energy characteristics of the fullerene–hydrogen and fullerene–halogen systems. In turn, creation of even a small thermodynamic database based on experimental results would facilitate development of new theoretical approaches to the description of these systems. For example, this would increase the accuracy of calculations of the relative stability of various fullerene derivatives. It appears rather unlikely that the thermochemical characteristics of endohedral or organic derivatives of fullerenes will be determined in the near future, because in the vast majority of cases, preparation of pure compounds of this class (free from side products and having a homogeneous isomer

composition) is associated with a tedious and expensive HPLC procedure.

Studies of fullerene derivatives in the gas phase will undoubtedly be continued in the near future, because insufficient amounts and purity of substances will not hold up mass-spectrometric measurements. For example, previously, ion–molecule equilibria have been studied successfully even with 3–5 mg samples of mixtures of endohedral metallofullerenes.

The number of objects with interesting ionisation characteristics is constantly extending. For example, mention should be made of a new class of endofullerenes with inner-sphere nitrogen clusters of lanthanides and recently discovered small fullerenes C₂₀¹⁴⁶ and C₃₆.¹⁴⁷

The synthetic works of fluorination of fullerenes would be carried out in the following directions. First, the search for pathways to the fully saturated compound C₆₀F₆₀ and fullerene hyperfluorides, the possibility of whose existence has been shown experimentally,^{65,66} still is of interest. The use of superoxidants, fluorides of metals in higher oxidation states, can lead to new compounds with unique properties. Naturally, it is necessary to continue the attempts to perform the targeted synthesis of compounds with low content of fluorine. These compounds could serve as convenient objects for investigating addition reactions and replacement of fluorine atoms by functional groups. A reaction of this type was first reported in 1997, when the compound C₆₀F₁₅Ph₃ (the product of the replacement of the three sterically most accessible fluorine atoms by three phenyl groups) was synthesised and its structure was characterised.¹⁴⁸

The development of reliable and effective procedures for the preparation of individual fluorofullerene derivatives accomplished in the last two or three years, the presence of data on their structure and purity, and determination of the key physical properties (thermal stability, solubility, air stability, volatility) make it possible to thoroughly and systematically research the chemical and physical properties of these compounds. The few publications on electrochemical properties of fluorofullerenes¹⁴⁹ indicate that fluorofullerenes can prove to be valuable materials for cathodic coatings in electrochemical cells. By varying the fluorine content in fluorofullerene molecules, it should be possible to design materials with desired electrochemical redox potentials; the reductive potential was found to increase by 0.5 V on passing from C₆₀F₃₆ to C₆₀F₄₈.⁴⁰

We have mentioned above that C₆₀F_x fluorofullerenes can be used as fluorinating agents or oxidants; however, this point has not been studied in detail. An interesting applied aspect is the use of C₆₀F₁₈ as a component in the construction of nanostructural charge transfer complexes. Quite recent works on the synthesis of such complexes with C₆₀ resulted in the design of solar batteries based on these compounds.¹⁵⁰ The replacement of [60]fullerene by C₆₀F₁₈ fluorofullerene, which is a more polar molecule with higher electron affinity, can markedly improve characteristics of light-sensitive devices. The exceptionally high polarity of the C₆₀F₁₈ molecule makes this fluorofullerene rather attractive for new fields of electronics; in particular, it could be of interest in the development of molecular transistors.

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Synthesis of C-vinylpyrroles

L N Sobenina, A P Demenev, A I Mikhaleva, B A Trofimov

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Abstract. The latest advances in the synthesis of C-vinylpyrroles are generalised and systematised. Methods for the synthesis based on reactions of acylpyrroles and dicarbonyl compounds or their synthetic equivalents are still of most importance. New promising methods for the synthesis of C-vinylpyrroles are considered, among them the reactions of alkenyl ketone oximes with acetylene in the KOH – DMSO system and base-catalysed condensation of pyrrolecarbodithioates, which have recently become available, with CH-acids. The bibliography includes 195 references.

I. Introduction

The chemistry of pyrroles attracts continuing interest because of the enormous biological potential of these compounds and the possibility of their use in the design of new pharmaceuticals as well as of electro- and photoconducting materials. Functionalised vinylpyrroles occupy a special place as promising intermediates in the synthesis of new heterocyclic compounds,^{1–4} valuable monomers^{5–8} and also as ligands for new photocatalysts and biologically active complexes.⁹

Fragments of 2-vinylpyrroles are involved in life-supporting systems, such as porphyrins, vitamin B₁₂, bile pigments, chlorins, florins, oxoflorins, biliverdins and stercobilins. 3-Vinylpyrrole structures are present in haemoglobin and myoglobin, which are responsible for oxygen transport from the lungs to tissue cells of organisms and for oxygen storage, respectively, and also in chlorophyll which is responsible for photosynthesis. C-Vinylpyrroles bearing functional groups at the double bond (or deprived of these groups) serve as reactive intermediates for the directed synthesis of conjugated and fused heterocyclic compounds simulating natural pyrrole ensembles. This generates

continuing interest in the development of new procedures for their synthesis and gives impetus to the examination of the reactivities and biological activities of C-vinylpyrroles.

1-Vinylpyrroles have been studied extensively and comprehensively in the last three decades. These compounds have become readily accessible owing to the discovery and development of a simple procedure for their synthesis from ketoximes and acetylene in the MOH – DMSO system, where M = Li, Na or K (Trofimov's reaction^{10–16}). The data on the synthesis, structures, reactivities and biological activities of 1-vinylpyrroles were exhaustively surveyed in monographs^{11, 13} and reviews.^{16–27}

Since the publication of the latest monographs^{16, 28, 29} covering different aspects of the structures, reactivities and synthesis of C-vinylpyrroles, a substantial body of literature has evolved, which called for systematisation, analysis and generalisation of the new data.

The present review is devoted to procedures for the synthesis of C-vinylpyrroles, including those containing different functional substituents both in the vinyl group and pyrrole ring, and surveys the data, which were published in the last decade and were not covered in monographs and reviews.

Procedures for the synthesis of C-vinylpyrroles can be classified into several main categories: (1) syntheses based on acylpyrroles; (2) syntheses starting from functionalised aliphatic compounds; (3) addition of pyrroles to compounds with an activated triple bond (C-vinylation); (4) substitution at a double bond.

II. Synthesis of C-vinylpyrroles from acylpyrroles

Presently, 2- and 3-acylpyrroles (primarily, formylpyrroles) are the most commonly used starting compounds in the synthesis of C-vinylpyrroles.

1. Condensation of formylpyrroles with CH-acids

The ability of 2- and 3-formylpyrroles to be readily involved in condensation with different CH-acids is widely used in the synthesis of C-vinylpyrroles.

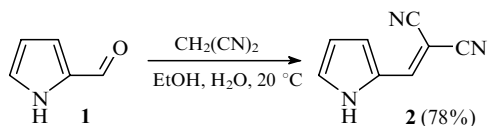
a. Condensation with malononitrile

2-(2,2-Dicyanovinyl)pyrrole (**2**) was prepared from 2-formylpyrrole (**1**) and malononitrile in the presence of glycine.³⁰

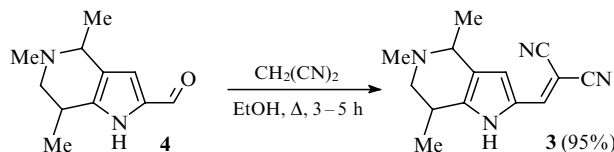
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Received 22 April 2002

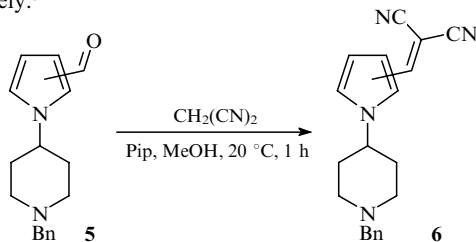
Uspekhi Khimii 71 (7) 641–671 (2002); translated by T N Safonova



Tetrahydropyrrollopyridine **3** was synthesised by refluxing 2-formyl derivative **4** with malononitrile.³¹

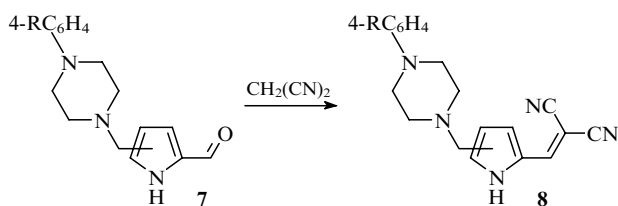


The reactions of 2- and 3-formylpyrroles **5** with malononitrile in the piperidine–methanol system afforded the corresponding 2- and 3-dicyanovinyl derivatives **6** in 87% and 75% yields, respectively.³²



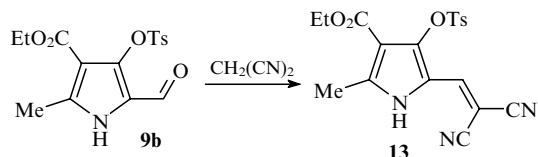
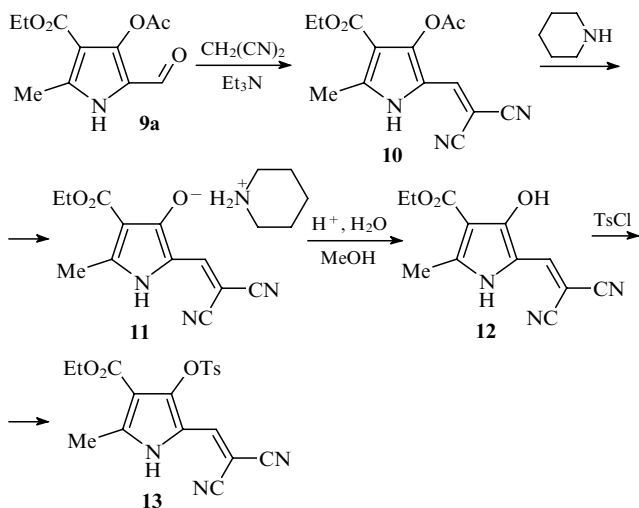
Pip is piperidine.

Under analogous conditions, 3-, 4- and 5-(piperazinylmethyl)-2-formylpyrroles **7** reacted with malononitrile to form the corresponding 2-(dicyanovinyl)pyrroles **8** in 49%–90% yields.³³



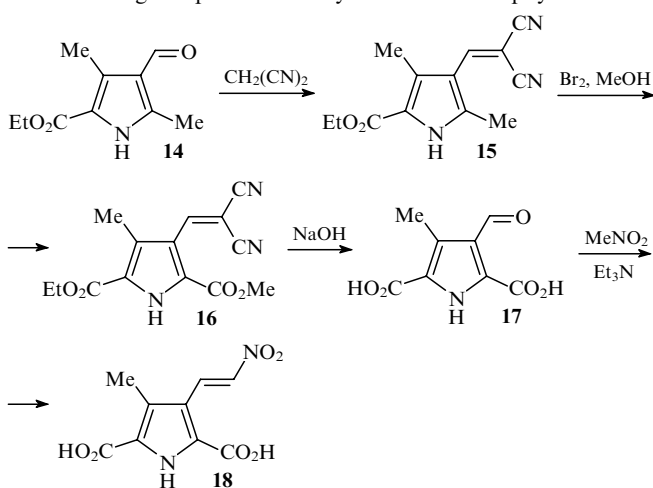
R = H, Cl.

Condensation of 4-acetoxy-3-ethoxycarbonyl-5-formyl-2-methylpyrrole (**9a**) with malononitrile in the presence of triethylamine gave rise to derivative **10** in high yield,³⁴ and subsequent heating of the latter with piperidine led to elimination of the acetyl group to form the stable piperidinium salt of 4-hydroxypyrrrole **11**. Subsequent acidification of the salt **11** produced 5-(2,2-dicyanovinyl)-3-ethoxycarbonyl-4-hydroxy-2-methylpyrrole (**12**). Tosyl derivative **13** was generated both in the reaction of the pyrrole **12**

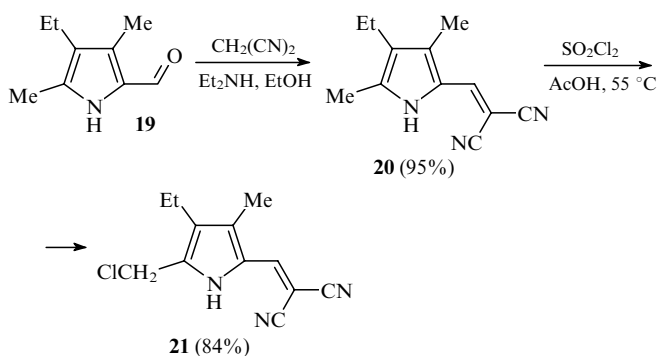


with *p*-toluenesulfonyl chloride and upon condensation of tosyl-oxy aldehyde **9b** with malononitrile.³⁴

The reactions of formylpyrroles with malononitrile or cyanoacetic ester yielding the corresponding vinylpyrroles are often used for protection of the aldehyde function in the synthesis of porphyrins. The aldehyde group is readily regenerated upon treatment of these pyrroles with alkali. Thus Woodward *et al.*³⁵ performed the synthesis of chlorophyll starting from 2,4-di(ethoxycarbonyl)-3,5-dimethylpyrrole (Knorr pyrrole) through condensation of 4-formyl-substituted pyrrole **14** with malononitrile, oxidation of the methyl group in compound **15** to the corresponding methyl ester **16** and hydrolysis, which resulted in regeneration of the aldehyde group to give pyrrole **17**. The latter was transformed into 4-(2-nitrovinyl)pyrrole **18** upon refluxing with nitromethane in the presence of triethylamine. The pyrrole **18** was used as the starting compound in the synthesis of chlorophyll.



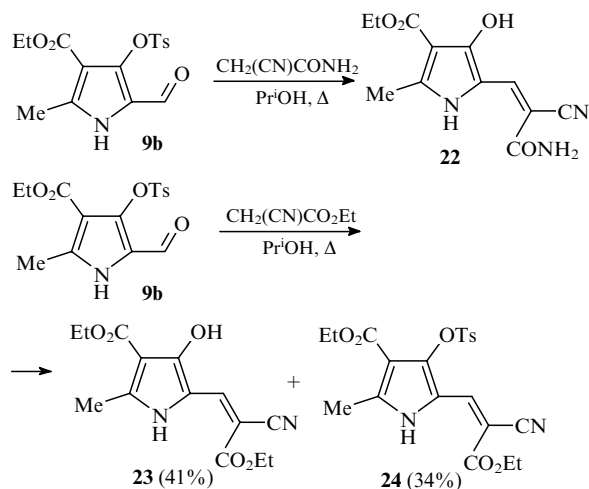
Analogously, the reaction of substituted 2-formylpyrrole **19** with malononitrile yielded 2-(2,2-dicyanovinyl)-4-ethyl-3,5-dimethylpyrrole (**20**) whose treatment with suluryl chloride afforded 5-chloromethyl-2-(2,2-dicyanovinyl)-4-ethyl-3-methylpyrrole (**21**).³⁵



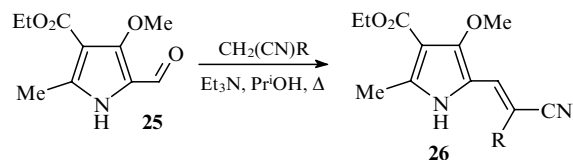
b. Condensation with alkoxycarbonyl- and amidomalnonitriles

Condensation of the tosyl-oxy aldehyde **9b** with ethyl cyanoacetate and cyanoacetamide proceeded upon refluxing in isopropyl alcohol in the presence of piperidine. Water that was liberated hydrolysed the sulfonate group either partially or completely. The reaction with cyanoacetamide afforded 5-(2-carbamoyl-2-cyano-vinyl)-4-hydroxypyrrrole **22**, whereas the reaction of ethyl cyanoacetate gave rise to 5-(2-cyano-2-ethoxycarbonylvinyl)-3-

ethoxycarbonyl-4-hydroxy-2-methylpyrrole (**23**) along with compound **24** containing the *p*-toluenesulfonate group.³⁶



The reaction of 5-formyl-substituted pyrrole **25** with cyanoacetamide or ethyl cyanoacetate produced the corresponding 5-vinylpyrroles **26**.³⁷

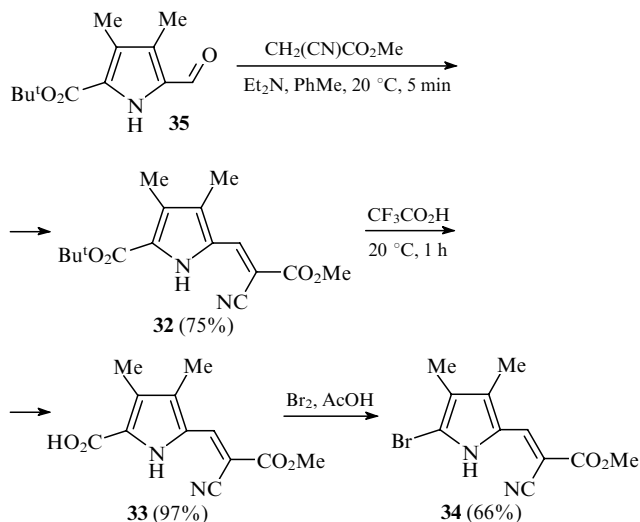


R = CONH₂, CO₂Et.

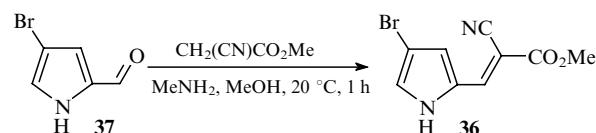
Condensation of aldehyde **27** with ethyl cyanoacetate was used for protection of the aldehyde group of pyrrole in the synthesis of the acetylene- and cumulene-containing porphyrinoid **28**.³⁸ Scheme 1 was employed for the preparation of functionalised vinylpyrroles **29–31**. Thus the 5-vinylpyrrole **29** generated in the first step was successively transformed into pyrrolecarboxylic acid **30** and then to iodopyrrole **31**, which gave 3,4-diethyl-2-formyl-5-iodopyrrole upon refluxing in methanol with NaOH. Subsequent cross-coupling and cyclisation afforded the porphyrinoid **28**.³⁸

Functionalised vinylpyrroles **32–34** were prepared by treatment of 2-*tert*-butoxycarbonyl-5-formyl-3,4-dimethylpyrrole (**35**)

with methyl cyanoacetate. Hydrolysis of the ester group in the resulting vinylpyrrole **32** under the action of trifluoroacetic acid yielded vinylpyrrolecarboxylic acid **33**, which was transformed into 5-bromo-2-vinylpyrrole **34**.³⁹

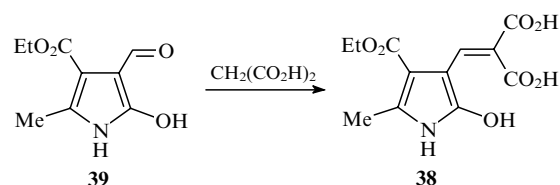


4-Bromo-2-(2-cyano-2-methoxycarbonylvinyl)pyrrole (**36**) was prepared by condensation of 4-bromo-2-formylpyrrole (**37**) with methyl cyanoacetate.⁴⁰

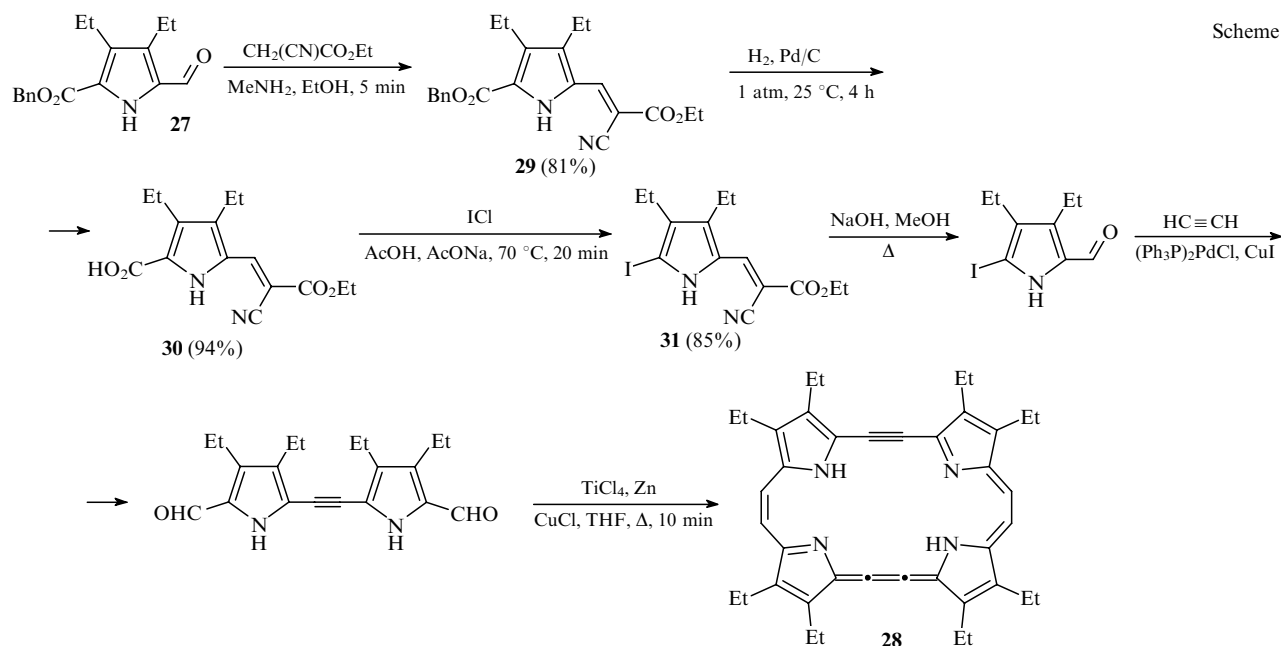


c. Condensation with malonic acid and its esters

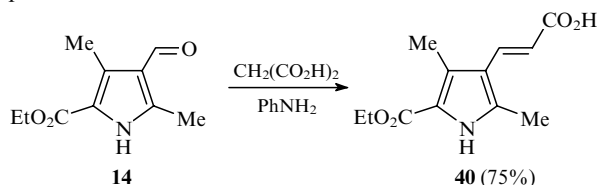
Functionalised 5-hydroxy-4-vinylpyrrole **38** was synthesised from 4-formyl-5-hydroxypyrrole **39** and malonic acid.⁴¹



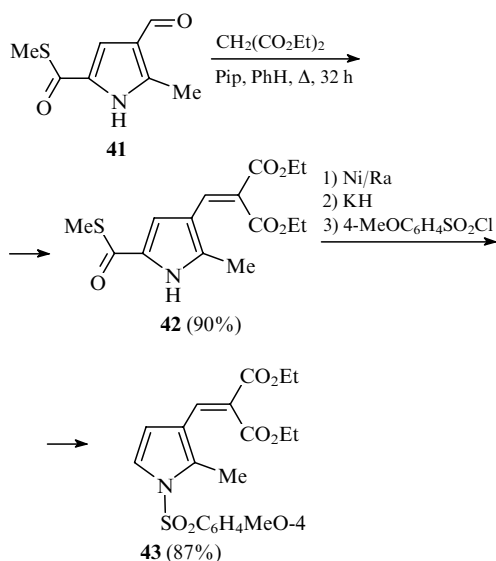
Scheme 1



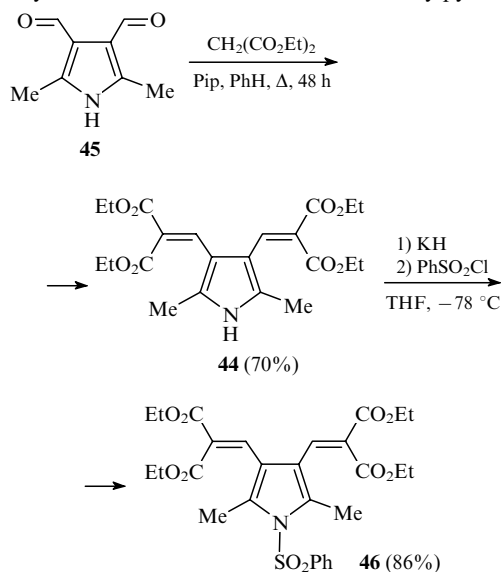
4-Vinylpyrrole **40** was prepared from the 4-formyl-substituted pyrrole **14** and malonic acid ³⁵ by decarboxylating condensation in the presence of aniline.



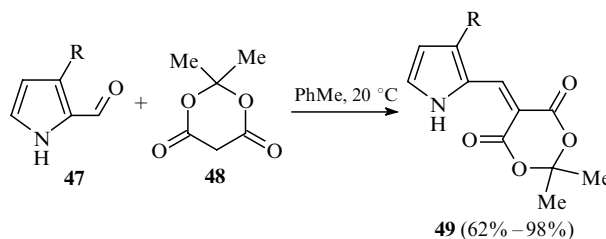
The reaction of 4-formyl-substituted pyrrole **41** with diethyl malonate afforded 4-vinylpyrrole **42**. Reductive elimination of the methylthiocarbonyl group from the pyrrole **41** under the action of Raney nickel (acetone, refluxing, 30 min) and successive treatment with potassium hydride and methoxybenzenesulfonyl chloride (THF, -78°C) gave rise to pyrrole **43**.⁴²



Functionalised 3,4-divinylpyrrole **44** was synthesised by condensation of 3,4-diformylpyrrole **45** with diethyl malonate. Treatment of the potassium derivative, which was prepared by the reaction of compound **44** with potassium hydride, with benzenesulfonyl chloride afforded *N*-substituted divinylpyrrole **46**.⁴²

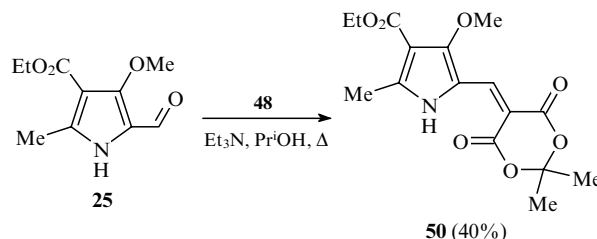


Classical Knoevenagel condensation of 2-formylpyrroles **47** with isopropylidene malonate (Meldrum's acid, **48**) in the presence of piperidinium acetate as a catalyst was used in the synthesis of 2-vinylpyrroles **49**.⁴³

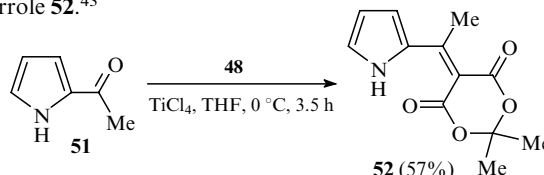


R = Me, MeO, CO₂Me.

The 5-formyl-substituted pyrrole **25** reacted with Meldrum's acid on refluxing in isopropyl alcohol in the presence of triethylamine to give 5-vinylpyrrole **50**.³⁷

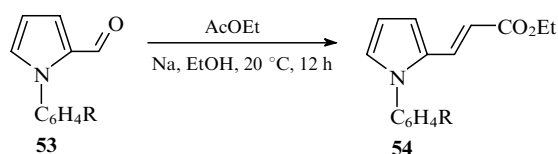


Condensation of 2-acetylpyrrole (**51**) with Meldrum's acid (**48**) in the presence of titanium tetrachloride produced 2-vinylpyrrole **52**.⁴³



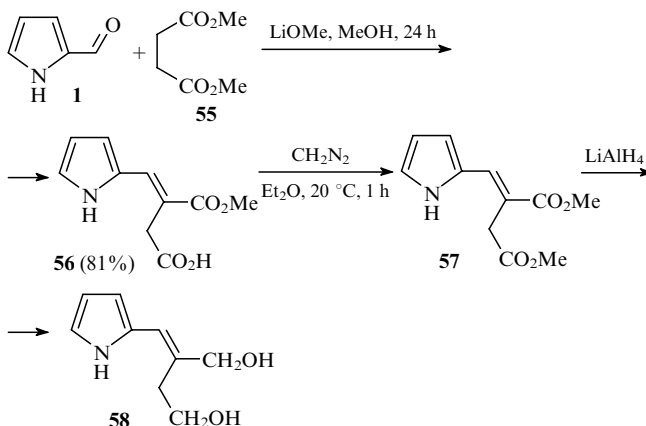
d. Condensation with acid derivatives containing the active methylene group

2-Vinylpyrroles **54** were synthesised by the Claisen reaction from 2-formylpyrroles **53** and ethyl acetate.⁴⁴

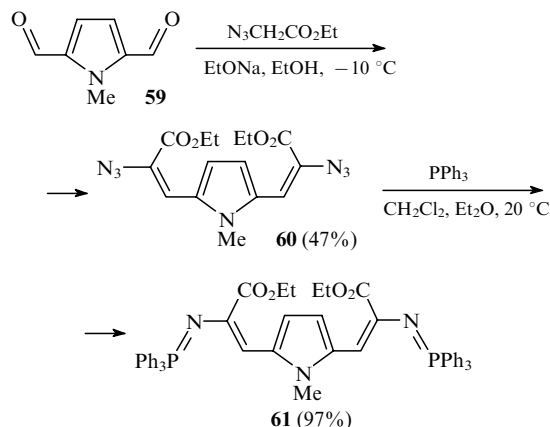


R = H, 4-MeO, 2-NO₂, 4-Cl.

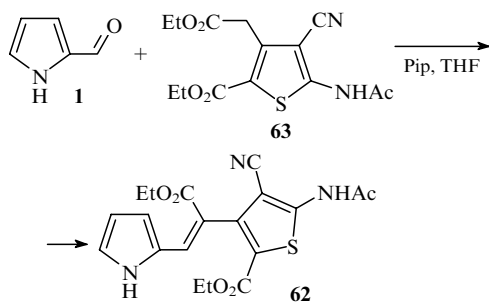
Stobbe condensation of 2-formylpyrrole (**1**) with dimethyl succinate **55** afforded functionalised 2-vinylpyrrole **56** from which diester **57** was obtained in quantitative yield. Reduction of the latter gave rise to 1,4-diol **58**.⁴⁵



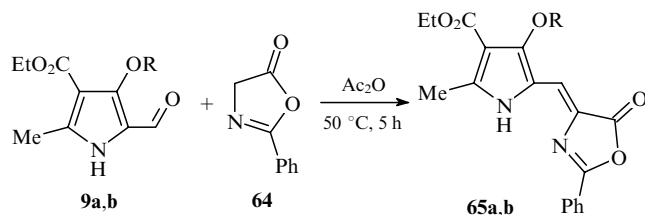
2,5-Diformyl-1-methylpyrrole (**59**) reacted with ethyl azidoacetate to form bis(azidovinyl)pyrrole **60**. Treatment of the latter with triphenylphosphine afforded divinylpyrrole **61** containing the iminophosphorane functional groups.⁴⁶



Substituted 2-vinylpyrrole **62** was prepared by refluxing 2-formylpyrrole (**1**) with 5-acetylamino-4-cyano-2-ethoxycarbonyl-3-ethoxycarbonylmethylthiophene (**63**).⁴⁷



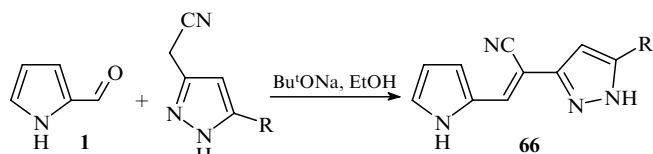
Heating of the formylpyrroles **9a,b** with hippuric acid (which was transformed into azlactone **64** under the reaction conditions) in acetic anhydride afforded 4-acetoxy- or 4-tosyloxy-5-pyrrolylmethyleneoxazolines **65a,b** containing the vinylpyrrole fragment.⁴⁸



$\text{R} = \text{Ac}$ (**a**), Ts (**b**).

e. Condensation with cyanomethylhetarenes and alkenes (hetaryl- and alkenylacetonitriles)

2-Formylpyrrole (**1**) undergoes condensation with nitriles of pyrazolylacetic acids to form the corresponding 1,2-dihetarylcyanoalkanes **66**. The ratio between the *Z* and *E* isomers of the compounds **66** depends on the temperature and reaction time.^{49, 50}

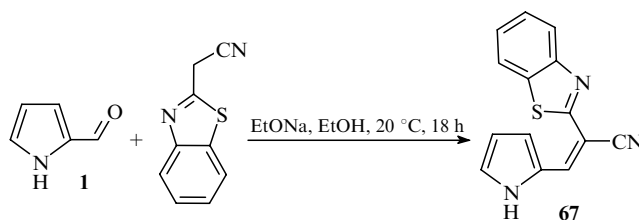


$\text{R} = \text{Ph}$, 4- MeC_6H_4 , 4- MeOC_6H_4 , 4- FC_6H_4 , 4- ClC_6H_4 , 4- BrC_6H_4 , 3- MeOC_6H_4 , 3- BrC_6H_4 .

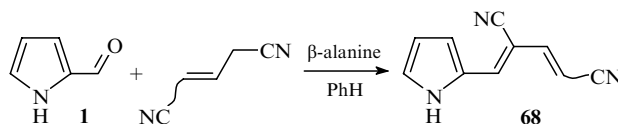
At 20°C , the *Z* isomers of the alkenes **66** were selectively generated during 4–5 h (the yields were 88%–95%). At

90 – 100°C (20–24 h), the thermodynamically more stable *E* isomers were obtained as the major reaction products (the yields were 52%–60%). In the latter case, the yields of the *Z* isomers were no higher than 25%–30%. The ratio between the isomers remained unchanged as the duration of heating was increased, which indicates that an equilibrium was established. Attempts to transform the *Z* isomers of the compounds **66** into the *E* isomers by refluxing in methanol were unsuccessful. However, the degree of isomerisation reached 100% upon the addition of Bu^tONa to the reaction mixture.⁴⁹

2-Formylpyrrole (**1**) reacted with 2-cyanomethylbenzothiazole to give 2-vinylpyrrole **67** in 85% yield.³⁰

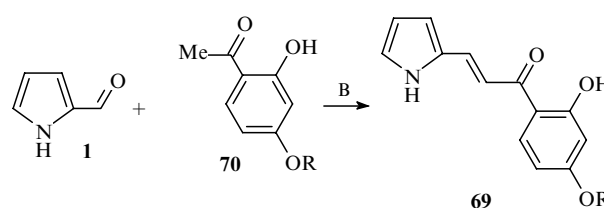


Condensation of 2-formylpyrrole (**1**) with glutakonitrile in the presence of β -alanine afforded butadiene derivative **68**.⁵¹



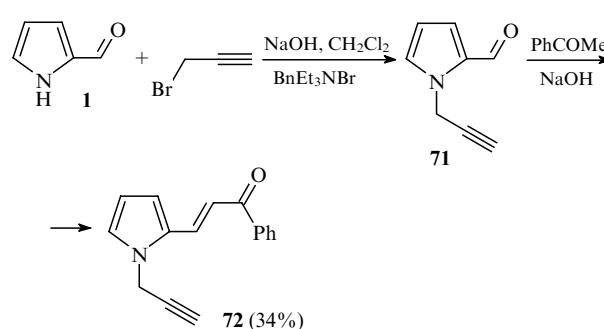
f. Condensation with ketones

2-Vinylpyrroles **69** were synthesised by base-catalysed condensation of 2-formylpyrrole (**1**) with aromatic ketones **70**.⁵²

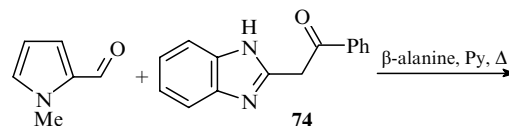


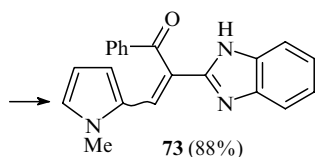
$\text{R} = \text{CH}_2\text{CO}_2\text{Et}$, $(\text{CH}_2)_2\text{OH}$.

2-Formyl-*N*-propargylpyrrole (**71**), which was prepared from 2-formylpyrrole (**1**) and propargyl bromide under the conditions of phase transfer catalysis, reacted with acetophenone in the presence of NaOH to give benzoylvinylpyrrole **72**.⁵³

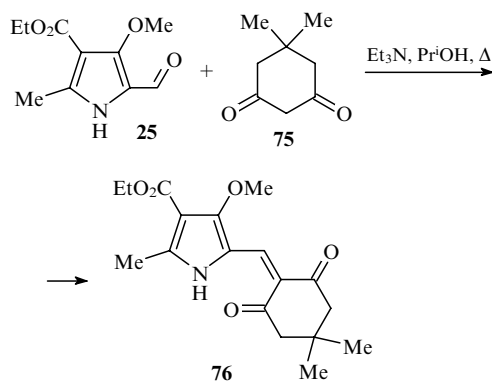


2-[2-Benzoyl-2-(benzimidazol-2-yl)]vinylpyrrole (**73**) was prepared by condensation of 2-formyl-1-methylpyrrole with ketone **74** in the presence of β -alanine.⁵⁴



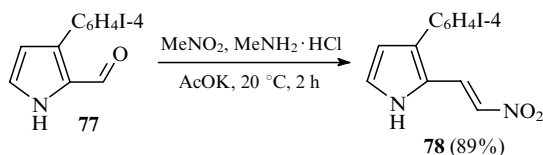


5-Vinylpyrrole **76** was synthesised from 5-formylpyrrole **25** and dimedone (**75**).³⁷

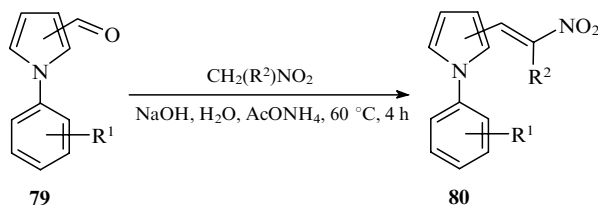


g. Condensation with nitroalkanes

The reaction of 2-formyl-3-(4-iodophenyl)pyrrole (**77**) with nitromethane in the presence of a small excess of methylamine hydrochloride afforded 2-(2-nitrovinyl)pyrrole **78**.⁵⁵

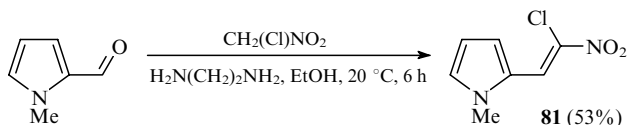


The reactions of *N*-aryl-2(3)-formylpyrroles **79** with nitroalkanes produced the *E* isomers of the corresponding 2- and 3-(2-nitrovinyl)pyrroles **80** in 64%–78% yields.^{44, 56}



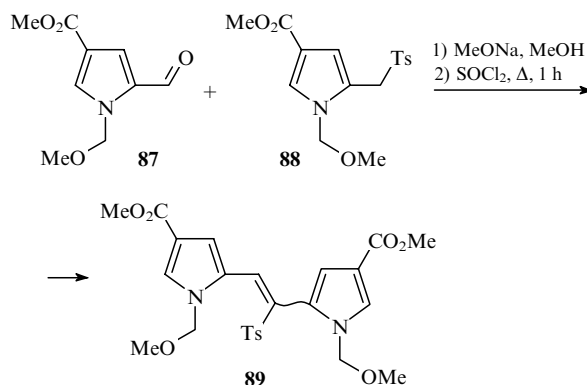
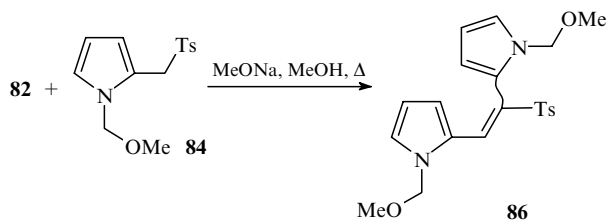
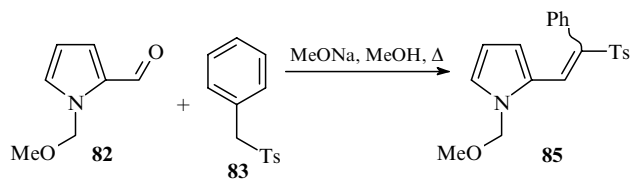
$R^1 = \text{H, 4-MeO, 2-NO}_2, 4\text{-Cl}$; $R^2 = \text{H, Me, Et}$.

2-(2-Chloro-2-nitrovinyl)-1-methylpyrrole (**81**) was synthesised by condensation of 2-formyl-1-methylpyrrole with nitrochloromethane in the presence of catalytic amounts of ethylenediamine.⁵⁷

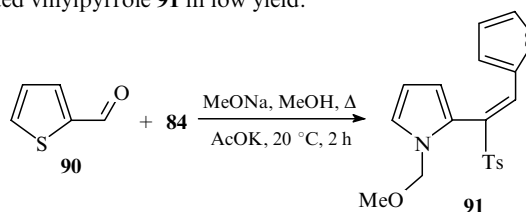


h. Condensation with sulfones

Condensation of 2-formyl-*N*-methoxymethylpyrrole (**82**) with sulfones **83** or **84** in the presence of 50 equiv. of sodium methoxide afforded 1,2-diaryl-1-sulfonyl-ethenes **85** and **86** in 76% and 78% yields, respectively.⁵⁸ Under these conditions, aldehyde **87** underwent condensation with sulfone **88** to give a mixture of diester **89** and a product of its hydrolysis with water generated in the course of the reaction. The compound **89** was isolated in 89% yield after treatment of the resulting mixture with thionyl chloride.

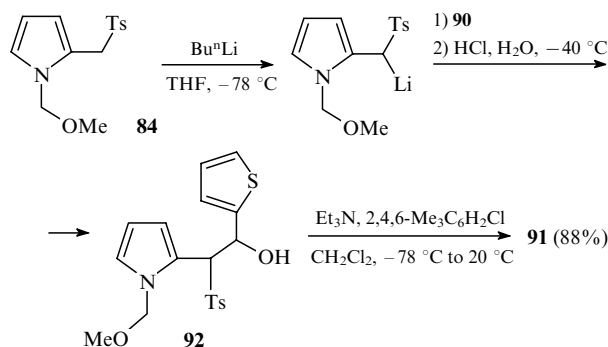


Under analogous conditions, the reaction of the sulfone **84** with thiophene-2-carbaldehyde (**90**) gave rise to thienyl-substituted vinylpyrrole **91** in low yield.



Apparently, the low yield is attributed to the Cannizzaro side reaction to which thiophenecarbaldehyde is more susceptible than aldehydes of the pyrrole series.

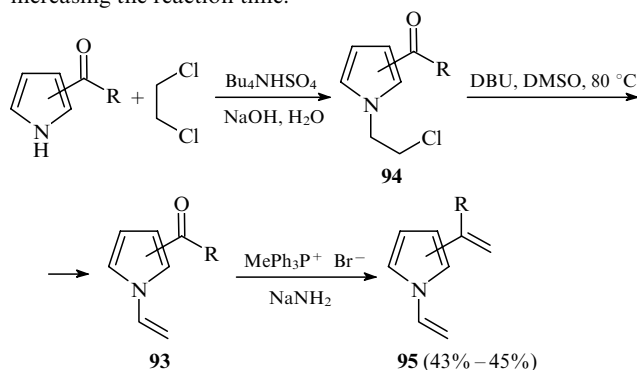
Condensation of thiophene-2-carbaldehyde (**90**) with the lithium derivative of sulfone **84** followed by hydrolysis with 10% HCl afforded a mixture of diastereomers of alcohol **92**. The latter was transformed into the alkene **91** by treatment with mesityl chloride.⁵⁸



2. Wittig reaction

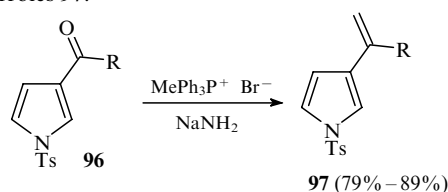
The reactions of formyl- and acetylpyrroles with alkylidenephosphoranes, which are generated upon dehydrohalogenation of quaternary phosphonium salts under the action of bases (Wittig reaction) is one of the most commonly used approaches to the synthesis of *C*-vinylpyrroles.^{59–78}

Carbonyl derivatives of 1-vinylpyrroles **93**, which were prepared by dehydrohalogenation of 1-(2-chloroethyl)pyrroles **94** under the action of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in DMSO at 80 °C, underwent methylenation upon treatment with methyltriphenylphosphonium bromide in the presence of sodium amide (the **93**:CH₂=PPh₃ ratio is 1:2) to give vinylpyrroles **95**. Dehydrohalogenation and methylenation of the chloroethyl derivatives **94** can be carried out in one step by using larger amounts of the phosphonium salt and sodium amide as well as by increasing the reaction time.⁵⁹



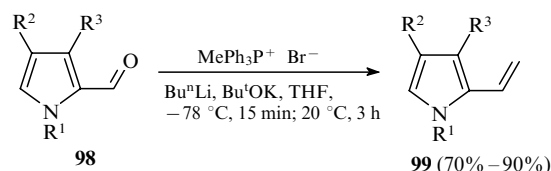
R = H, Me.

The analogous reactions of 3-acyl-1-tosylpyrroles **96** with methyltriphenylphosphonium bromide afforded 1-tosyl-3-vinylpyrroles **97**.⁶⁰



R = Me, Prⁱ, Ph.

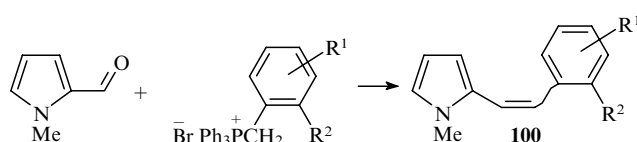
The same procedure was used for the synthesis of substituted 2-vinylpyrroles **99** from 2-formylpyrroles **98** and methyltriphenylphosphonium bromide.^{61, 62}



R¹ = Me, Ts, CO₂Bu^t (Boc); R² = H, Me, NO₂;

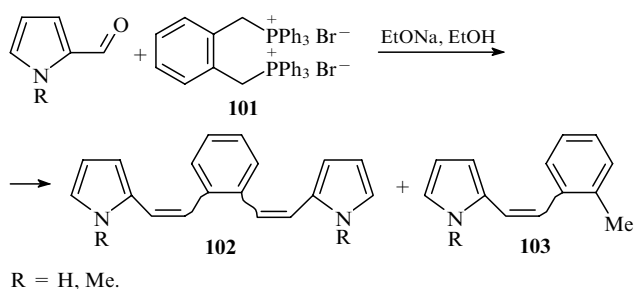
R³ = H, Me, (CH₂)₂CN.

The reactions of 2-formyl-1-methylpyrrole with substituted benzyltriphenylphosphonium bromides produced (*E*)- and (*Z*)-*N*-methyl(styryl)pyrroles **100**.⁶³ In some cases, isomers were separated by column chromatography. Photochemical isomerisation of the initially formed *Z* isomers into *E* isomers was observed.⁶³



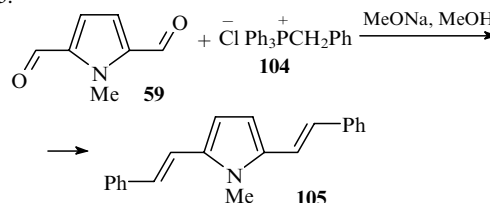
R¹ = 4-Br, 3-CN, 4-CN, 3-NO₂, 4-Cl; R² = H, Cl.

The Wittig reaction of diphosphonium salt **101** proceeded with two 2-formylpyrrole molecules to give 2,2'-(1,2-phenylenedivinyl)dipyrroles **102** (a mixture of stereoisomers) in 32% (R = H) and 40% (R = Me) yields.⁶⁴

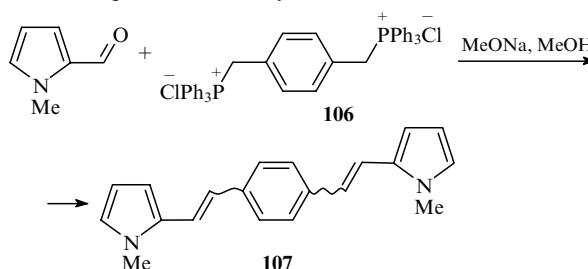


2-Styrylpyrroles **103** were generated as by-products due, apparently, to steric hindrances caused by the *o*-substituents in the diphosphonium salt **101**, which prevent the reaction of this salt with the second aldehyde molecule.⁶⁴

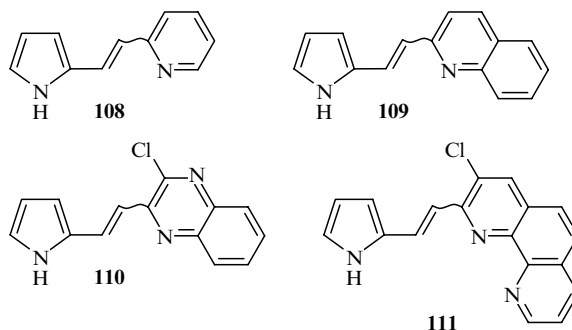
The reaction of the dialdehyde **59** with phosphonium salt **104** proceeded at both aldehyde groups to yield 2,5-distyrylpyrrole **105**.⁶⁵



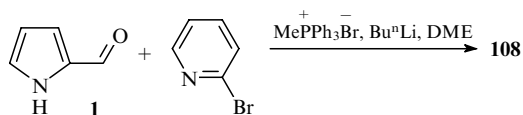
Under the analogous conditions, the reaction of *p*-xylylenebis(triphenylphosphonium) chloride **106** with 2-formyl-1-methylpyrrole proceeded selectively to produce 1,1-dimethyl-2,2'-(1,4-phenylenedivinyl)dipyrrole (**107**) in 50% yield.⁶⁵ The initially formed mixture of the *E,E*, *E,Z* and *Z,Z* isomers of the compound **107** was isomerised into the pure *E,E* isomer upon refluxing in toluene in the presence of catalytic amounts of iodine.



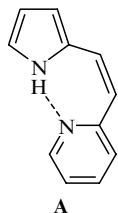
A series of studies performed by Arai and co-workers^{66–70} was devoted to the examination of isomerisation of 2-(2-hetarylvinyl)pyrroles **108–111** containing the pyridine,^{66, 67} quinoxaline,⁶⁶ quinoxaline⁶⁸ or phenanthroline substituents.⁶⁹



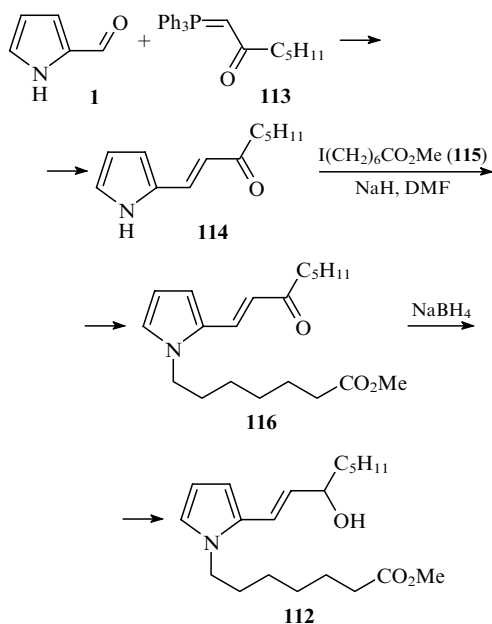
The compounds **108–111** were prepared by the reactions of 2-formylpyrrole (**1**) with ylides generated from the corresponding halogen-containing heterocycles and methylenetriphenylphosphorane. For example, the pyridine-substituted 2-vinylpyrrole **108** was synthesised from 2-formylpyrrole (**1**), 2-bromopyridine and methyltriphenylphosphonium bromide.⁶⁶



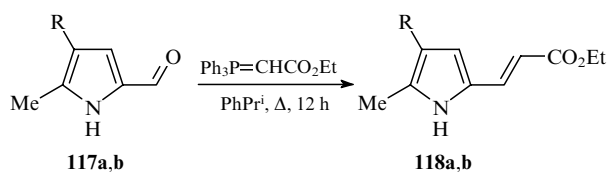
When irradiated with UV light ($\lambda = 366 \text{ nm}$) in methanol, benzene or acetonitrile at 20°C under an atmosphere of nitrogen, the initially formed *E* isomers of the compounds **108–111** were transformed into the *Z* isomers due, apparently, to intramolecular hydrogen bonding between the proton of the NH group of the pyrrole fragment and the nitrogen atom of the heterocycle. For example, the structure **A** was obtained in the case of 2-[2-(2-pyridyl)]vinylpyrrole **108**. The reverse transformation of the *Z* isomers into the *E* isomers proceeded in the presence of NiCl_2 .⁶⁹



The pyrrole analogue of prostaglandins **112** was synthesised from 2-formylpyrrole (**1**) and phosphorane **113** followed by alkylation of the pyrrole fragment of compound **114** with methyl 7-iodoheptanoate (**115**) and reduction of the carbonyl group in the reaction product **116** with sodium borohydride.⁷¹

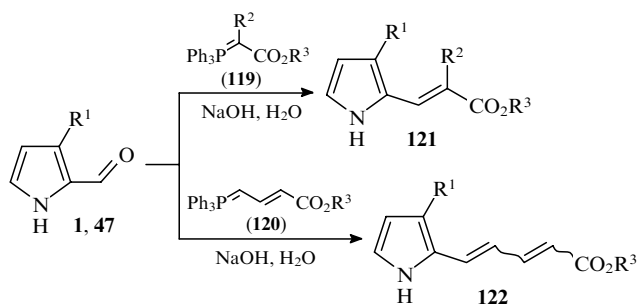


The reactions of 2-formyl-5-methylpyrrole (**117a**) and 3-acetyl-5-formyl-2-methylpyrrole (**117b**) with ethoxycarbonylmethylenephosphorane afforded 2-vinylpyrroles **118a,b** in 93% and 73% yields, respectively.⁷²



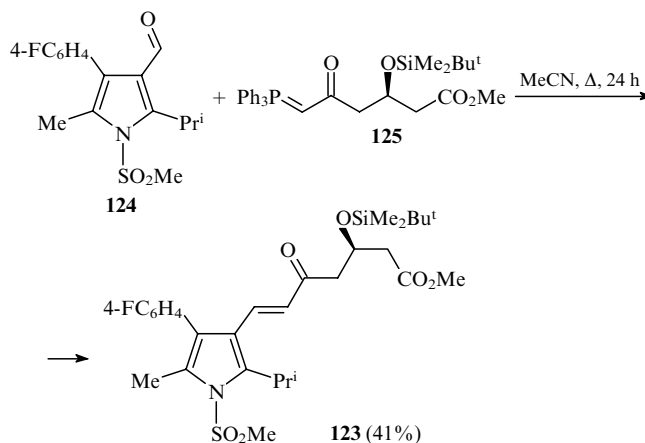
R = H (**a**), Ac (**b**).

2-Vinylpyrroles **121** and **122** (a mixture of the *E,E*, *E,Z* and *Z,Z* isomers) were synthesised by the reactions of 2-formylpyrroles **1** and **47** with phosphoranes **119** and **120**, respectively.⁷³

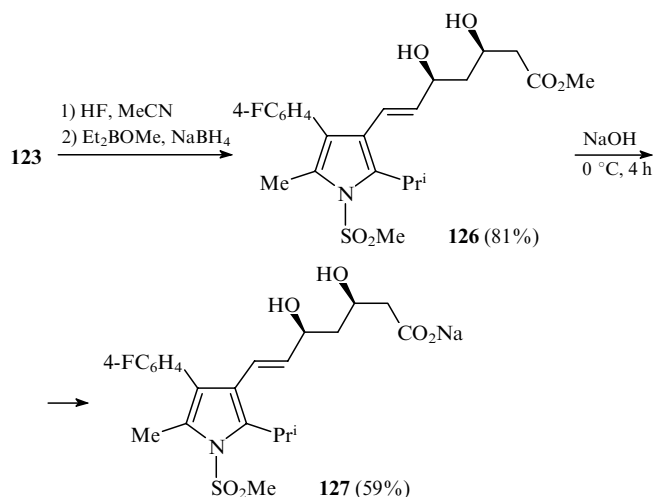


$\text{R}^1 = \text{H}$ (**1**), Me (**47**); $\text{R}^2 = \text{H}$, Me, MeO, CO_2Me , CN; $\text{R}^3 = \text{Me}$, Et.

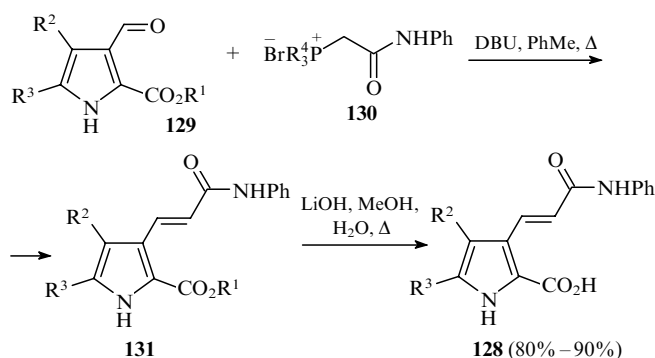
Optically active 3-vinylpyrrole **123** was prepared by refluxing unstable 3-formylpyrrole **124** with chiral Wittig reagent **125** in acetonitrile.⁷⁴



The sodium salt of functionally substituted 3-vinylpyrrole **127**, which is a potential inhibitor of HMG-CoA reductase, was prepared by a series of transformations of the vinylpyrrole **123** involving removal of the silyl protective group, stereoselective reduction of the carbonyl group and hydrolysis of methyl ester **126**.⁷⁵

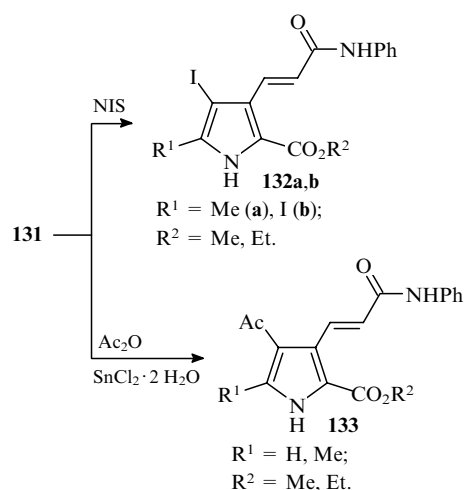


A broad spectrum of (*E*)-3-[2-(*N*-phenylcarbamoyl)vinyl]pyrrole-2-carboxylic acids **128** containing various substituents at positions 4 or 5 of the pyrrole ring were synthesised by olefination of the corresponding 3-formylpyrroles **129** with phosphoranes, which were prepared from triphenyl- or tri-*tert*-butyl(*N*-phenylcarbamoyl)methylphosphonium bromides **130** followed by hydrolysis of the ester group in the resulting compounds **131**.^{76,77}

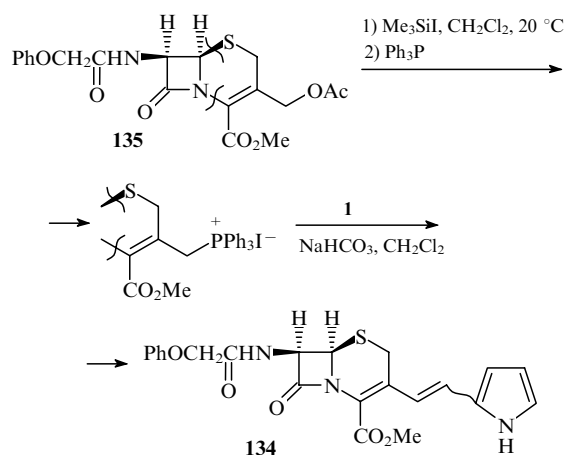


$\text{R}^1 = \text{Me, Et; R}^2 = \text{H, Me, Et, Pr}^i, \text{OEt, OBn, Br, Cl;}$
 $\text{R}^3 = \text{H, Me, Et, Pr}^i, \text{Ph, 2,4-Cl}_2\text{C}_6\text{H}_3, \text{Br; R}^4 = \text{Bu}^t, \text{Ph.}$

4-Iodo-5-methyl-3-[2-(*N*-phenylcarbamoyl)vinyl]pyrroles (**132a**) and 4,5-diiodo-3-[2-(*N*-phenylcarbamoyl)vinyl]pyrroles (**132b**) were synthesised by iodination of the pyrroles **131** ($\text{R}^2 = \text{H}$, $\text{R}^3 = \text{H}$ or Me) with one or two equivalents of *N*-iodosuccinimide (NIS). Vinylpyrroles **133** were prepared by Friedel–Crafts acylation of the pyrroles **131** ($\text{R}^2 = \text{H}$).⁷⁶



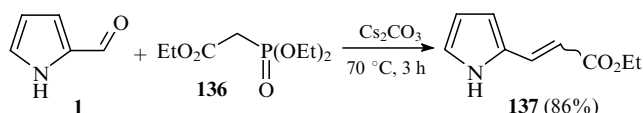
The active antibiotic, *viz.*, 3-[2-(2-pyrrolyl)vinyl]cefalosporin **134**, was prepared as a mixture of *E* and *Z* isomers in a ratio of 1 : 3 in a total yield of 30% from 7-aminocefalosporanic acid **135**. The scheme for the synthesis involves the transformation of the acetoxymethyl group into the iodomethyl group, the formation of the phosphonium salt through the reaction of the 3-iodomethyl derivative with triphenylphosphine and its reaction with 2-formylpyrrole (**1**).⁷⁸



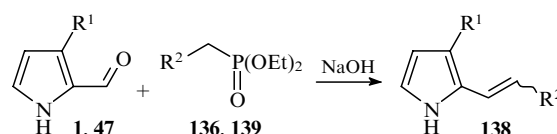
3. Horner reaction

Procedures for the synthesis of C-vinylpyrroles from acylpyrroles and dialkyl phosphonates in the presence of bases (Horner or Wittig–Horner reactions) are being extensively developed.^{73, 79–87}

Olefination of 2-formylpyrrole (**1**) with phosphonate **136** was carried out with the use of $\text{Cs}_2\text{CO}_3 \cdot 3\text{H}_2\text{O}$ (1.5-fold excess) as a base. The reaction was conducted in dioxane in a two-phase system to yield 2-[2-(ethoxycarbonyl)vinyl]pyrrole **137**.⁷⁹



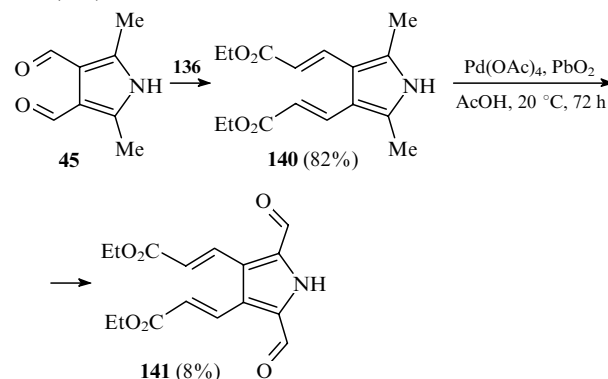
Functionalised 2-vinylpyrroles **138** (*E* and *Z* isomers) were prepared from the 2-formylpyrroles **1** and **47** and the phosphonates **136** and **139**.⁷³



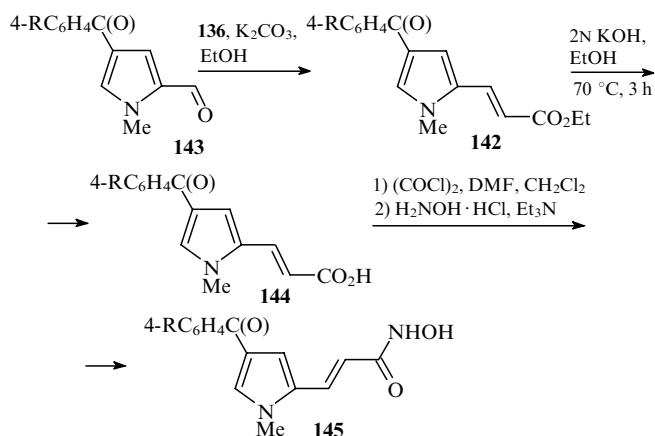
$\text{R}^1 = \text{H (1), Me, MeO, CO}_2\text{Me, CN (47);}$

$\text{R}^2 = \text{CO}_2\text{Et (136), CO}_2\text{Me (139).}$

Bis(ethoxycarbonylvinyl)pyrrole **140** was synthesised by the Horner reaction from 3,4-diformyl-2,5-dimethylpyrrole **45** and the phosphonate **136**. Oxidation of the methyl groups in the latter compound afforded 3,4-bis(2-ethoxycarbonylvinyl)-2,5-diformylpyrrole (**141**).⁸⁰

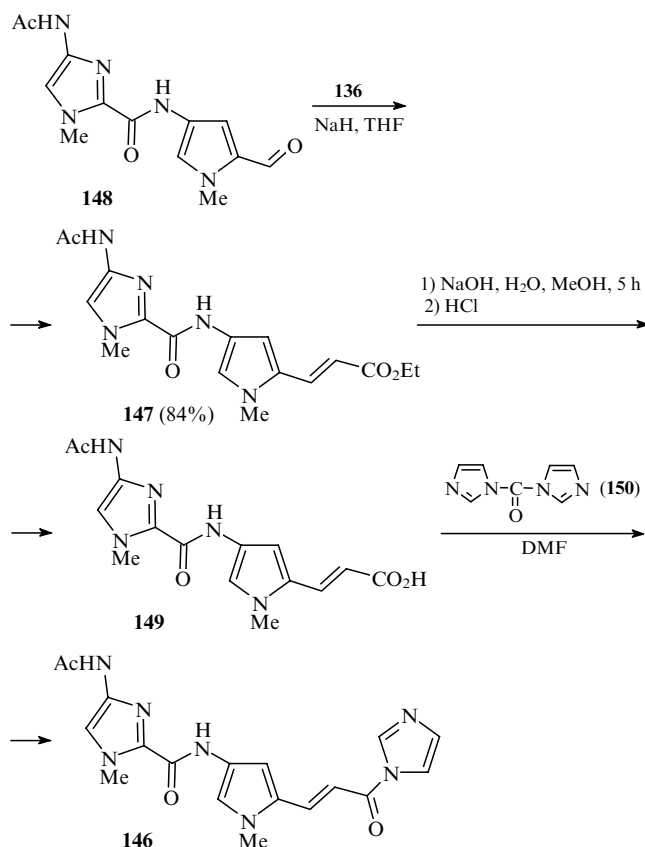


Ethyl (*E*)-3-[4-(4-*R*-benzoyl)-1-methylpyrrol-2-yl]acrylates **142** were prepared by the reactions of 4-(4-*R*-benzoyl)-2-formyl-1-methylpyrroles **143** with the phosphonate **136**. Alkaline hydrolysis of the esters **142** in ethanol afforded the corresponding acids **144**, which were transformed into [2-(*N*-hydroxyamido)vinyl]pyrroles **145**.⁸¹

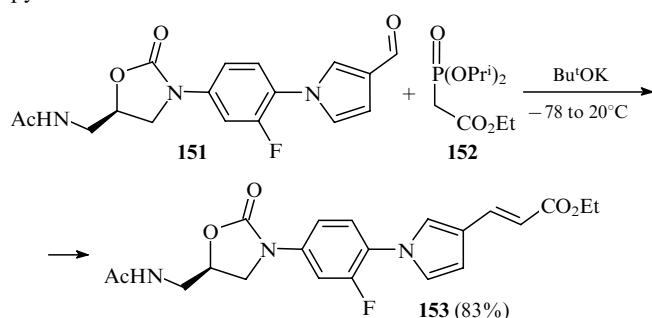


$\text{R} = \text{H, NO}_2, \text{Cl, F, MeO, NMe}_2, \text{imidazol-1-yl.}$

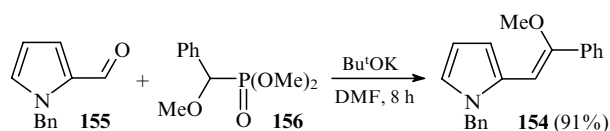
Substituted 2-vinylpyrrole **147**, which was prepared from 2-formylpyrrole **148** and the phosphonate **136**, served as the key intermediate in the synthesis of the precursor of the DNA-dialkylating agent, *viz.*, activated amide **146**. Subsequent hydrolysis of the compound **147** followed by acidification with HCl gave rise to acid **149** in 67% yield. When treated with 1,1'-carbonyldiimidazole (**150**) in DMF, the latter was transformed into the target 2-vinylpyrrole **146**.⁸²



N-Substituted 3-formylpyrrole **151** reacted with phosphonate **152** in the presence of Bu^tOK to produce 3-ethoxycarbonylvinylpyrrole **153**.⁸³

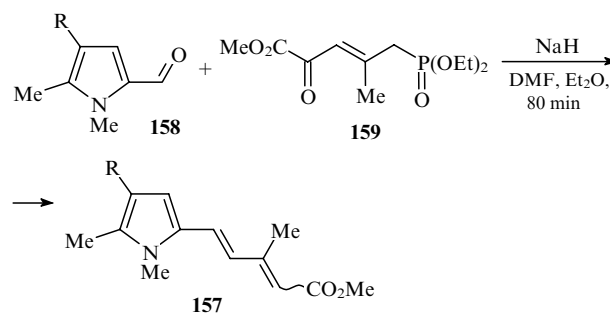


The scheme for the synthesis of the benzannulated analogue of the antibiotic CC-1065 involves the Horner reaction as the first step. *N*-Benzyl-2-(2-methoxy-2-phenylvinyl)pyrrole (*E*-**154**) was synthesised from 1-benzyl-2-formylpyrrole **155** and phosphonate **156** in dry DMF by the portionwise addition of Bu^tOK during 8 h.⁸⁴



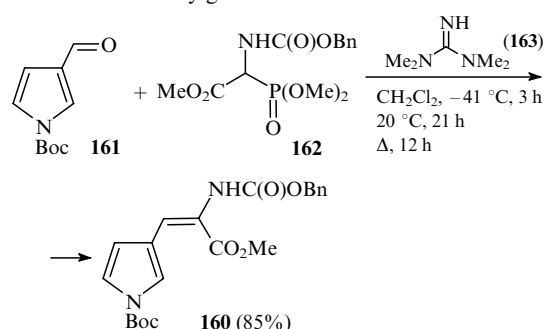
2-Butadienylpyrroles **157**, which are used in the synthesis of retinoids, were prepared as a mixture of the *E,E* and *E,Z* isomers

in a ratio of 7 : 3 by the reactions of 2-formyl-1,5-dimethylpyrroles **158** with phosphonate **159**.⁸⁵

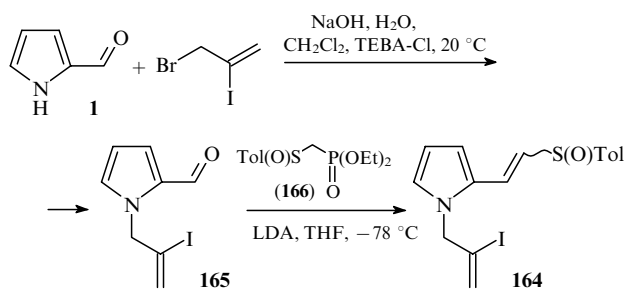


R = Ac (77%), CO₂Et (82%).

Functionalised 3-vinylpyrrole **160** was synthesised by the Horner–Emmons reaction from 3-formylpyrrole **161** and trimethyl *N*-(benzyloxycarbonyl)phosphonoglycine (**162**) in the presence of tetramethylguanidine **163**.⁸⁶



The two-step synthesis produced a mixture of the *E* and *Z* isomers of 2-(4-tolylsulfinyl)vinylpyrrole **164** (in a ratio of 67 : 33) in a total yield of 82%.⁸⁷ The process involved *N*-allylation of 2-formylpyrrole (**1**) with 3-bromo-2-iodopropene followed by olefination of aldehyde **165** with phosphonate **166**.

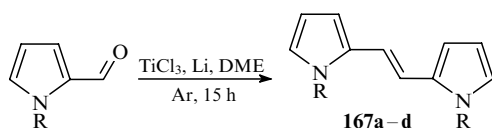


TEBA-Cl is benzyltriethylammonium chloride; LDA is Pr₂NLi; Tol is 4-MeC₆H₄.

4. Dimerisation of acylpyrroles

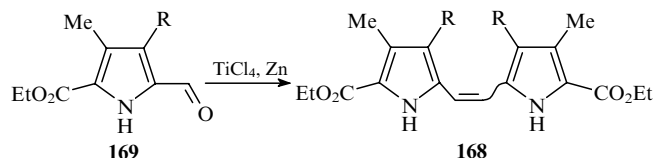
The intermediates in the synthesis of *meso*-substituted porphyrinoids, *viz.*, 1,1- and 1,2-dipyrrolylethenes, are often prepared by reductive dimerisation of 2-formylpyrroles. In these reactions, titanium compounds are generally used as catalysts.^{88–95}

Thus dipyrrolylethenes **167a–d** were prepared by refluxing *N*-substituted 2-formylpyrroles with TiCl₃ in dry dimethoxyethane in the presence of metal lithium in argon.⁸⁸ The yields of the reaction products depend on the nature of the substituent. The reactions of 2-formyl- and 2-formyl-1-methylpyrroles proceeded non-selectively to give complex mixtures of products, whereas dimerisation of 1-ethoxycarbonyl- and 1-acetyl-2-formylpyrroles afforded dipyrrolylethenes **167c,d** in 30% and 50% yields, respectively.⁸⁸



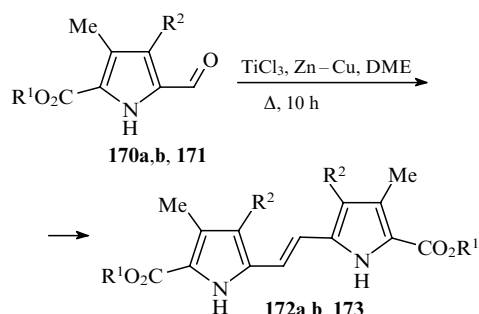
R = H (**a**), Me (**b**), COMe (**c**), CO₂Et (**d**).

1,2-Di(pyrrol-2-yl)ethenes **168** (*E* and *Z* isomers) were synthesised from pyrroles **169** in the presence of TiCl₄ and Zn.^{89, 90}



R = Et, COMe, CO₂Et, CH₂CH₂CO₂Et.

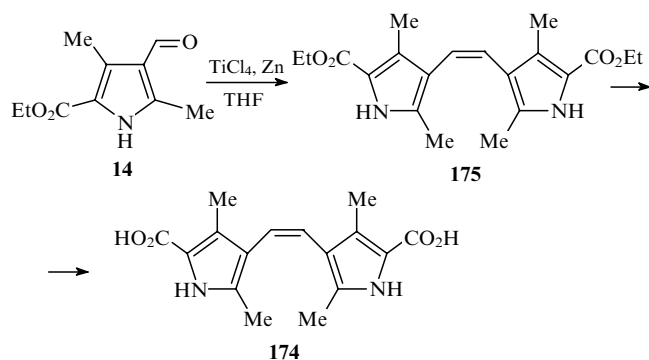
Refluxing of 2-formylpyrroles **170a–c** with the TiCl₃·(DME)_{1.5} complex in dimethoxyethane in the presence of the Zn–Cu system (15 equiv.) afforded the *E* isomers of 1,2-di(pyrrol-2-yl)ethenes **171a–c**.^{91, 92} The lower yields of the pyrroles **171b, c** are apparently attributed to lability of the methoxycarbonyl and *tert*-butoxycarbonyl ester groups in the presence of the titanium reagent.



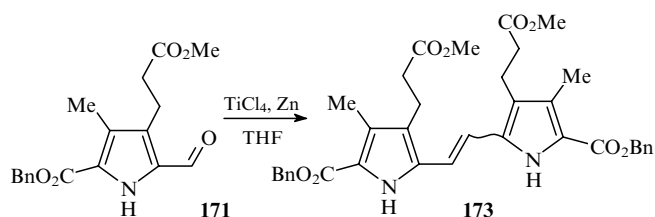
Compound	R ¹	R ²	Yield (%)
172a	Bn	Me	81
172b	Bu ^t	Et	22
173	Bn	(CH ₂) ₂ CO ₂ Me	46

An attempt to perform cross-coupling of the pyrroles **170a** and **170c** to obtain mixed 1,2-di(pyrrol-2-yl)ethene failed; instead, the reaction afforded the pyrrole **171a** as the major product (20%).⁹¹

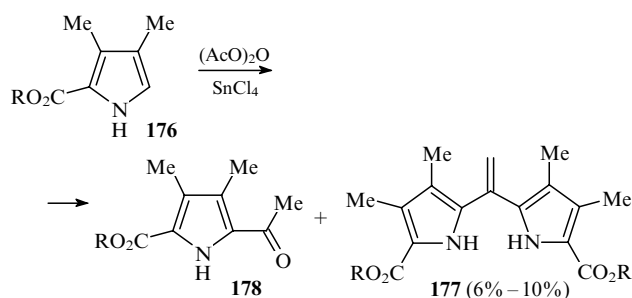
Treatment of ethyl 4-formyl-3,5-dimethylpyrrole-2-carboxylate (**14**) with the TiCl₄–Zn system in THF gave rise to a complex mixture of the reaction products. From this mixture, acid **174** was isolated in 10% yield through dimerisation of the 3-formylpyrrole **14** followed by hydrolysis of the ester groups in dimer **175**.⁹³



However, the reaction of the 5-formylpyrrole **171** performed under the same conditions afforded reductive dimerisation product **173** (*E*:*Z* = 1:4) in 86% yield. In this case, hydrolysis of the ester groups did not take place.⁹³

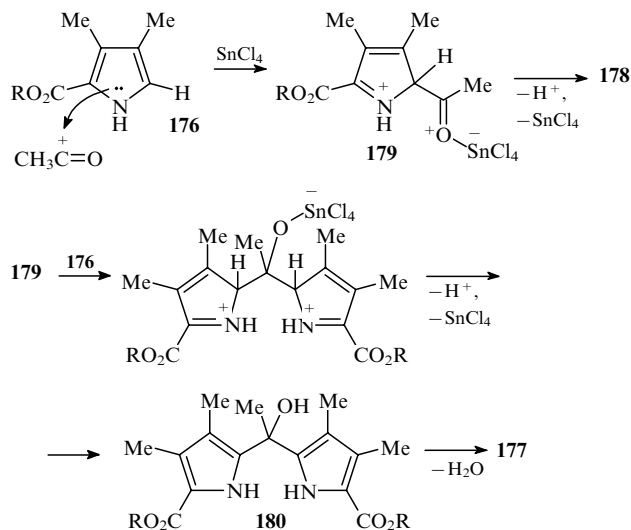


Friedel–Crafts acylation of 3,4-dimethylpyrrole-5-carboxylates **176** containing no substituents at position 2 with acetic anhydride in the presence of tin chloride afforded symmetrical 1,1-di(pyrrol-5-yl)ethenes **177** as by-products due to condensation of ketones **178** with the starting pyrroles **176**, which proceeded under the reaction conditions.^{91, 94}

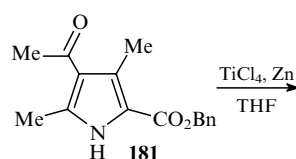


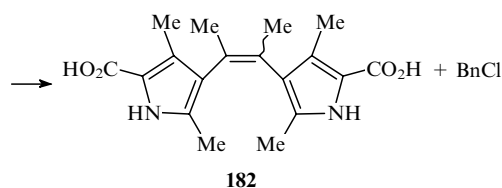
R = H, Et, Bn.

The proposed⁹¹ reaction mechanism involves the electrophilic attack of the acylium ion on the pyrrole **176** giving rise to the cationoid intermediate **179**. The latter lost the proton at the α position to form the 2-acetylpyrrole **178**. The cation **179** can attack the second molecule of the pyrrole **176** to generate intermediate hydroxydipyrrolyethane **180** whose dehydration afforded the 1,1-di(pyrrol-2-yl)ethene **177**.⁹¹

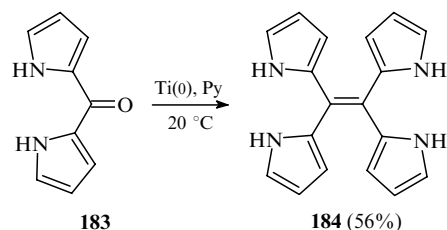


Ketone **181** reacted with the TiCl₄–Zn system to give 2,3-dipyrrolylbut-2-ene **182** in low yield. The reaction produced benzyl chloride rather than benzyl alcohol as a by-product. Cheng *et al.*⁹³ believed that this fact indicates that it is not the treatment that led to hydrolysis of the ester groups.



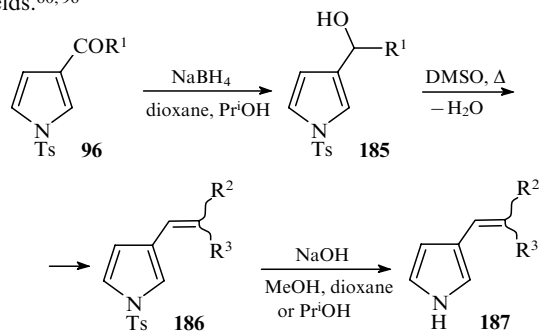


Reductive dimerisation of di(pyrrol-2-yl) ketone **183** in the presence of Ti(0) yielding 1,1,2,2-tetra(pyrrol-2-yl)ethene **184** may also be assigned to this type of reactions.⁹⁵



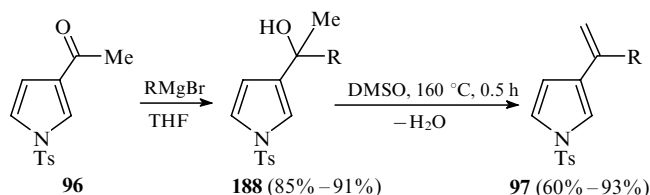
5. Other reactions involving acylpyrroles

Dehydration of 3-(1-hydroxyalkyl)-1-tosylpyrroles **185**, which were synthesised by reduction of 3-acylpyrroles **96** with sodium borohydride, afforded 3-vinylpyrroles **186**.⁹⁶ Detosylation of the latter with NaOH gave rise to 3-vinylpyrroles **187** in 66%–87% yields.^{60, 96}



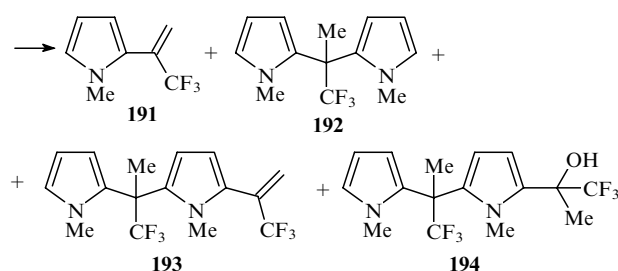
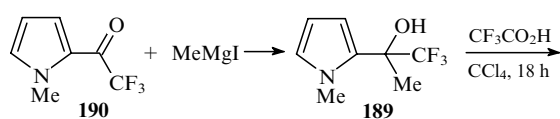
$R^1 = \text{Me}, R^2 = R^3 = \text{H}; R^1 = \text{Et}, R^2 = \text{H}, R^3 = \text{Me};$
 $R^1 = \text{Bn}, R^2 = \text{H}, R^3 = \text{Ph}; R^1 = \text{Pr}^i, R^2 = R^3 = \text{Me}.$

The reactions of 3-acetyl-1-tosylpyrrole (**96**) with Grignard reagents in THF produced 3-(1-hydroxyethyl)-1-tosylpyrroles **188**, which lost water upon heating in DMSO to give 3-(1-*R*-vinyl)pyrroles **97**.⁶⁰

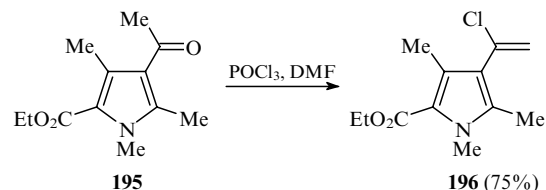


$R = \text{Me}, \text{Pr}^i, \text{Ph}.$

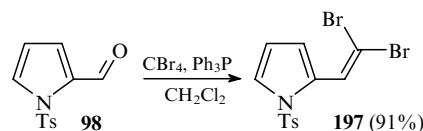
The reaction of alcohol **189**, which was synthesised from 1-methyl-2-trifluoroacetylpyrrole **190** and methylmagnesium iodide, with trifluoroacetic acid (0.1 M solution in CCl_4) afforded a mixture of products from which pyrroles **191**–**194** were isolated by chromatography in a ratio of 4 : 7 : 8 : 74.⁹⁷



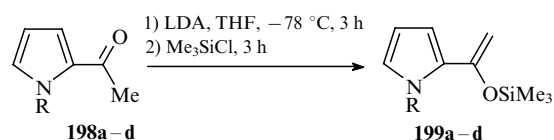
The reaction of 4-acetyl-2-ethoxycarbonyl-1,3,5-trimethylpyrrole (**195**) with POCl_3 gave rise to 3-(1-chlorovinyl)pyrrole **196**.⁹⁸



The reaction of 2-formyl-*N*-tosylpyrrole (**98**) with tetrabromomethane in the presence of triphenylphosphine yielded 2-(2,2-dibromovinyl)pyrrole **197**.⁶¹

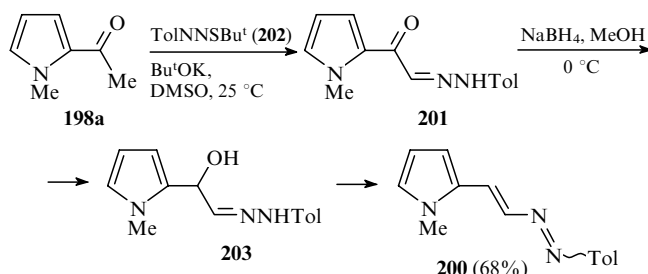


Successive treatment of 2-acetylpyrroles **198a–c** with lithium diisopropylamide and trimethylchlorosilane produced 2-[1-(trimethylsilyloxy)vinyl]pyrroles **199a–c**.⁹⁹ Silylation of 2-acetyl-1-ethoxycarbonylpyrrole **198d** in acetonitrile at 20 °C in the presence of triethylamine and catalytic amounts of ZnCl_2 afforded compound **199d**.⁹⁹



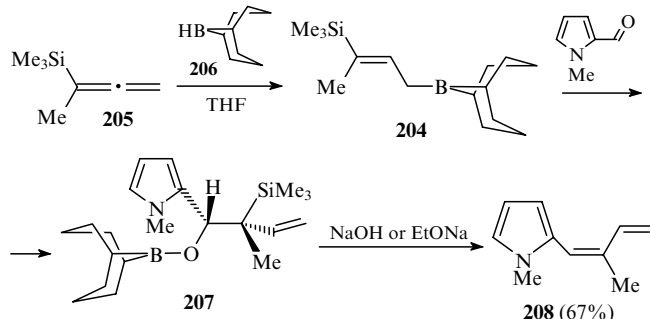
$R = \text{Me}$ (**a**, 85%), Me_3Si (**b**), SO_2Ph (**c**, 85%), CO_2Et (**d**, 93%).

1-(1-Methylpyrrol-2-yl)-2-(*p*-tolylazo)alkene **200** (predominantly, the *E* isomer) was prepared from 2-acetyl-1-methylpyrrole **198a** in three steps.

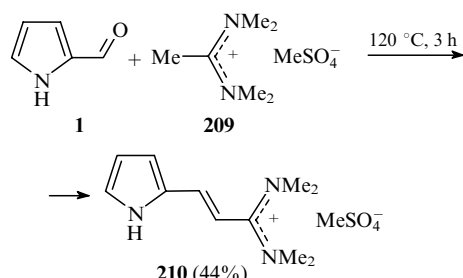


In the first step, diketone hydrazone **201** was prepared by the reaction of the enol form of 2-acetyl-1-methylpyrrole (**198a**) with *tert*-butyl *p*-tolylazo sulfide **202**. The second step involves selective reduction of the carbonyl group of the compound **201** with sodium borohydride. Hydrazone **203** was dehydrated to the diazadiene **200** either in a two-phase system (dilute sulfuric acid–diethyl ether) at 25 °C or in an acetic anhydride–pyridine mixture at 50 °C.¹⁰⁰

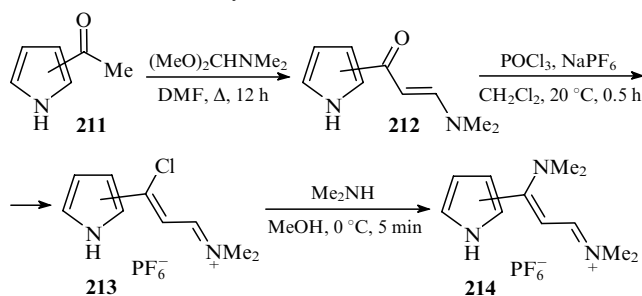
Condensation of γ -(trimethylsilyl)crotylborane **204**, which was prepared from trimethylsilyllallene **205** and 9-borabicyclo[3.3.1]nonane (**206**), with 2-formyl-1-methylpyrrole afforded intermediate **207**. Treatment of the latter with a base (to initiate Peterson olefination) led to the virtually selective formation of the *Z* isomer of 1-(pyrrol-2-yl)isoprene **208**.¹⁰¹



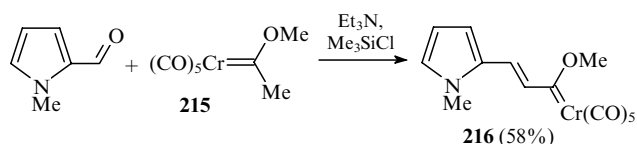
2-Formylpyrrole (**1**) smoothly reacted with *N,N,N',N'*-tetramethylacetimidium methyl sulfate **209** to produce *N,N,N',N'*-tetramethyl-3-(2-pyrrolyl)acrylamidinium methyl sulfate **210**.¹⁰²



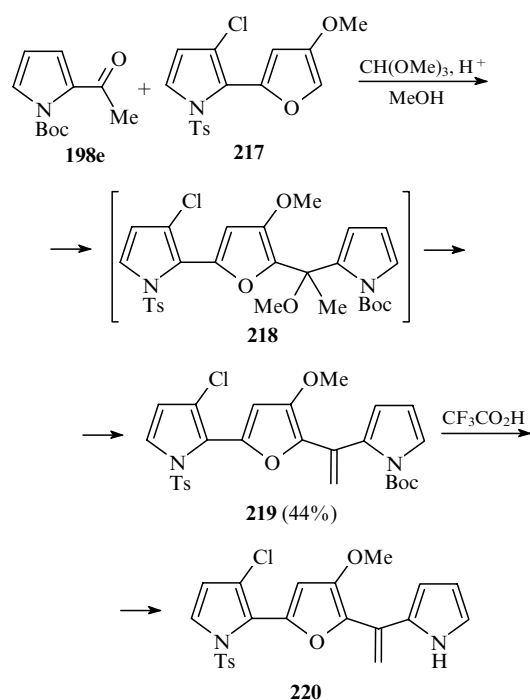
Aminomethylation of 2- and 3-acetylpyrroles **211** with dimethylformamide dimethyl acetal afforded 2- and 3-aminovinyl ketones **212** in 92% and 93% yields, respectively. The reactions of these ketones with POCl₃ in the presence of sodium hexafluorophosphate gave rise to (1-chlorovinyl)pyrroles **213** in 75% and 78% yields, respectively. The latter were transformed into (amino-vinyl)pyrroles **214** (the yields were 64% and 69%, respectively) by treatment with dimethylamine.¹⁰³



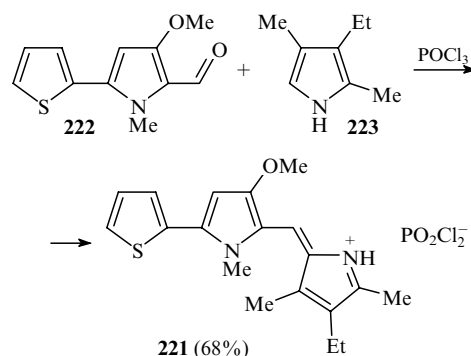
Condensation of the chromium carbene complex **215** with 2-formyl-1-methylpyrrole yielded product **216**.¹⁰⁴



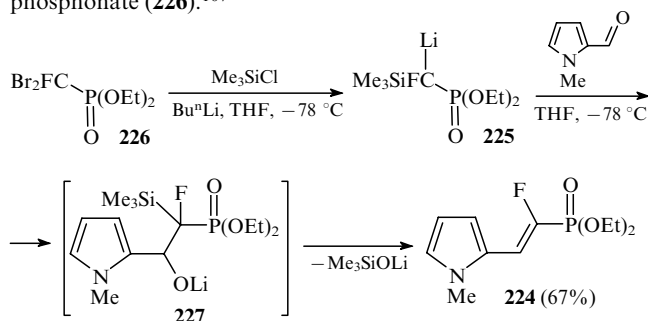
Protected 2-acetylpyrrole **198e** reacted with furylpyrrole **217** in the presence of methyl orthoformate and catalytic amounts of chlorosulfonic acid. The initially formed unstable compound **218** was transformed into 2-vinylpyrrole **219**, which was subsequently transformed into 2-vinylpyrrole **220** after removal of the *tert*-butoxycarbonyl protection.¹⁰⁵



2-Vinylpyrrole **221**, which is an analogue of the natural antibiotic prodigiosin, was synthesised by condensation of formylpyrrole **222** with 3-ethyl-2,4-dimethylpyrrole (**223**) in the presence of POCl₃.¹⁰⁶



2-(2-Diethoxyphosphoryl-2-fluorovinyl)-1-methylpyrrole (**224**, a mixture of the *E* and *Z* isomers in a ratio of 76:24) was prepared by condensation of 2-formyl-1-methylpyrrole with diethyl α -fluoro- α -lithio- α -(trimethylsilyl)methylphosphonate (**225**), which was synthesised from diethyl dibromofluoromethylphosphonate (**226**).¹⁰⁷

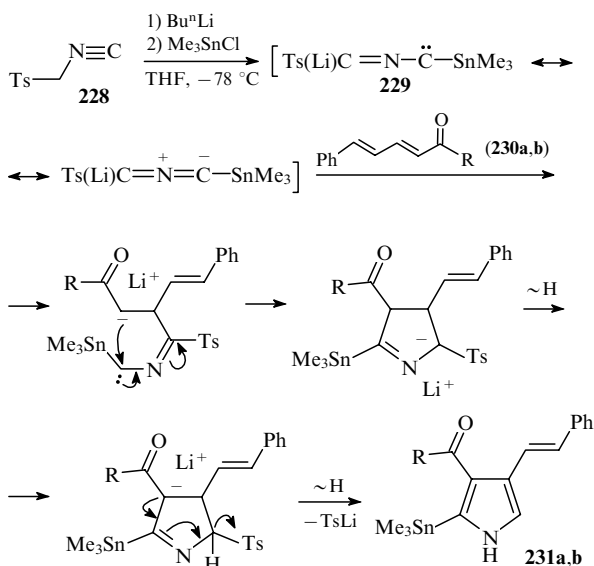


The reaction proceeded instantaneously in spite of the presence of the (EtO)₂PO group stabilising the carbanion. Attempts to isolate the intermediate pyrrole after hydrolysis of alkoxide **227** failed. β -Elimination of the trimethylsilyloxy group from the initially formed intermediate **227** took place, *i.e.*, exclusively Peterson olefination (rather than the Wittig–Horner reaction) proceeded under these conditions.¹⁰⁷

III. Synthesis of C-vinylpyrroles from functionalised aliphatic compounds

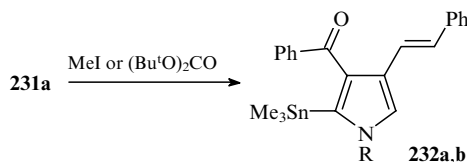
1. Synthesis from tosylmethyl isocyanide and activated alkenes

In the last decade, a procedure for the preparation of 4-vinylpyrrole derivatives containing no substituents at positions 1 and 5 has been extensively developed. This procedure relies on the base-catalysed addition of tosylmethyl isocyanide to activated alkenes.^{22, 61, 108–115} The successive reactions of isocyanide **228** with BuⁿLi and then with an excess of Me₃SnCl afforded derivative **229**, which reacted with dienones **230a,b** to give 3-acetyl- (**231a**) or 3-benzoyl-4-(*E*)-styryl-2-(trimethylstannyl)-pyrroles (**231b**).¹⁰⁸ The reactions unexpectedly gave rise to 2-stannylpyrroles rather than to 5-stannylpyrroles, which are adducts of TsCLi(SnMe₃)N≡C with dienones. In this process, the stannylated isocyanide derivative **229** serves, apparently, as the reactive species. In the study,¹⁰⁸ the possibility of the migration of the Me₃Sn group from position 5 to position 2 of the pyrrole ring was also not excluded.



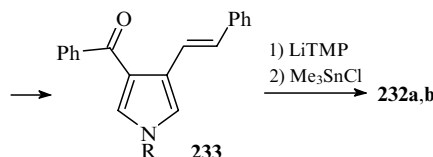
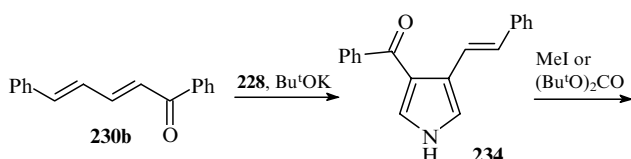
R = Me (**a**), Ph (**b**).

N-Substituted 2-(trimethylstannyl)pyrroles **232a,b** containing the styryl group at position 4 were prepared either by methylation of the pyrrole **231b** under the conditions of phase transfer catalysis or by acylation of di-*tert*-butyl carbonate.¹⁰⁸



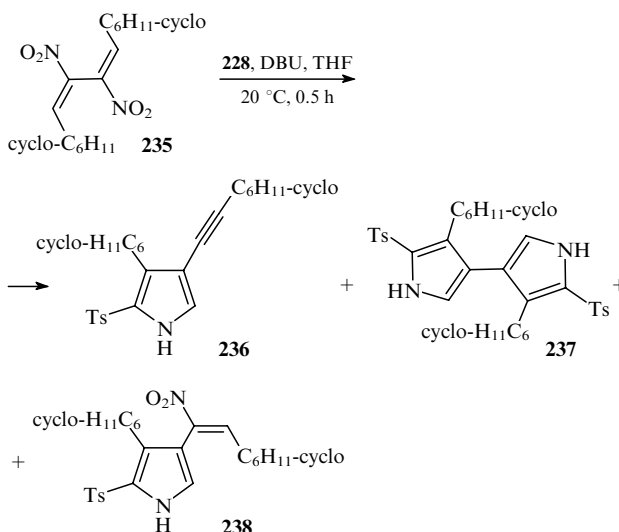
R = Me (**232a**), Boc (**232b**).

The compounds **232a,b** were also prepared by the introduction of the trimethylstannyl group into pyrroles **233**, which were synthesised by the reaction of the tosylmethyl isocyanide **228** with the dienone **230b** in the presence of Bu^tOK followed by alkylation or acylation of intermediate **234**.¹⁰⁸

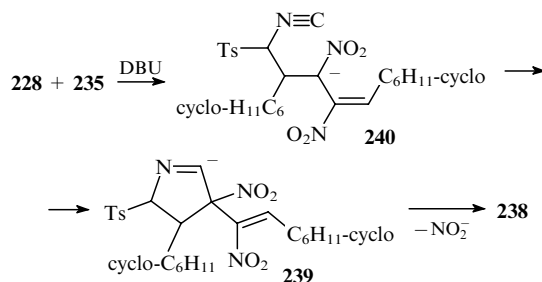


R = Me, Boc; LiTMP is lithium 2,2,6,6-tetramethylpiperidide.

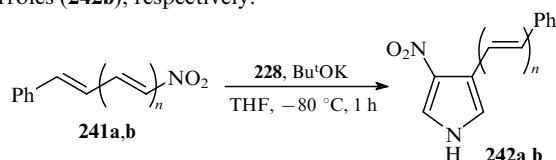
The reaction of the isocyanide **228** with an equimolar amount of 1,4-dicyclohexyl-2,3-dinitrobuta-1,3-diene (**235**) in THF in the presence of diazabicycloundecene afforded a mixture of ethynylpyrrole **236** (58%), 4,4'-bipyrrole **237** (9%) and nitrovinylpyrrole **238** (12%).¹⁰⁹



Intermediate **239**, which is a precursor of the pyrrole **238**, was generated through the addition of the tosylmethyl isocyanide anion to one nitrovinyl group of the dinitrobutadiene system and intramolecular cyclisation of the resulting anion **240**.¹⁰⁹

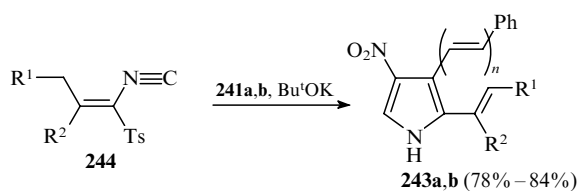


Conjugated nitrodiene **241a** and nitrotriene **241b** reacted with the isocyanide **228** in the presence of an excess of Bu^tOK in THF to form 4-styryl- (**242a**) and 4-(4-phenylbuta-1,3-dienyl)-3-nitropyrroles (**242b**), respectively.¹¹⁰



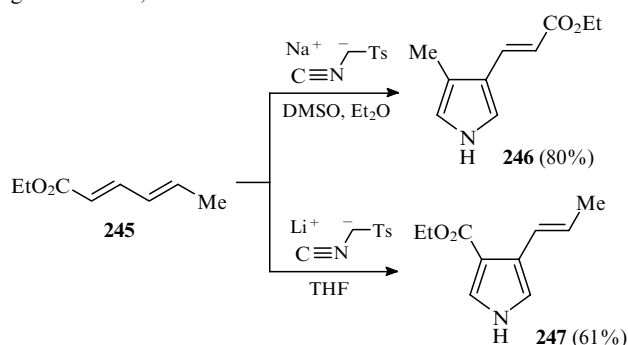
n = 1 (**a**, 73%), 2 (**b**, 75%).

2,3-Dialkenyl-4-nitropyrroles **243** were prepared by the analogous reactions of the nitrodiene **241a** or the nitrotriene **241b** with 1-isocyano-1-tosyl-2,2-disubstituted alkenes **244**, which are products of condensation of tosylmethyl isocyanide **228** with ketones.^{110–112}

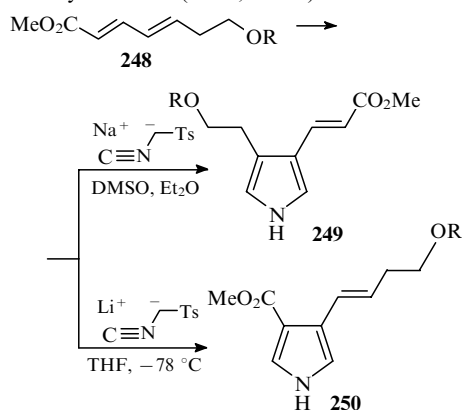


$n = 1$ (**a**), 2 (**b**); $\text{R}^1 = \text{H}, \text{Me}$; $\text{R}^2 = \text{Me}, \text{Ph}$; $\text{R}^1 - \text{R}^2 = (\text{CH}_2)_4$.

The synthesis with the use of ethyl hexa-2,4-dienoate **245** as the Michael acceptor afforded isomeric pyrroles **246** and **247**. The direction of the reaction depends on its conditions. Thus the use of a more polar solvent in combination with a more dissociated ionic pair facilitates the addition of the anion derived from the isocyanide **228** to the δ position of the ester **245** bearing the highest positive charge. For example, the reaction of the sodium derivative of the isocyanide **228** with the ester **245** in a DMSO– Et_2O mixture afforded pyrrole **246**, whereas the reaction of the lithium derivative of the isocyanide **228** in tetrahydrofuran gave rise to 1,2-adduct **247**.¹¹³

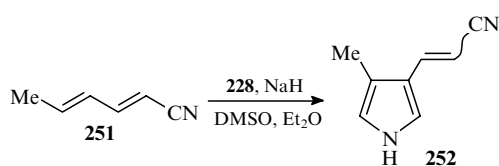


Condensation of ester **248** with the sodium derivative of the isocyanide **228** in the DMSO– Et_2O system produced a mixture of regioisomers **249** and **250** in a ratio of 7 : 1 in 55% yield. The use of the lithium derivative in THF at -78°C afforded only pyrrole **250** with an impurity of the starting isocyanide **228**. The compound **250** was isolated as the *N*-benzyl derivative after treatment with benzyl bromide (NaH , DMF).¹¹³



$\text{R} = \text{Bu}^t\text{Me}_2\text{Si}$.

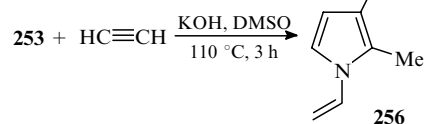
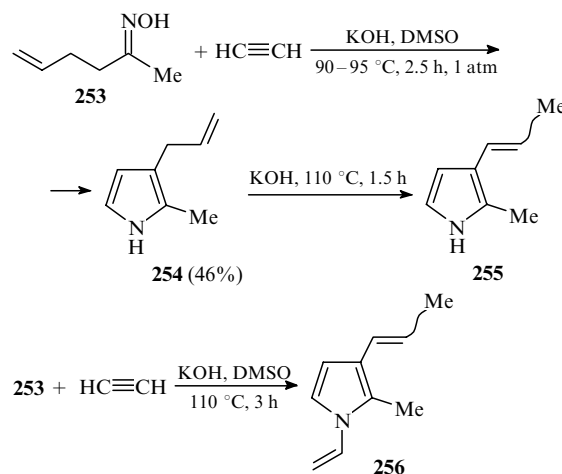
The reaction of nitrile **251** with the isocyanide **228** in the presence of sodium hydride in the DMSO– Et_2O system produced a mixture of (*E*)- and (*Z*)-3-(2-cyanovinyl)pyrroles **252**.⁶¹



2. Synthesis from unsaturated ketone oximes and acetylene

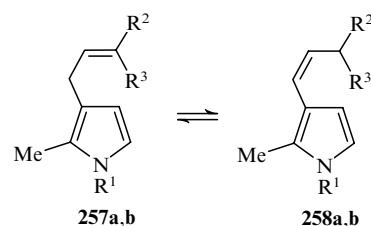
Heterocyclisation of unsaturated ketone oximes with acetylene in the superbasic KOH–DMSO system (Trofimov's reaction) is a promising procedure for the synthesis of C-vinylpyrroles.^{114,115} This procedure enables one to carry out a two-step transformation of readily available ketones to pyrroles and their 1-vinyl derivatives (in the presence of an excess of acetylene).

For example, 2-methyl-3-(prop-2-enyl)pyrrole (**254**) was prepared from hex-5-en-2-one oxime **253** and acetylene.¹¹⁴ Heating of compound **254** with calcined KOH under an atmosphere of nitrogen led to prototropic isomerisation to form an equilibrium mixture of the *E* and *Z* isomers (in a ratio of 7 : 3) of 2-methyl-3-(prop-1-enyl)pyrrole (**255**) in a total yield of 93%.



The reaction with an excess of acetylene afforded only 2-methyl-3-(prop-1-enyl)-1-vinylpyrrole (**256**) (the yield was 80%, a mixture of the *E* and *Z* isomers in a ratio of 7 : 3).¹¹⁵ Hence, the prop-1-enyl substituents are thermodynamically more favourable for these compounds due, apparently, to conjugation of the double bond with the pyrrole ring.

Isomerisation of 3-allylpyrroles **257a,b** in the KOH–DMSO (120°C , 1 h, the molar ratio KOH : pyrrole **257** = 1 : 1) or Bu^tOK –DMSO system ($60-65^\circ\text{C}$, 1 h) afforded an equilibrium mixture of the pyrroles **257a,b** and (*E*)- and (*Z*)-3-(prop-1-enyl)pyrroles **258a,b**.¹¹⁵



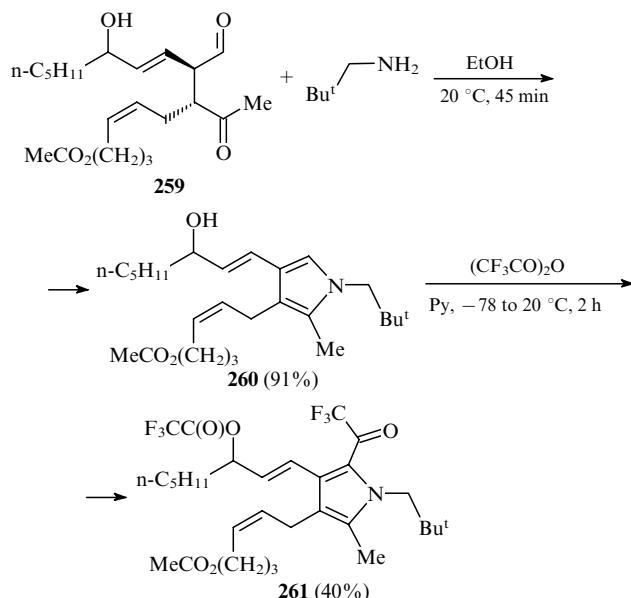
$\text{R}^1 = \text{H}, \text{CH}=\text{CH}_2$; $\text{R}^2 = \text{R}^3 = \text{Me}$ (**a**), $\text{R}^2 - \text{R}^3 = (\text{CH}_2)_5$ (**b**).

The allyl substituents in the 1-vinylpyrroles **257a,b** are isomerised into the corresponding prop-1-enyl substituents by 75%–100%. For the corresponding 1*H*-pyrroles, the conversion was at most 30%. The higher conversion in the case of 1-vinylpyrroles results from conjugation between the 3-(alk-1-enyl) and 1-vinyl fragments through the double bonds and the nitrogen atom of the pyrrole ring.¹¹⁵

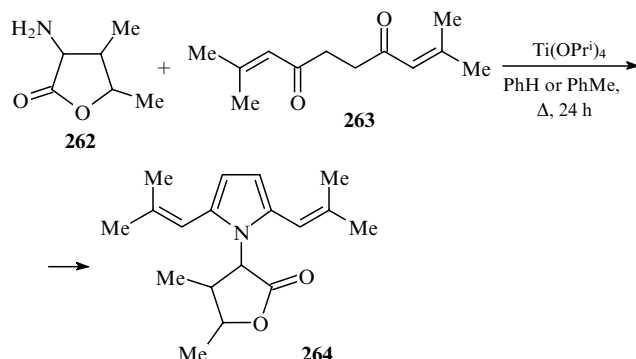
3. Synthesis from 1,4-dicarbonyl compounds

One of the most commonly used procedures for the preparation of pyrroles involves the transformation of 1,4-dicarbonyl compounds into pyrroles under the action of ammonia or amines (Paal–Knorr synthesis). In some cases, this procedure is applicable also to the synthesis of C-vinylpyrroles. These reactions performed with the use of unsaturated γ -ketoaldehydes, such as an analogue of levuglandin **259**, as the dicarbonyl component and

neopentylamine as the amino component, afforded pyrrole **260**.¹¹⁶ Condensation was performed in dry degassed ethanol at 20 °C. However, the pyrrole **260** is unstable and completely decomposes in one day even under an atmosphere of argon. Stable functionalised β -C-vinylpyrrole **261** was prepared from the pyrrole **260** under the action of trifluoroacetic anhydride under an atmosphere of argon.¹¹⁶

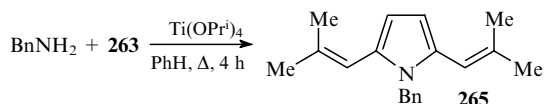


Refluxing of aminolactone **262** with 2,9-dimethyldeca-2,8-diene-4,7-dione (**263**) in benzene or toluene in the presence of titanium isopropoxide for 24 h afforded 2,5-diisobutenylpyrrole **264** in 53% yield.^{117, 118}



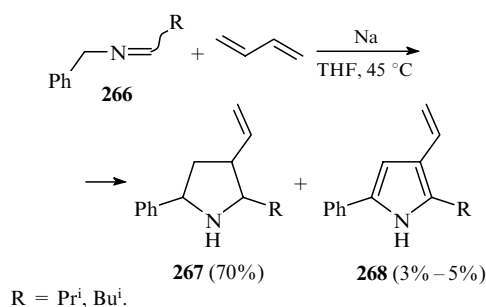
It should be noted that TiCl_4 , which is widely used as a catalyst in the Paal–Knorr synthesis, is inefficient in this reaction. Thus, the pyrrole **264** was obtained only in trace amounts.

Under analogous conditions, the reaction of the diketone **263** with benzylamine gave rise to 1-benzyl-2,5-diisobutenylpyrrole (**265**) in 63% yield.¹¹⁸



4. Synthesis from imines and butadiene

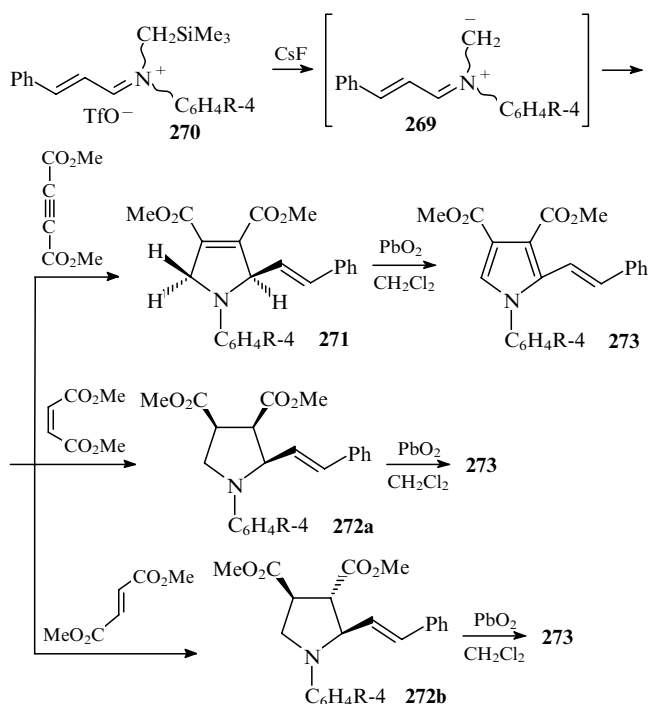
Condensation of alkylidenebenzylamines **266** with butadiene in the presence of catalytic amounts of sodium metal proceeded as the [3 + 2]-cycloaddition accompanied by imine–imine isomerisation to give a complex mixture of products containing alkyl(vinyl)phenylpyrrolidines **267** as the major component and pyrroles **268** (in small amounts).^{119–121}



$\text{R} = \text{Pr}^i, \text{Bu}^i$.

The pyrroles **268** can also be prepared by catalytic dehydrogenation of the pyrrolidines **267** in the presence of Pd/C (250 °C, 5 h, the yield was 52%).¹¹⁹

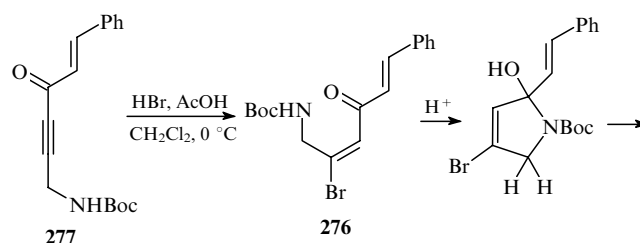
Ylide **269**, which was generated upon desilylation of a mixture of the *E,Z* and *E,E* isomers of salt **270**, reacted with different dipolarophiles, such as dimethyl acetylenedicarboxylate, dimethyl maleate or dimethyl fumarate, to form dihydropyrroles **271** or stereoisomeric pyrrolidine derivatives (**272a,b**).¹²² Oxidation of the dihydropyrroles **271** and pyrrolidines **272a,b** gave rise to 2-styrylpyrroles **273**.¹²²

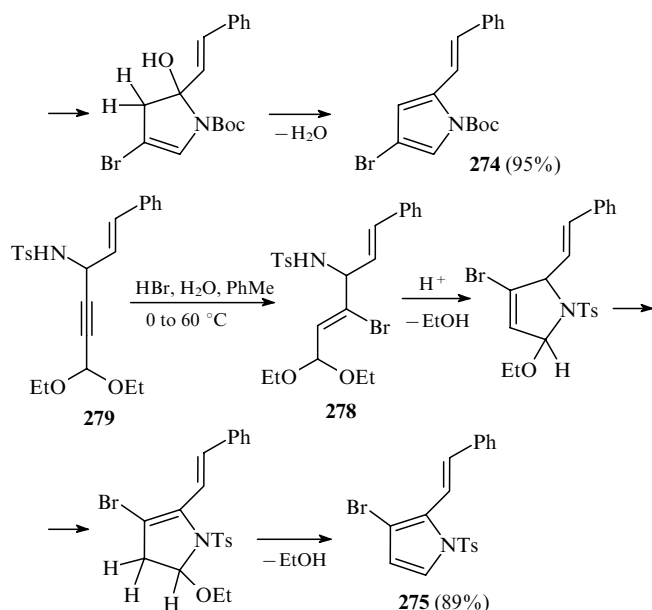


$\text{R} = \text{H}, \text{Me}, \text{MeO}, \text{Cl}$.

5. Synthesis from vinylacetylenic amides

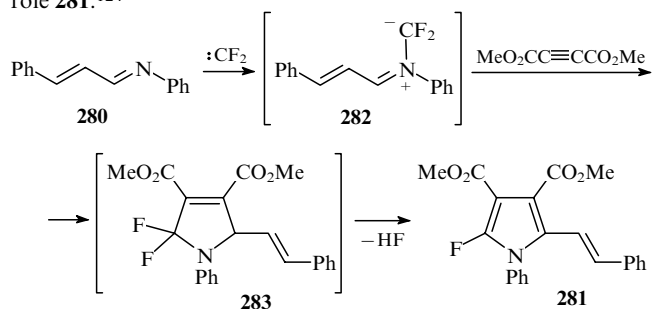
Nitrogen-protected β -bromo- α -styrylpyrroles **274** and **275** were synthesised by cyclisation of diene amidoketones **276** (generated from vinylacetylenic amidoketones **277**) or aminoacetals **278** (prepared from vinylacetylenic aminoacetals **279**) in the presence of HBr.¹²³





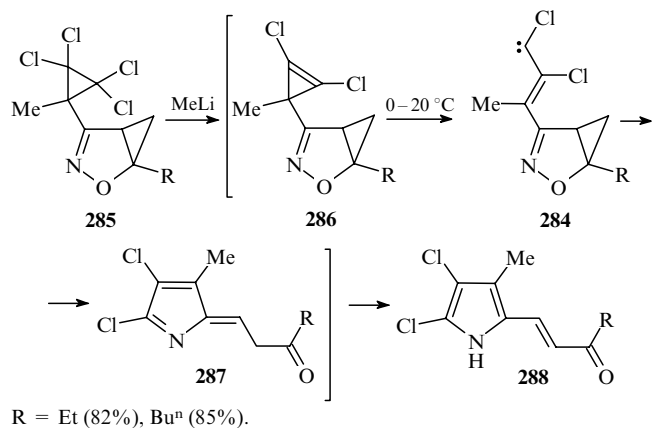
6. Synthesis involving carbenes

Imine **280** reacted with difluorocarbene in the presence of dimethyl acetylenedicarboxylate to give 5-fluoro-2-(*E*)-styrylpyrrole **281**.¹²⁴



Apparently, difluorocarbene attacks the lone electron pair of the nitrogen atom to form azomethine ylide **282**, which adds as the 1,3-dipole to acetylenedicarboxylic ester to form dihydropyrrole **283**. Its subsequent dehydrofluorination affords the pyrrole **281**.¹²⁴

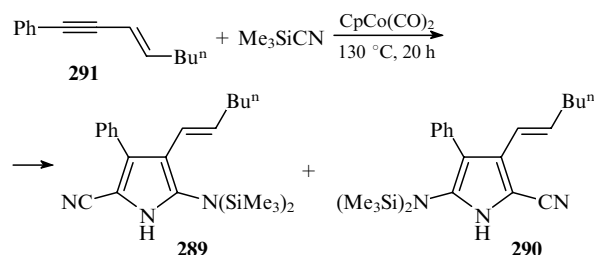
Vinylcarbenes **284** were prepared from 1-(2,2,3,3-tetrachloro-1-methylcyclopropyl)isoxazolines **285** by treatment with methyl-lithium followed by isomerisation of the resulting 1,2-dichlorocyclopropenes **286**. The attack of the carbene centre on the isoxazoline substituent was accompanied by rearrangement to give methylene-2*H*-pyrroles **287**, which underwent aromatisation under the reaction conditions to give 2-(2-acylvinyl)pyrroles **288**.¹²⁵



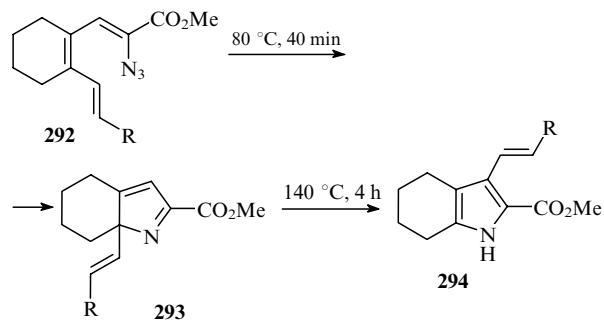
R = Et (82%), Buⁿ (85%).

7. Other procedures for the synthesis

A mixture of isomeric pyrrole-2-carbonitriles **289** and **290** (in a ratio of 1 : 4) containing a hex-1-enyl substituent at the β position was prepared in a total yield of 53% from 1-phenyloct-3-en-1-yne (**291**) and trimethylsilyl cyanide in the presence of the cobalt cyclopentadienyl complex.¹²⁶

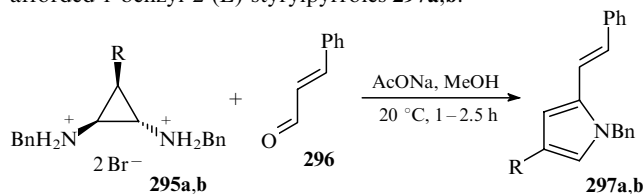


Thermolysis of β -cyclohexenyl α -azidoacrylates **292** in a solution of xylene, cyclohexane or DMF proceeded quantitatively to give substituted tetrahydrobenzo-2*H*-pyrroles **293** stable up to 130 °C.¹²⁷ Upon refluxing in xylene, the latter compounds were slowly rearranged through, apparently, the double 1,5-shift of the vinyl group to give 4,5,6,7-tetrahydro-2-methoxycarbonyl-3-vinylindoles **294**.¹²⁷



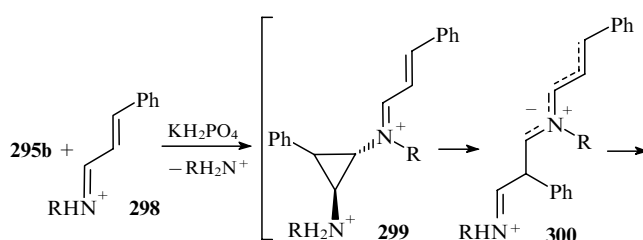
R = H, Ph, CH=CHPh.

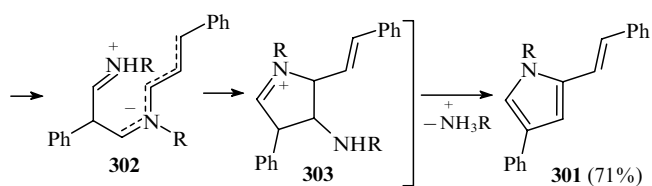
Treatment of *trans*-1,2-di(*N*-benzylammonio)cyclopropane dibromides **295a,b** with cinnamaldehyde (**296**) in an acetate buffer afforded 1-benzyl-2-(*E*)-styrylpyrroles **297a,b**.^{128, 129}



R = H (**a**, 54%), Ph (**b**, 71%).

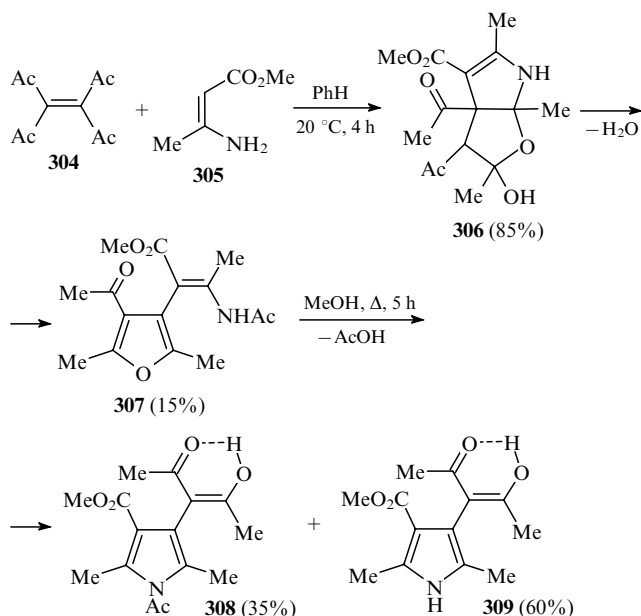
The reactions of K_2HPO_4 with salts of 3-phenylcyclopropane-1,2-diamines **295b** (R = Me, Bn) proceeded with the opening of the three-carbon ring to produce imminium ions **298**. The latter reacted with the salts **295** to give cyclopropane intermediates **299**. The ring opening in these intermediates afforded bipolar ions **300**. 2-Styrylpyrroles **301** were generated by cyclisation of intermediates **302** followed by aromatisation of 3,4-dihydro-2*H*-pyrroles **303**. The styrylpyrroles **301** were also derived from two molecules of the salt **295b** upon treatment with an aqueous solution of K_2HPO_4 (the yield was 59%) or AcONa (the yield was 60%).¹²⁹



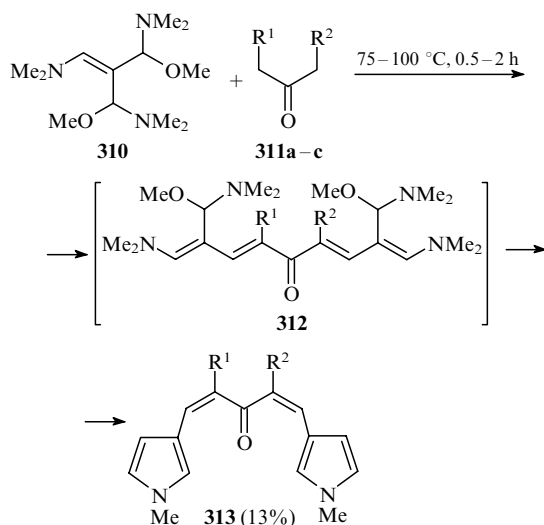


R = Me, Bn.

Tetraacetylene (**304**) reacted with methyl 3-aminobut-2-enoate (**305**) under mild conditions to give a mixture of dihydropyrrole **306** and tetrasubstituted furan **307**.¹³⁰ Upon refluxing in methanol, the latter underwent recyclisation to produce a mixture of *N*-acyl- (**308**) and NH-pyrroles (**309**).¹³⁰



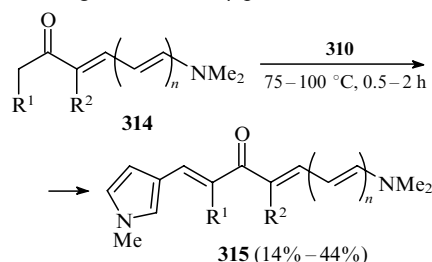
Condensation of 1,3-bis(dimethylamino)-2-[dimethylamino(methoxy)methyl]-1-methoxyprop-2-ene (**310**) with ketones **311a–c** did not furnish the expected polyenic bis(dimethylamino) ketones **312** containing the *N,O*-acetal groups at the γ, γ' positions; instead, products of their intramolecular cyclisations, *viz.*, di[β -(*N*-methylpyrrol-3-yl)vinyl] ketones **313**, were isolated.^{131–133}



R¹ = R² = H (**a**), R¹–R² = (CH₂)₂ (**b**), (CH₂)₃ (**c**).

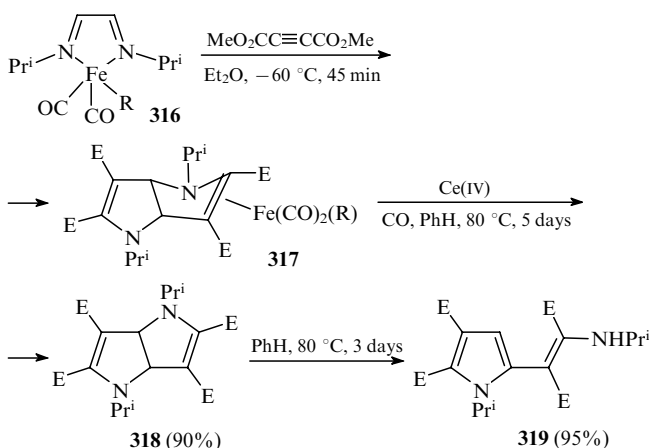
The reactions of conjugated dimethylamino ketones **314** with the compound **310** taken in an equimolar ratio proceeded analog-

ously to give unsaturated amino ketones **315** containing the pyrrole ring in one of the β positions.^{131–133}



R¹ = R² = H; R¹ = , R² = H; R¹–R² = (CH₂)₂, (CH₂)₃; n = 0–2.

The reactions of complexes **316** with dimethyl acetylenedicarboxylate proceeded as the 1,3-dipolar cycloaddition to the Fe–N=C fragment to form the 1,4,3*a*,6*a*-dihydropyrrolo[3,2-*b*]pyrrole complexes **317** in good yields. Treatment of the latter with Ce(IV) led to liberation of dihydropyrrolo[3,2-*b*]pyrrole **318**.¹³⁴ Heating of the compound **318** in benzene caused the ring opening to give vinylpyrrole **319**.

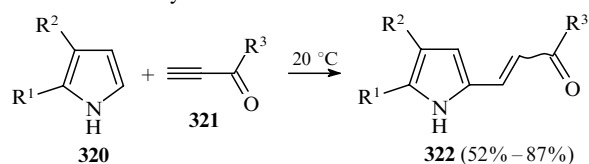


E = CO₂Me; R = CO, CNBu^t, CNBn, CNC₆H₁₁-cyclo, CNC₆H₄Me-2, CNC₆H₃Me₂-2,6.

IV. Addition of pyrroles to acetylenes

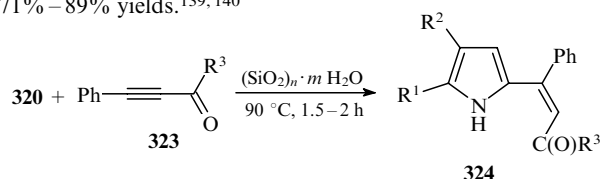
The direction of the reaction of pyrroles with activated acetylenes depends on the reaction conditions and the structures of the starting reagents. For example, diene condensation as well as C- or N-nucleophilic attack on the triple bond can occur.^{16,28,29} In recent years, the addition of pyrroles as C-nucleophiles to the electron-deficient triple bond has been extensively studied because this reaction provides the most direct approach to functionally substituted *C*-vinylpyrroles.

Thus, the non-catalytic reactions of pyrroles **320** with terminal acylacetylenes **321** proceeded under mild conditions both without a solvent and in protic (methanol or ethanol) or aprotic (diethyl ether, benzene, hexane or acetonitrile) solvents to give 2-(2-acylvinyl)pyrroles **322** (predominantly, the *Z* isomers).^{135–139} In the course of isolation and purification and even upon storage, the *Z* isomers are readily transformed into the *E* isomers.^{135–139}



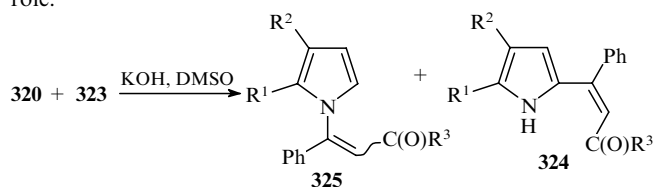
R¹ = H, Prⁿ, Ph; R² = H, Me, n-C₇H₁₅; R¹–R² = (CH₂)₄; R³ = Ph, 2-thienyl.

Unlike the alkynes **321**, 1-acyl-2-phenylacetylenes **323** are less reactive and do not react with pyrroles at 20 °C. The latter reaction was performed upon heating of equimolar amounts of the reagents in the presence of a 5–10-fold excess of silica gel. The *Z* isomers of 2-(2-acyl-1-phenylvinyl)pyrroles **324** were obtained in 71%–89% yields.^{139, 140}



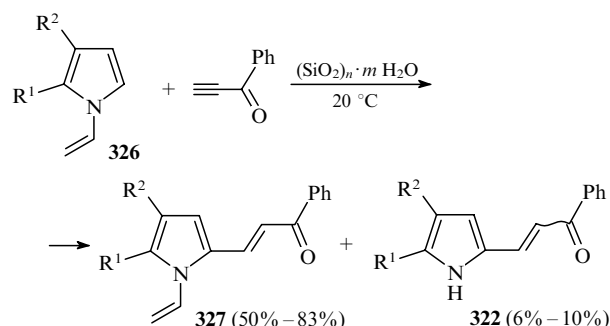
$\text{R}^1 = \text{H, Ph}; \text{R}^2 = \text{H}; \text{R}^1-\text{R}^2 = (\text{CH}_2)_4;$
 $\text{R}^3 = \text{Ph, 2-thienyl, 2-furyl, CCl}_3.$

The reactions of the pyrroles **320** with ethynyl ketones **323** ($\text{R}^3 = \text{Ph, 2-furyl}$) in the superbasic KOH–DMSO system afforded a mixture of N- (**325**, *E* and *Z* isomers) and C-adducts (**324**, *Z* isomers) (in a total yield of 60%–80%), the ratio of the products being dependent on the structure of the starting pyrrole.¹⁴¹



$\text{R}^1 = \text{H, Ph}; \text{R}^2 = \text{H}; \text{R}^1-\text{R}^2 = (\text{CH}_2)_4; \text{R}^3 = \text{Ph, 2-furyl}.$

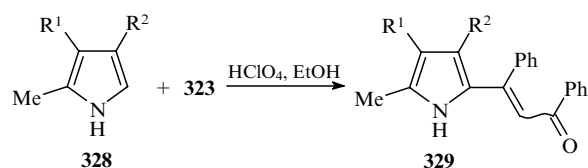
Regio- and stereospecific C-vinylation of 1-vinylpyrroles **326** with benzoylacetylene proceeded at 20 °C on the surface of silica gel under the conditions of mechanochemical activation to form *E* isomers of 1,2-divinylpyrroles **327**.¹⁴²



$\text{R}^1 = \text{H, Me, Bu}^n, 2,5\text{-Me}_2\text{C}_6\text{H}_3, \text{Ph}; \text{R}^2 = \text{H, Me, Et, Pr}^n.$

The reactions of the pyrroles **326** ($\text{R}^1 = \text{Me}$ and $\text{R}^2 = \text{Pr}^n$ or $\text{R}^1 = \text{Ph}$ and $\text{R}^2 = \text{Et}$) afforded compounds **327** along with the adducts **322**, which do not contain the vinyl substituent at the nitrogen atom. The formation of the latter compounds is associated with hydrolysis of the *N*-vinyl group both in the starting pyrroles **326** and in the reaction products **327** that occurs on SiO_2 .¹⁴²

Trisubstituted pyrroles **328** reacted with phenylbenzoylacetylene (**323**, $\text{R}^3 = \text{Ph}$) in ethanol in the presence of HClO_4 to give vinylpyrroles **329** (mixtures of the *E* and *Z* isomers).¹⁴³

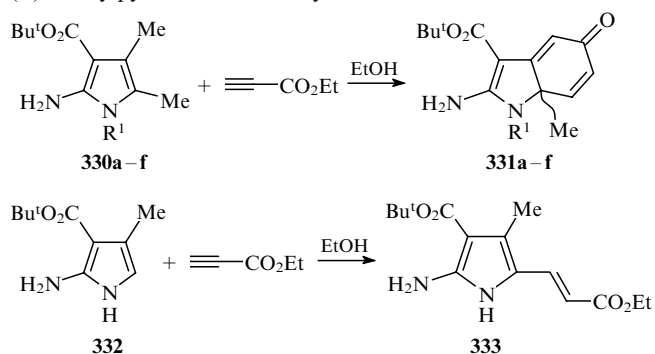


$\text{R}^1 = \text{COMe, CO}_2\text{Me, CO}_2\text{Et}; \text{R}^2 = \text{Me, (CH}_2)_2\text{CO}_2\text{H}.$

The yields of the vinylpyrroles **329** and the ratio of the *E* and *Z* isomers depend substantially on the structures of the starting

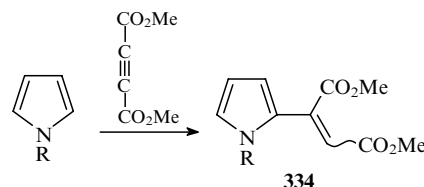
compounds **328**. At $\text{R}^1 = \text{CO}_2\text{Me}$ and $\text{R}^2 = \text{Me}$, the yield of the corresponding adduct **329** was 75% (the ratio *E*:*Z* = 7:1), whereas the adducts were obtained in yields of only 56% (*E*:*Z* = 2:1) and 12% (*E*:*Z* = 9:1) at $\text{R}^1 = \text{CO}_2\text{Me}$, $\text{R}^2 = (\text{CH}_2)_2\text{CO}_2\text{H}$ and $\text{R}^1 = \text{COMe}$, $\text{R}^2 = (\text{CH}_2)_2\text{CO}_2\text{H}$, respectively.¹⁴³

The reactions of substituted 2-amino-4,5-dimethylpyrroles **330a–f** with ethyl propiolate proceeded predominantly as the cycloaddition resulting in functionalised dihydroindoles **331a–f**. Under the analogous conditions, the reaction of pyrrole **332**, which contains no substituents at positions 1 and 2, gave rise to (*E*)-2-vinylpyrrole **333** in 68% yield.¹⁴⁴



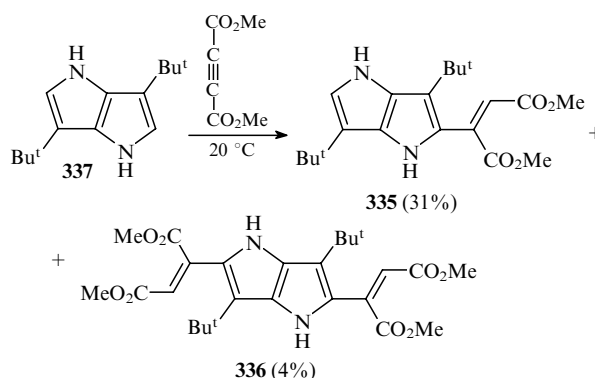
$\text{R}^1 = \text{Pr}^n$ (**a**), $(\text{CH}_2)_2\text{OMe}$ (**b**), $(\text{CH}_2)_2\text{Ph}$ (**c**), **Bn** (**d**),
 2-pyridylmethyl (**e**), 3-pyridylmethyl (**f**).

N-Substituted pyrroles add to dimethyl acetylenedicarboxylate to form mixtures of the *E* and *Z* isomers of 2-vinylpyrroles **334**. The reactions proceed upon stirring of the reagents at 20 °C or upon ultrasonic irradiation. In the latter case, the pyrroles are produced in substantially higher yields.¹⁴⁵

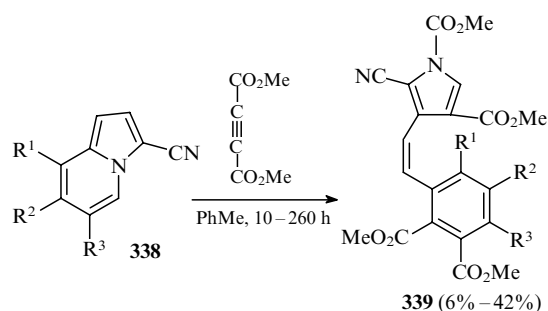


$\text{R} = \text{Me, (CH}_2)_2\text{CN, Ph}.$

A mixture of 2-vinyl- (**335**) and *E,Z*-2,5-divinylpyrrolo[3,2-*b*]pyrroles **336** was obtained in the reaction of pyrrolopyrrole **337** with an excess of dimethyl acetylenedicarboxylate at 20 °C.¹⁴⁶ A mixture of the *E* and *Z* isomers of the divinylpyrrole **336** (in 24% and 47% yields, respectively) can also be prepared by the addition of the monoadduct **335** to dimethyl acetylenedicarboxylate under the same conditions.¹⁴⁶

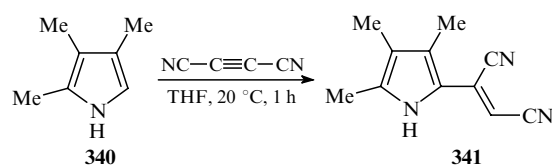


Recyclisation of indolizine-3-carbonitriles **338** under the action of dimethyl acetylenedicarboxylate selectively afforded the *Z* isomers of functionally substituted 3-styrylpyrroles **339**.¹⁴⁷

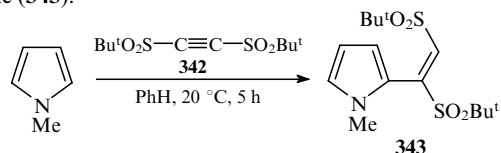


$R^1 = \text{H, Me; } R^2 = \text{H, Me, CN, Bn; } R^3 = \text{H, Me.}$

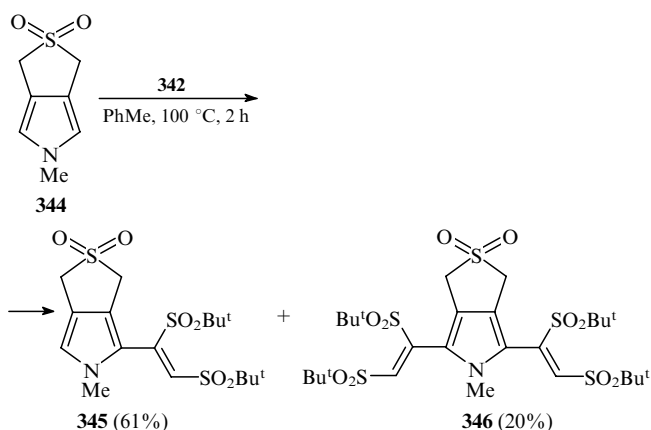
The reaction of 2,3,4-trimethylpyrrole (**340**) with dicyanoacetylene produced (*E*)-2-(1,2-dicyanovinyl)pyrrole **341** as the major product (in 63% yield), whereas the yield of the *Z* isomer was only 9%.¹⁴⁸



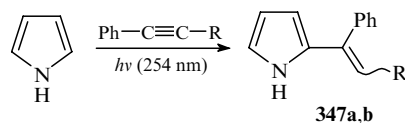
1-Methylpyrrole reacted with di(*tert*-butylsulfonyl)acetylene (**342**) to give (*E*)-2-[1,2-di(*tert*-butylsulfonyl)vinyl]-1-methylpyrrole (**343**).¹⁴⁹



Heating of pyrrolisosulfolene **344** with the acetylene **342** produced a mixture of *E* isomers of 2-vinyl- (**345**) and 2,5-divinylpyrroles (**346**).¹⁵⁰



The photochemical reactions of pyrrole with phenyl- and diphenylacetylenes afforded 2-(1-phenylvinyl)- (**347a**) and 2-(1,2-diphenylvinyl)pyrroles **347b** (a mixture of the *E* and *Z* isomers in approximately equal amounts) in yields of only 7% and 9%, respectively.¹⁵¹



$R = \text{H (a), Ph (b).}$

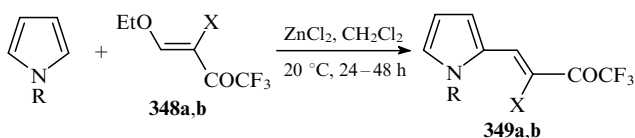
The low yields of the adducts were accounted¹⁵¹ for by photoinduced dimerisation of arylacetylenes and the instability of the adduct **347a** in air.

V. Substitution reactions at the double bond

1. Substitution of functional groups in electron-deficient alkenes

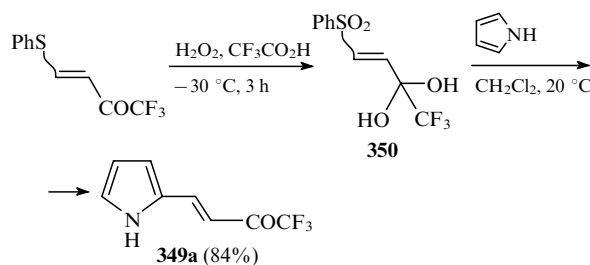
In recent years, the substitution of functional groups at the electrophilic double bond or the catalytic replacement of the hydrogen atom of the alkene fragment by halogenopyrroles (Heck and Stille reactions) have found wide use in the synthesis of *C*-vinylpyrroles.

The reactions of 1*H*- and 1-methylpyrroles with 4-ethoxy-1,1,1-trifluorobut-3-en-2-one (**348a**) and 3-(ethoxymethylidene)-1,1,1,5,5,5-hexafluoropentane-2,4-dione (**348b**), which are products of mono- and bistrifluoroacetylation of ethyl vinyl ether, respectively, led to the substitution of the ethoxy group and the formation of 2-(2-trifluoroacetyl)vinylpyrroles **349a,b**. The reactions proceeded under mild conditions in the presence of 25 mol.% ZnCl_2 . In the presence of other Lewis acids, the reactions are accompanied by substantial resinification. The reaction of the ketone **348a** proceeded stereospecifically to produce the *E* isomer.^{152–154}

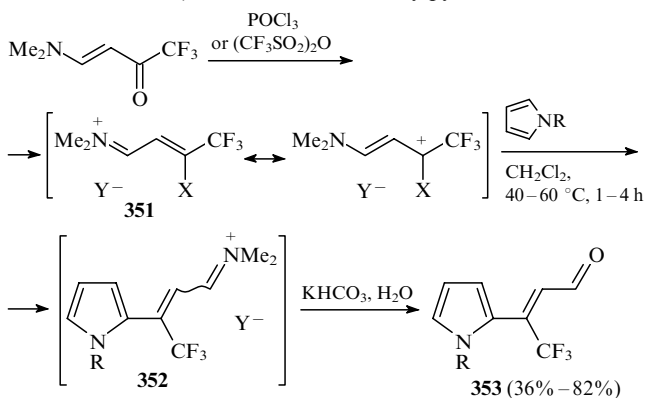


$R = \text{H, Me; } X = \text{H (a, 53%), COCF}_3 \text{ (b, 88%).}$

The pyrrole **349a** ($R = \text{H}$) was also synthesised from 1*H*-pyrrole and 1,1,1-trifluoro-4-(phenylsulfonyl)but-3-ene-2,2-diol (**350**), which was prepared by oxidation of the trifluoroacetylation product of vinyl sulfide. The reaction proceeded under mild conditions as addition–elimination.^{154, 155}

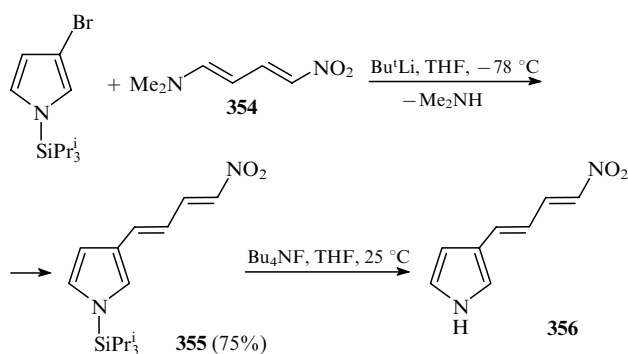


The reactions of iminium complex **351**, which was generated in the reaction of 4-dimethylamino-1,1,1-trifluorobut-3-en-2-one with POCl_3 or trifluoromethanesulfonic anhydride, with pyrroles proceeded stereospecifically to give finally (after hydrolysis of intermediates **352**) the *E* isomers of 2-vinylpyrroles **353**.^{154, 156}

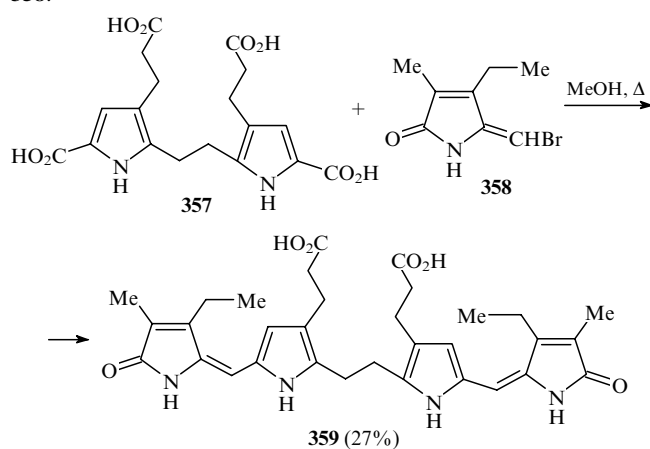


$R = \text{H, Me, Ph; } X = \text{OP(O)Cl}_2, \text{CF}_3\text{SO}_2\text{O; } Y = \text{Cl, POCl}_2, \text{CF}_3\text{SO}_2\text{O.}$

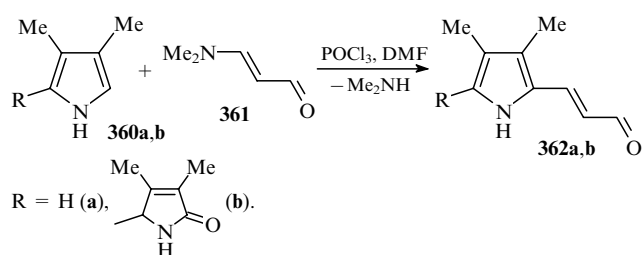
Condensation of 3-bromo-1-(triisopropylsilyl)pyrrole with nitrodieneamine **354** led to the replacement of the dimethylamino group to form 3-(4-nitrobuta-1,3-dienyl)-1-(triisopropylsilyl)pyrrole (**355**). Desilylation of the latter afforded pyrrole **356**.¹⁵⁷



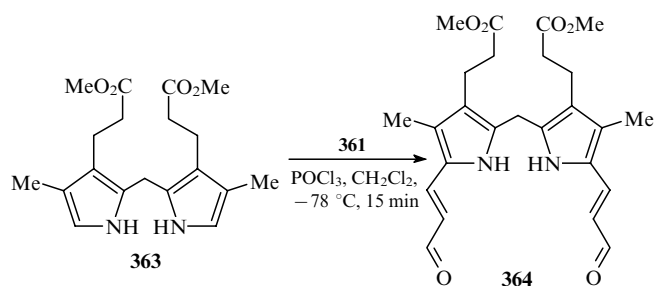
Refluxing of bispyrrole **357** with bromomethylidene-2,5-dihydropyrrol-2-one **358** in methanol produced homorubin **359**.⁹⁰ Initially, the compound **357** underwent α -decarboxylation and then the α -unsubstituted pyrrole reacted with the compound **358**.⁹⁰



Vilsmeier double formylation of 3,4-dimethylpyrrole **360a**^{158, 159} and dipyrinone **360b**¹⁵⁹ with 3-(dimethylamino)-acrolein (**361**) afforded 2-vinylpyrroles **362a,b**.

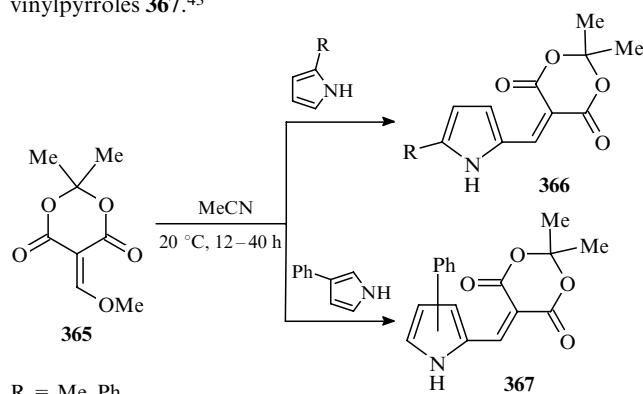


Bispyrrole **363** was formylated with the acrolein **361** at both α positions to give bis[(formylvinyl)pyrrol-2-yl]methane **364**.¹⁶⁰

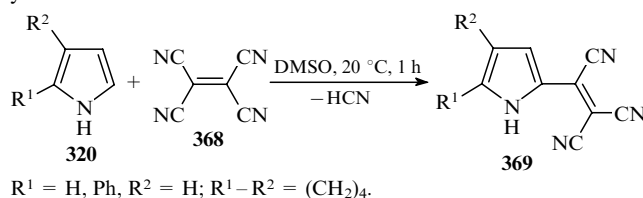


The reactions of 2-methyl- and 2-phenylpyrroles with the methoxymethylidene derivatives of Meldrum's acid **365** proceeded regioselectively under mild conditions to give 2-vinylpyrroles **366** in 60% and 70% yields, respectively.⁴³ Under analogous conditions, the reaction of 3-phenylpyrrole with the

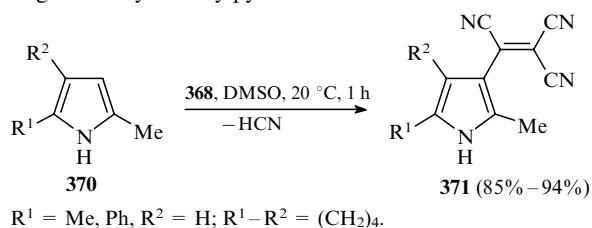
compound **365** produced a mixture ($\sim 1:1$) of 3- and 4-phenyl-2-vinylpyrroles **367**.⁴³



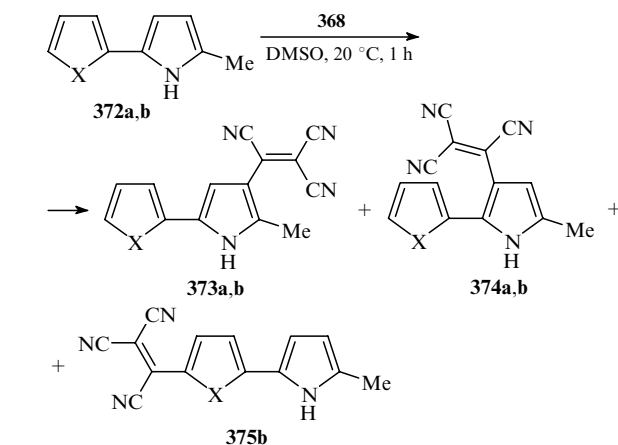
In the reactions of the pyrroles **320** with tetracyanoethylene (**368**), one of the nitrile groups in the latter compound was replaced to form 2-(tricyanovinyl)pyrroles **369** in quantitative yields.¹⁶¹



The pyrroles **370** containing substituents at both α positions reacted with tetracyanoethylene (**368**) under the same conditions to give 3-tricyanovinylpyrroles **371**.^{162, 163}

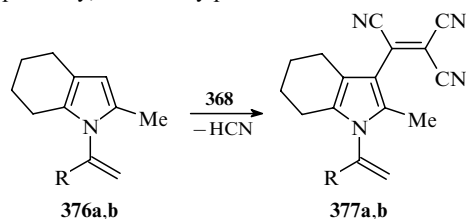


5-Methyl-2-(2-thienyl)pyrrole (**372a**) reacted with tetracyanoethylene (**368**) to yield 3-tricyanovinyl isomer **374a** along with 4-tricyanovinyl derivative **373a**.^{162, 163} Under these conditions, 2-(2-furyl)-5-methylpyrrole (**372b**) behaved differently, *viz.*, the major direction of the reaction with tetracyanoethylene involves the attack on the α position of the furan ring giving rise to product **375b**.



X	Yield (%)		
	373	374	375
S (a)	75	15	—
O (b)	18	9	67

The reactions of 1-vinyl- and 1-prop-2-enyl-substituted pyrroles **376a,b** with tetracyanoethylene (**368**) taken in equimolar amounts in DMSO afforded 3-tricyanovinyl-1-vinyl- (**377a**) and 1-(prop-2-enyl)-3-tricyanovinyl-substituted (**377b**) derivatives, respectively, as the only products.^{162, 163}

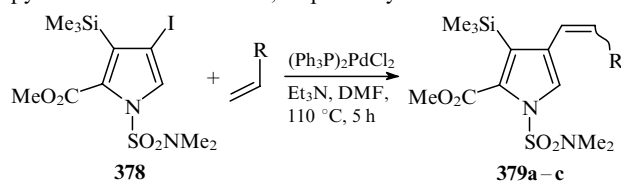


R = H (**a**, 92%), Me (**b**, 91%).

Hence, the *N*-alkenyl substituent in the pyrroles **376a,b** does not react with tetracyanoethylene according to the [2 + 2]-cycloaddition mechanism typical of other 1-vinyl-substituted heterocyclic compounds.¹⁶⁴

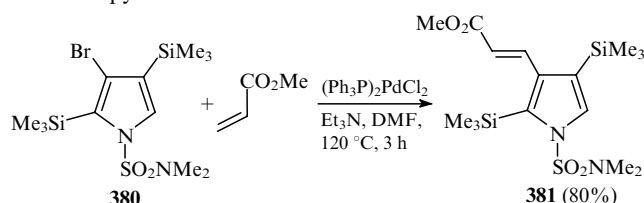
2. Catalytic vinylation of halogenopyrroles

The Heck reaction of 4-iodopyrrole **378** with acrylonitrile in the presence of bis(triphenylphosphine)palladium chloride afforded a mixture of (*E*)- and (*Z*)-4-vinylpyrroles **379a** in 45% and 17% yields, respectively. The corresponding reactions involving methyl acrylate or methyl vinyl ketone proceeded stereoselectively to give pyrroles **Z-379b** or **E-379c**, respectively.¹⁶⁵

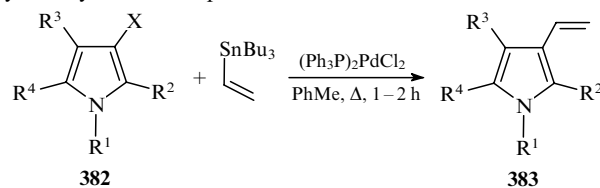


R = CN (**a**), CO₂Me (**b**), COMe (**c**).

Under analogous conditions, the reaction of 3-bromopyrrole **380** with methyl acrylate also proceeded selectively to form the *E* isomer of pyrrole **381**.¹⁶⁵



The reactions of 4-halogenopyrroles **382** with vinyltributyltin (Stille reaction) were examined. 4-Iodopyrroles produced 4-vinylpyrroles **383** in 80%–92% yields. The reactions proceeded upon refluxing of the reagents in toluene in the presence of bis(triphenylphosphine)palladium chloride. Under analogous conditions, 4-bromopyrrole gave the corresponding 4-vinylpyrroles in low yields (10%–15%), whereas the reaction of 4-chloropyrrole with vinyltributyltin did not proceed at all.¹⁶⁶



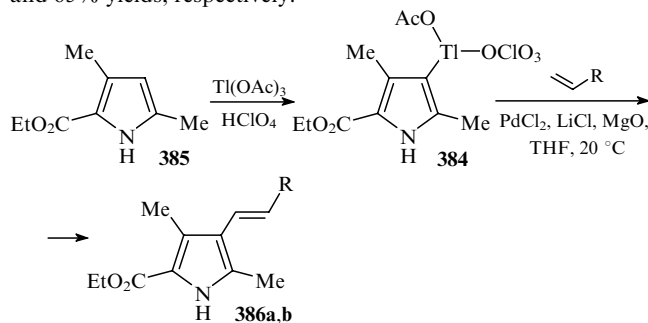
R¹ = H, Me, C(=O)Ph, Ts; R² = H, Me; R³ = H, Me;

R⁴ = CHO, CO₂Et; X = Cl, Br, I.

Alkenyl derivatives of heteroaromatic compounds can also be prepared by Tl(III)–Pd(II) transmetalation. This reaction does not require thorough drying of the reagents and solvents and the use of an inert atmosphere and proceeds under mild conditions

(often regio- and stereospecifically), Pd(II) complexes being used in catalytic amounts.

Thus hydrogen was readily replaced in methyl acrylate and styrene under the action of ethyl 4-[(acetoxypyrrolyl)thallio]-3,5-dimethylpyrrole-2-carboxylate (**384**), which was synthesised from ethyl 3,5-dimethylpyrrole-2-carboxylate (**385**) and Tl(OAc)₃.¹⁶⁷ Olefination was carried out in the presence of PdCl₂, MgO or LiCl with the molar ratio pyrrole:alkene: (PdCl₂–LiCl) = 1 : (5–10) : 0.1. It is necessary to add a base (generally, magnesium oxide or potassium carbonate) with the aim of preventing side reactions of pyrroles, which proceed in the presence of strong acids generated in the course of alkenylation. The reactions proceeded selectively to give pyrroles **386a,b** in 43% and 65% yields, respectively.¹⁶⁷



R = CO₂Me (**a**), Ph (**b**).

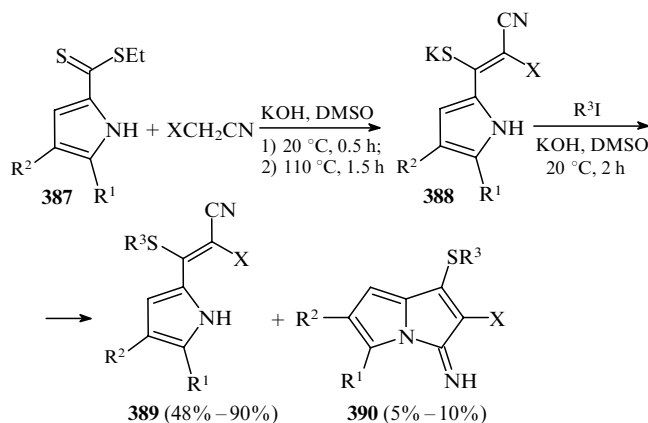
VI. Other procedures for the introduction of the vinyl group into the pyrrole ring

1. Synthesis from pyrrolecarbodithioates

Once a convenient and versatile procedure has been developed for the synthesis of pyrrole-2- and -3-carbodithioates by the direct reactions of pyrroles with carbon disulfide in the KOH–DMSO system,^{168–178} these compounds found wide use in the synthesis of functionalised *C*-vinylpyrroles.^{178–181}

The reactions of pyrrole-2-carbodithioates **387** with CH-acids (malononitrile, cyanoacetamide and ethyl cyanoacetate) in the KOH–DMSO system followed by alkylation of intermediate thiolates **388** with alkyl halides produced 2-vinylpyrroles **389**.^{179–181} All three steps of the reactions were carried out in one pot.

The reactions of the pyrrole-2-carbodithioates **387** with malononitrile and cyanoacetamide afforded 2-vinylpyrroles **389** along with small amounts of products of their intramolecular cyclisation, viz., 3-imino-3*H*-pyrrolizines **390**. The reactions of the pyrrole-2-carbodithioates **387** with ethyl cyanoacetate gave rise to pyrrolizin-3-ones **391** as the major condensation products.



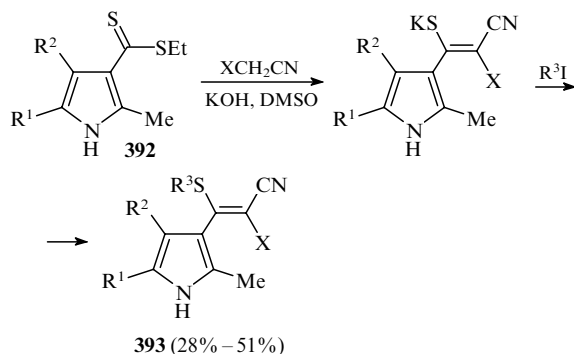
X = CN, CONH₂.



$\text{R}^1 = \text{Me, Pr}^n, \text{Bu}^n, \text{Ph}$; $\text{R}^2 = \text{H, Me, Et, Pr}^n$; $\text{R}^1 - \text{R}^2 = (\text{CH}_2)_4$;

$\text{R}^3 = \text{Me, Et, Bu}^n, \text{Al}$; $\text{X} = \text{CN, CONH}_2, \text{CO}_2\text{Et}$.

Under analogous conditions, pyrrole-3-carbodithioates **392** selectively reacted with nitriles containing the activated methylene group to form 3-vinylpyrroles **393**.¹⁷⁸

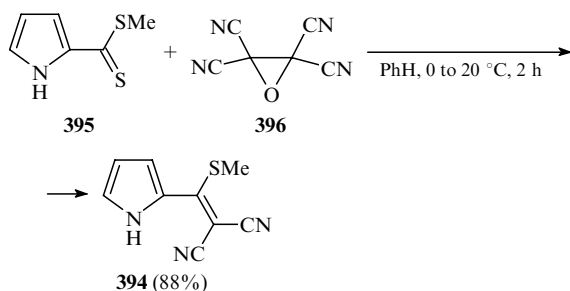


$\text{R}^1 = \text{Me, Ph}$; $\text{R}^2 = \text{H, Me}$; $\text{R}^1 - \text{R}^2 = (\text{CH}_2)_4$;

$\text{R}^3 = \text{Me, Et}$; $\text{X} = \text{CN, CONH}_2, \text{CO}_2\text{Et}$.

3-Vinylpyrroles **393** were obtained in low yields due to instability of the pyrrole-3-carbodithioates **392**, which partially (by 10%–20%) decomposed to 3-unsubstituted pyrroles under the reaction conditions.

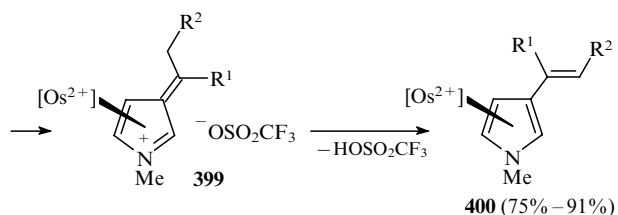
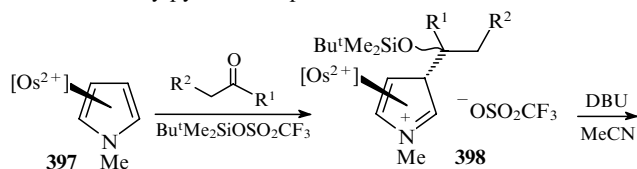
(2,2-Dicyano-1-methylthiovinyl)pyrrole (**394**) was synthesised from methyl pyrrole-2-carbodithioate **395** and epoxide **396**.¹⁸²



2. Vinylation of osmium complexes of pyrroles

In the pentaammineosmium complex of 1-methylpyrrole **397**, which was prepared from 1-methylpyrrole and $\text{Os}(\text{NH}_3)_5(\text{OTf})_3$ in quantitative yield, the electrophilic activity of the C(3) atom is much higher than that of the C(3) atom in free pyrrole. This complex can be readily transformed into the 3-vinylpyrrole complexes according to several procedures.^{183–186}

One procedure involves the reaction of complex **397** with a twofold excess of ketone in the presence of 1 equiv. of *tert*-butyldimethylsilyl triflate to form silylated aldol adducts **398**. Diazabicycloundecene-catalysed elimination of silanol $\text{HOSiMe}_2\text{Bu}^t$ followed by deprotonation of azafulvenium intermediates **399** afforded 3-vinylpyrrole complexes **400**.^{183, 185}

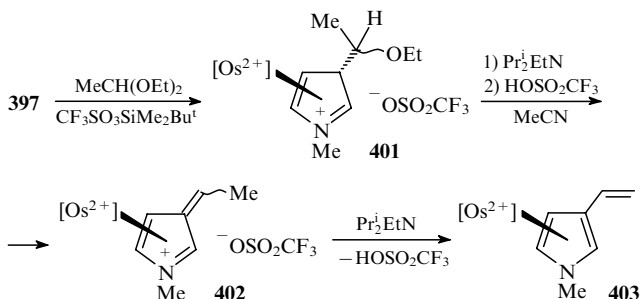


Hereinafter, $[\text{Os}^{2+}] = [\text{Os}^{\text{II}}(\text{NH}_3)_5]^{2+}$; $\text{R}^1 = \text{Me, Et, Pr}^i, \text{Ph}$;

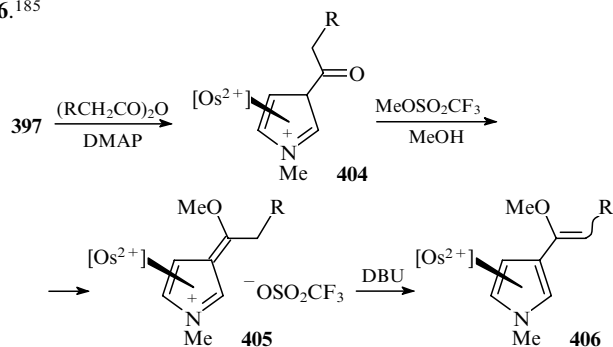
$\text{R}^2 = \text{H, Me}$; $\text{R}^1 - \text{R}^2 = (\text{CH}_2)_4$.

Another procedure involves the reaction of the complex **397** with acetaldehyde diethyl acetal in the presence of *tert*-butyldimethylsilyl triflate. In this case, 3*H*-pyrrole adduct **401** is generated. After deprotonation and elimination of ethanol catalysed by trifluoromethanesulfonic acid, compound **401** gives azafulvenium complex **402** in 93% yield (a mixture of stereoisomers in a ratio of 3:2).

Deprotonation of the complex **402** afforded unstable complex **403**, which was isolated as a product of the reaction with *N*-phenylmaleimide.¹⁸⁵

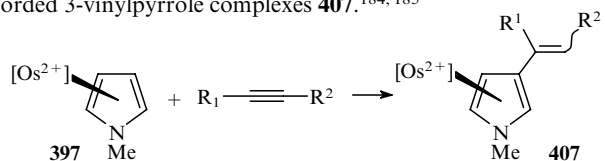


Yet another approach to 3-vinylpyrrole complexes of osmium is based on acylation of the pyrrole **397** with acid anhydrides in the presence of 4-dimethylaminopyridine (DMAP). Due to the nucleophilic properties, the oxygen atom of the carbonyl group in complex **404** can be methylated with methyl trifluoromethanesulfonate to give 2-azafulvenium complex **405**. The addition of diazabicycloundecene to the complex **405** led to deprotonation and the formation of methoxy-substituted 3-vinylpyrrole complex **406**.¹⁸⁵



$\text{R} = \text{H, Me}$.

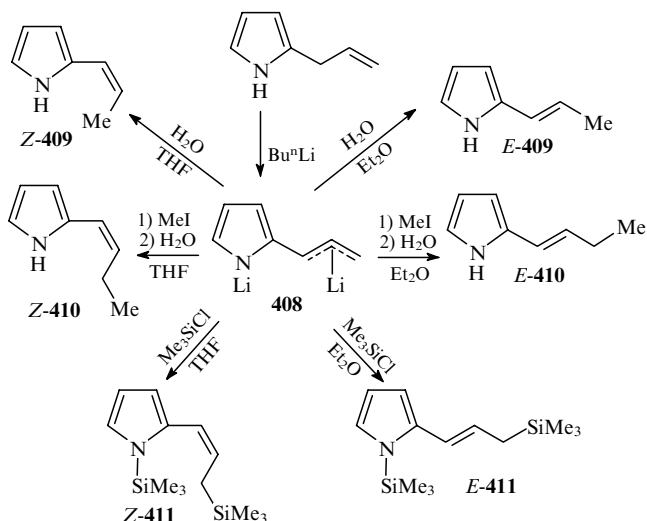
The addition of the complex **397** to activated acetylenes also afforded 3-vinylpyrrole complexes **407**.^{184, 185}



$\text{R}^1 = \text{H, CO}_2\text{Me, Ph}$; $\text{R}^2 = \text{COMe, CO}_2\text{Me}$.

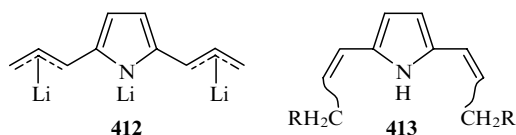
3. Synthesis from allyl derivatives

2-Allylpyrrole was transformed into *N,C*-dilithium derivative **408** in high yield under the action of 2 equiv. of Bu^nLi in the hexane–diethyl ether system. The compound **408** selectively reacts with various electrophilic agents (H_2O , MeI, Me_3SiCl) to form 2-(alk-1-enyl)pyrroles **409–411**.¹⁸⁷



The reactions in Et_2O at 0°C gave rise to the *E* isomers, whereas the reactions in THF afforded the *Z* isomers of compounds **409–411**.

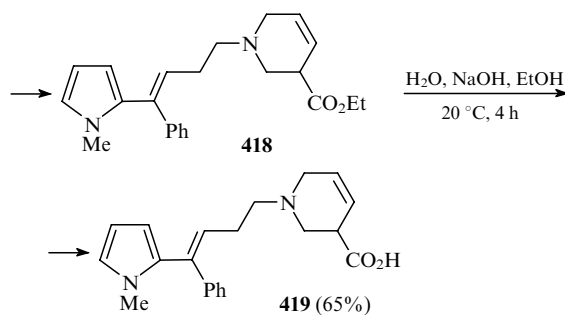
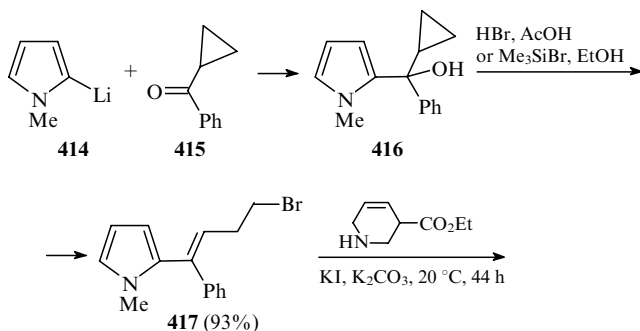
The reactions of the *N,C,C*-trilithium derivative of 2,5-diallylpyrrole **412** with electrophiles (H_2O , D_2O , MeI, Me_3SiCl and Me_3SnCl) in THF proceed selectively to produce the *Z* isomers, whereas these reactions in the hexane–diethyl ether system give rise to mixtures of the *E* and *Z* isomers of 2,5-di(alk-1-enyl)pyrroles **413**.¹⁸⁸



$\text{R} = \text{H}, \text{Me}, \text{SiMe}_3, \text{SnMe}_3$.

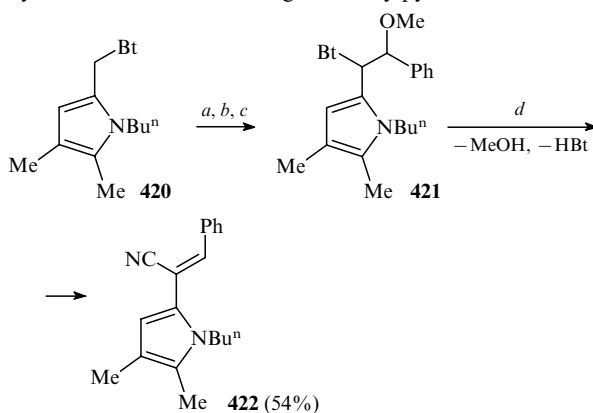
4. Condensation with carbonyl compounds and their synthetic equivalents

2-Lithio-1-methylpyrrole (**414**) reacted with cyclopropyl phenyl ketone (**415**) to form alcohol **416** whose three-carbon ring was opened under the action of either HBr in AcOH or Me_3SiBr in EtOH to give (*E*)-4-bromo-1-(1-methylpyrrol-2-yl)-1-phenylbut-1-ene (**417**).¹⁸⁹



Alkylation of ethyl 1,2,3,6-tetrahydropyridine-3-carboxylate with the bromine-containing derivative **417** followed by hydrolysis of ester **418** produced acid **419**.¹⁸⁹

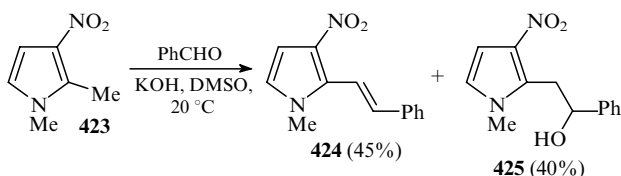
Successive treatment of pyrrole **420** with Bu^nLi , benzaldehyde and methyl iodide in hexamethylphosphoramide (HMPA) afforded pyrrole **421**. The nucleophilic replacement of the benzotriazole group in the latter compound by the nitrile group followed by elimination of methanol gave 2-vinylpyrrole **422**.¹⁹⁰



$\text{Bt} =$; (a) Bu^nLi , THF, -78°C ; (b) PhCHO, THF, -78°C ;

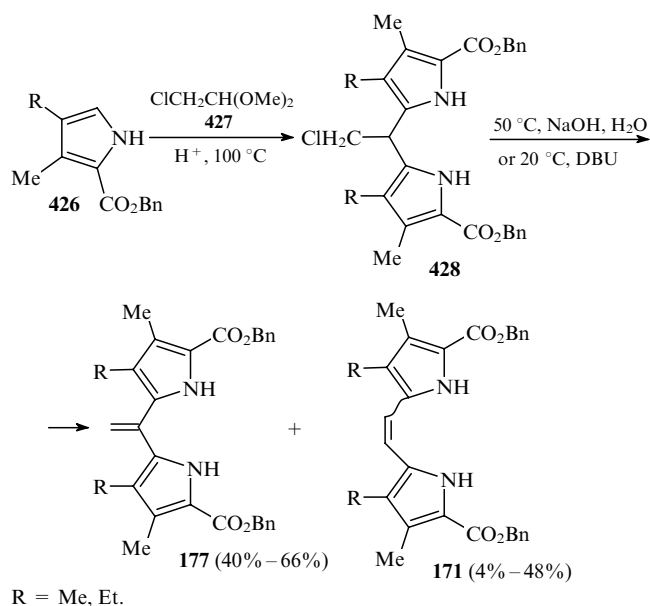
(c) MeI, HMPA, -78 to 20°C ; (d) NaCN, DMF, Δ , 12 h.

Base-catalysed condensation of 1,2-dimethyl-3-nitropyrrole (**423**) with benzaldehyde in the KOH–DMSO system afforded a mixture of 2-vinylpyrrole **424** and alcohol **425**.¹⁹¹

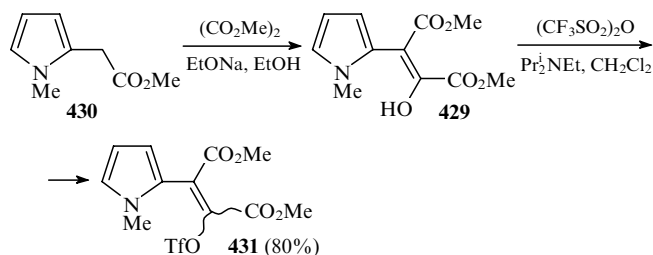


Condensation of pyrrole **426** with chloroacetaldehyde dimethyl acetal **427** proceeded upon heating in the presence of *p*-toluenesulfonic acid to form (chloromethyl)di(pyrrol-5-yl)methanes **428** in 75%–91% yields. The use of montmorillonite K-10 as an acid catalyst makes it possible to perform this process at 20°C with retention of high yields of dipyrrolylmethanes **428**.⁹¹

Elimination of HCl from (chloromethyl)dipyrrolylmethanes **428** afforded 1,2-di(pyrrol-5-yl)ethenes **171** (a mixture of the *E* and *Z* isomers) along with 1,1-di(pyrrol-5-yl)ethenes **177**. This pathway allows one to prepare the 1,1-di(pyrrol-5-yl)ethenes **177** in higher yields compared to those obtained by acylation of the 3,4-dimethylpyrrolecarboxylic esters **176** (see Section II.4).^{91, 94}

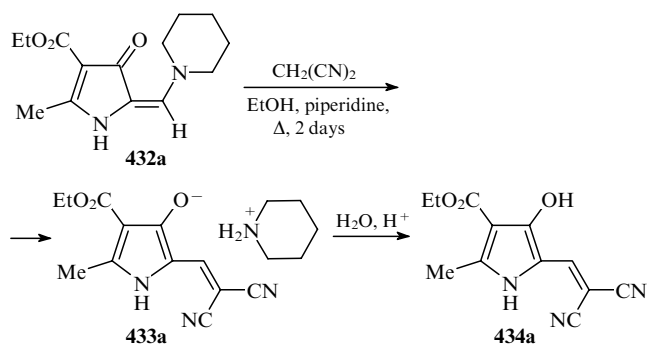


Treatment of substituted 2-vinylpyrrole **429**, which was synthesised from 2-(methoxycarbonylmethyl)-1-methylpyrrole **430** and dimethyl oxalate, with trifluoromethanesulfonic anhydride afforded a mixture of *E*- and *Z*-triflates **431** in a ratio of 5:1.¹⁹²

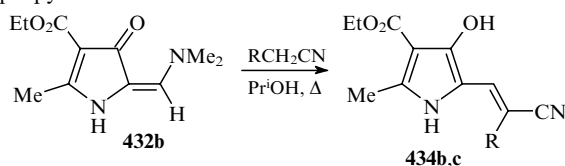


5. Synthesis from enaminoketones of the pyrrole series

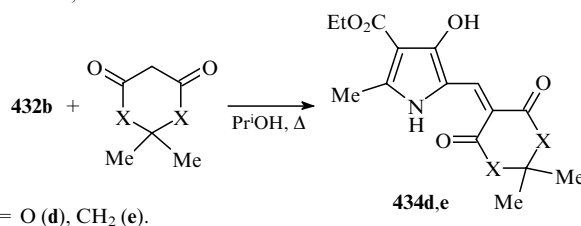
Enaminoketone **432a** reacted with malononitrile to form salt **433a** whose acidification gave rise to 5-(2,2-dicyanovinyl)-3-ethoxycarbonyl-4-hydroxy-2-methylpyrrole **434a**.^{34, 37}



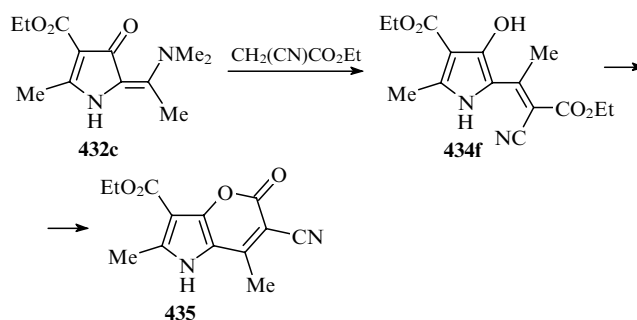
Vinylpyrroles **434b,c** were synthesised from enaminoketone **432b** and derivatives of cyanoacetic acid upon refluxing in isopropyl alcohol.³⁴



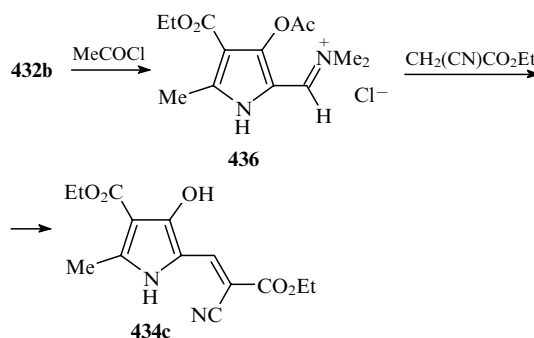
Under the same conditions, the enaminoketone **432b** reacted with Meldrum's acid and dimedone to give vinylpyrrole derivatives **434d,e**.³⁴



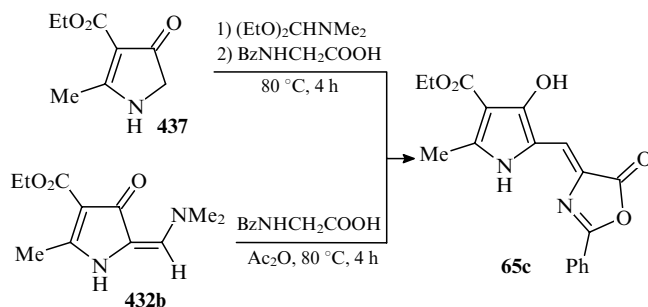
Condensation of the enaminoketone **432c** with ethyl cyanoacetate was accompanied by further cyclisation of pyrrole **434f** to 6-cyano-3-ethoxycarbonyl-2,7-dimethyl-5-oxopyrano[3,2-*b*]pyrrole (**435**).³⁴



Vinylpyrrole **434c** can be prepared from immonium salt **436**, which was generated upon treatment of the enaminoketone **432b** with acetyl chloride.³⁶



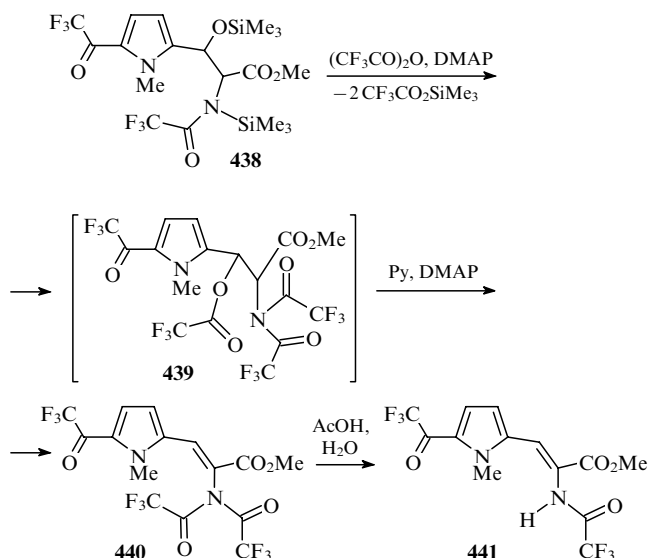
The pyrrole **65c** containing the azlactone substituent at the vinyl group was synthesised according to two procedures, viz., by aminomethylation of ketone **437** with dimethylformamide diethyl acetal followed by the reaction of hippuric acid and by the reaction of the enaminoketone **432b** with hippuric acid in acetic anhydride.⁴⁸



6. Other reactions

Elimination of trimethylsilyl trifluoroacetate $[(\text{CF}_3\text{CO})_2\text{O}$, DMAP, dichloroethane] from compound **438** afforded intermediate **439**, which produced functionalised 2-vinylpyrrole **440** in the

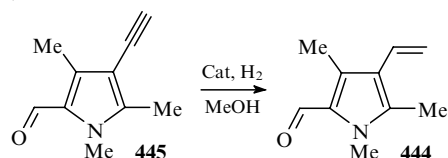
presence of pyridine and DMAP.¹⁹³ The compound **440** is unstable due to its high sensitivity to hydrolysis and is transformed into vinylpyrrole **441** after treatment with dilute acetic acid.¹⁹³



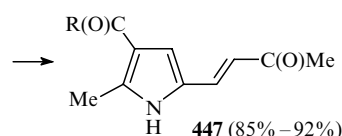
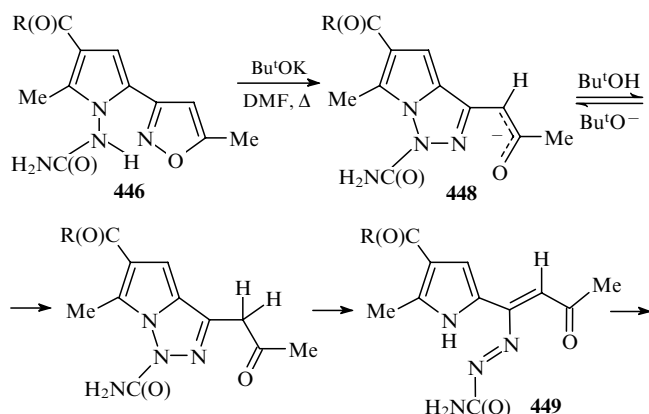
Refluxing of substituted pyrrole **442** in DMF in the presence of potassium carbonate led to elimination of benzotriazole to give 2-(pent-1-enyl)pyrrole **443** in 57% yield (*E*:*Z* = 3:1).¹⁹⁰



4-Vinylpyrrole **444** was prepared in 65% yield by selective hydrogenation of 4-ethynylpyrrole **445** in the presence of the Lindlar catalyst partially deactivated with 3,6-dithiaoctane-1,8-diol.⁹⁸

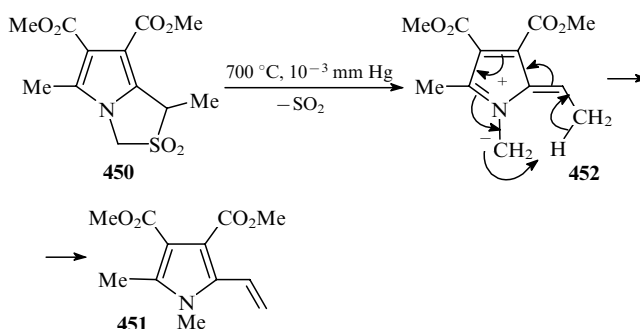


Substituted *N*-ureidopyrroles **446** were transformed into 5-vinylpyrroles **447** with the *E* configuration upon refluxing in DMF in the presence of Bu^tOK .¹⁹⁴ Their formation was attributed to the intramolecular nucleophilic attack of the deprotonated ureido group on the isoxazole nitrogen atom followed by isomerisation of intermediate **448** to azocarbonyl compound **449**, which gave the pyrroles **447** under the reaction conditions.



R = Me, OEt.

Vacuum pyrolysis of dihydrothienopyrrole *S,S*-dioxide **450** led to elimination of SO_2 to give 2-vinylpyrrole **451** whose formation proceeded, apparently, through the [1,8-*H*]-shift in the 1,7-bipolar system **452**.¹⁹⁵



VII. Conclusion

The data surveyed in the present review demonstrate considerable advances in the synthesis of functionalised *C*-vinylpyrroles achieved in the last decade. Known procedures for the synthesis, which are based on reactions of acylpyrroles with CH-acids and the Wittig and Wittig–Horner reagents, are being improved and new preparative reactions, which could enable one to prepare *C*-vinylpyrroles from more readily accessible starting compounds, are being searched for. In particular, the reactions of alkenyl ketone oximes with acetylene in the KOH–DMSO system and base-catalysed condensation of pyrrolocarbodithioates, which have recently become available, with CH-acids are being extensively developed. These reactions provide simple approaches to groups of *C*-vinylpyrroles, which have previously been not easily accessible or unknown, starting from available compounds.

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Modern applications of NMR tomography in physical chemistry. The characteristic features of the technique and its applications to studies of liquid-containing objects

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Abstract. This review concerns the state-of-the-art in the field of NMR tomography. The scope and limitations of the method, its capabilities, and some of the most widely used applications in physical chemistry are discussed. It is demonstrated that the technique is able to provide a vast variety of information about the state of objects under study and on the physicochemical processes occurring in them, which can be gained owing to the specific features of the technique. The review predominantly covers the studies of the structure and properties of various liquid-containing objects. The bibliography includes 232 references.

I. Introduction

Nuclear magnetic resonance tomography, or magnetic resonance imaging (MRI), has long been used in medical and biological research. Currently, this technique is being utilised for not only diagnosis of diseases but also operative control in clinical therapy and in studies of functional activity of the human brain. Recently, magnetic resonance imaging has also been used in studies of various objects of inanimate matter. Modern methods of multi-nuclear magnetic resonance allow one to image the internal structure of a vast variety of samples and to investigate the properties of and processes occurring in materials with a spatial resolution of the order of hundreds and even tens of micrometres.

Today, an extensive literature on the physicochemical applications of MRI has evolved, concerning a vast variety of applications. Therefore, the authors of this review tried to give the readers an idea of the most widespread avenues of applications of this technique and to present some appropriate illustrative examples. The choice of both applications and examples is to a great extent subjective. In most cases, it was dictated by authors' opinion about the importance of a particular application and by the field of research they are involved in.

There is also a number of objective factors that preclude unambiguous classification of particular experiments. For

instance, any NMR experiment can in principle be carried out with spatial resolution, which leads to an almost infinite number of possible imaging experiments. This review leaves the communications concerned with obtaining spectral rather than spatial information as well as the NMR studies performed without spatial resolution out of consideration. The authors also leave aside specific biological and medical applications of this technique in spite of enormous literature in this field. It should be noted that there are no fundamental differences between particular experimental techniques employed in medical experiments and those used in physicochemical studies and that many physicochemical research strategies were initially developed for medical applications of MRI. A vast variety of processes occurring in living organisms, *e.g.*, pulsatory flow of liquids, gas diffusion in porous media, *etc.*, are also of considerable interest for chemists. At the same time, many experimental techniques employed in medical research have initially been tested and evaluated using model objects of inanimate matter. Therefore, it is impossible to leave biomedical applications of MRI out of consideration altogether.

Some features basically differentiate MRI from other modern methods of imaging the internal structure of various objects. Therefore, this review pays considerable attention to specific features of the technique, which is of great importance for assessing possible fields of its applications. The review mainly covers the publications concerned with the imaging and studies of the properties of liquid-containing objects.

II. The nuclear magnetic resonance imaging technique

1. General remarks

Magnetic resonance imaging^{1–4} undoubtedly owes its origin to the emergence and development (in the mid-1940s) of radio-spectroscopy as a field of experimental science and first of all to successful pioneering ESR experiments by Zavoiskii⁵ and studies on the observation of NMR signals in condensed matter carried out by the research groups headed by Bloch⁶ and Purcell.⁷ Studies of the spin echo carried out by Hahn⁸ in the 1950s are also of great importance for the development of MRI, since recording the spin echo signals serves as the basis for many particular MRI techniques. In 1966, Ernst and Anderson⁹ proposed a promising method of extracting spectral information using the Fourier transform. This was a breakthrough in the development of modern pulsed NMR^{10–12} which is the basis of magnetic resonance imaging. Since the early 1970s, commercial NMR spectrometers have been equipped with computers for acquisition, processing and presentation of experimental data. Modern experi-

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ments are so sophisticated and the amount of information is so large that computers are an integral part of NMR equipment. In 1971, Jeener[†] proposed the use of two-dimensional Fourier transform in NMR and thus laid the groundwork for multidimensional NMR spectroscopy.^{13–16} In essence, magnetic resonance images represent a kind of multidimensional NMR spectra.¹⁷ Moreover, both NMR spectroscopy and MRI can be considered as particular cases of multidimensional NMR experiments in a generalised space of coordinates, frequencies and time. In 1973, Lauterbur¹⁸ reported the first tomographic image obtained using the ¹H NMR signals. Commercial NMR tomographs for medical research have been produced since the early 1980s. The mid-1980s were marked by the development of hardware, design of novel experimental techniques, which allowed considerable enhancement of spatial resolution and the emergence of NMR microtomography or magnetic resonance microimaging (MRM).

It should be noted that it is hard to discriminate between MRI and MRM.[‡] Similarly to the commonly accepted term ‘microscopy’, a formal line between them can be drawn through a volume element of the order of (0.1 mm)³, which represents the resolution limit for the naked eye.¹⁹ Nevertheless, even such a conventional distinction is sometimes ambiguous, since the spatial resolution is often anisotropic. For instance, many experiments are performed with an in-plane resolution of tens of micrometres and a slice thickness of several millimetres.

2. Obtaining an image

The basis for nuclear magnetic resonance is the interaction between the nuclear spins and the static and alternating magnetic fields. In practice, a spin system usually represents an ensemble of nuclear spins which is described by the total magnetisation vector **M**. At thermal equilibrium in a static magnetic field **B**₀, the nuclear spins tend to line up with the field so that the vector **M** is directed along **B**₀. Conventionally, the magnetic field is aligned along the *z* axis of the laboratory frame of reference, **B**₀ = **B**_{0z}. A 90° flip of the longitudinal magnetisation vector **M** = **M**_z about the *x* axis creates the transverse magnetisation **M**_y ⊥ **B**₀. In pulsed NMR, the magnetisation vector is flipped by applying the radiofrequency (RF) pulses for which the magnetic field **B**_{1x} is perpendicular to the field **B**₀ while the flip angle, α, depends on the amplitude of the field **B**_{1x} and the duration of the RF pulse. In particular, the pulse that flips the magnetisation vector 90° is called the 90°-pulse. After the flip, the transverse magnetisation vector experiences free precession about the **B**_{0z} direction and creates the observed signal at the resonance frequency ω equal to the spin precession frequency in the external field **B**₀.

Precession of the transverse magnetisation vector is accompanied by its irreversible decay with the characteristic time *T*₂ as a result of transverse, or spin-spin, relaxation. Often, the actual decay time, *T*₂^{*}, of the observed signal is shorter than *T*₂ (*T*₂^{*} < *T*₂) owing to different spin precession frequencies that can be due to the differences in the local magnetic fields. For a system of immobile spins such a dephasing is reversible and the spin system can be rephased by reversal of the applied field gradient or by inversion of the phase of the spin precession by applying a 180°-pulse. Rephasing of the magnetisation leads to creation of the spin echo signal. In the case of NMR, the width of a spectral line is determined by the time *T*₂ (*T*₂^{*}). Return of the spin system to thermal equilibrium and recovery of the longitudinal magnetisation vector **M**_z ∥ **B**₀ is associated with the effect of the longitudinal, or spin-lattice, relaxation occurring with the

characteristic time *T*₁. Knowledge of the relaxation times *T*₁, *T*₂, *T*₂^{*} and the relaxation time in the rotating frame of reference, *T*_{1ρ}, allows one to extract valuable information on the structure of and processes in the objects under study. Generally, the relaxation times depend on the magnitude of the applied magnetic field and the relaxation time measurements have been a routine procedure in the NMR experiments.^{10–12}

The basics of MRI are very simple. The position of a single line in the NMR spectrum is determined by the resonance frequency, ω, which is to a first approximation proportional to the applied external magnetic field **B**₀:

$$\omega = \gamma \mathbf{B}_0, \quad (1)$$

where γ is the gyromagnetic ratio of the nucleus under study with a nonzero spin. The NMR spectrum of water in two tubes placed in a uniform magnetic field (see Fig. 1) will exhibit a single, relatively narrow line (see Fig. 1*a*) regardless of the amount of water in the tubes and their arrangement. However, if the magnetic field is nonuniform (*i.e.*, it is a function of the spatial coordinates), the resonance frequency also becomes a function of the spatial coordinates of the nuclear spin. Most of experiments are carried out using constant magnetic field gradient; in this case the magnitude of the magnetic field is a linear function of coordinate:

$$\mathbf{B}_z = \mathbf{B}_{0z} + \left(\frac{d\mathbf{B}_z}{dx} \right) x = \mathbf{B}_{0z} + G_x x, \quad (2)$$

(here, the magnetic field gradient, *G*_x, is applied along the *x* axis). It should be emphasised that applying the *G*_x gradient does not change the orientation of the total magnetic field at any point of the sample along the *z* axis, while the magnetic field amplitude becomes a linear function of the coordinate *x*. Usually, the second term in expression (2) is smaller than the first one. The gradients *G*_y and *G*_z are defined analogously.

Thus, if two tubes shown in Fig. 1 are placed in a magnetic field given by expression (2), different locations of the tubes on the *x* axis denote that they experience different magnetic fields and, hence, give the NMR signals at different frequencies (Fig. 1*b*). Moreover, inhomogeneity of the magnetic field within each tube leads to different resonance frequencies of microscopic volumes of

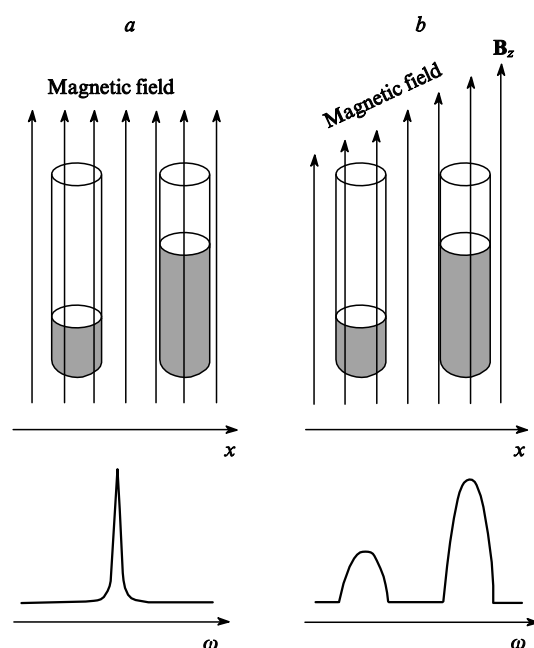


Figure 1. A schematic representation of the NMR spectrum of water in two tubes placed in the magnetic field **B**_z. Homogeneous magnetic field (*a*), magnetic field strength is a linear function of coordinate *x* (*b*).

[†] See J Jeener, in *Ampere International Summer School, Basko Polje, Yugoslavia, 1971*

[‡] The term ‘MRI’ is mostly used in medical literature; however, many non-medical applications of the method cannot also be called ‘microimaging’. Since in fact we deal with the same experimental method, in this review we prefer to use a more general term, ‘MRI’, while the term ‘MRM’ is used in those cases where high spatial resolution should be emphasised.

water at different coordinates x . It is easily seen that applying the G_x gradient allows one to obtain an integrated projection of the sample under study on the direction of the gradient vector.

The approach illustrated in Fig. 1 can be used in NMR spectroscopy for simultaneous analysis of several samples to increase the throughput of experimental technique, which is of particular importance in, *e.g.*, combinatorial chemistry.²⁰

Even such a simple one-dimensional (1D) experiment allows the obtaining of useful information in studies of samples of appropriately chosen symmetry. For instance, by applying the field gradient along the axis of a cylindrical sample one can obtain the 1D profiles of the liquid content. Experiments with sequential recording of the 1D profiles in studies of the adsorption of water on a cylindrical bead pack of the adsorbent particles are illustrated in Fig. 2. The advantages of this technique are its simplicity and the possibility of fast recording the 1D profiles (data acquisition times are of the order of hundreds of microseconds), since in this case the signal is recorded after a single application of the pulse sequence. In the MRI studies the pulse sequence includes the RF pulses and pulsed magnetic field gradients G_i , which are applied between the RF pulses or simultaneously with them.

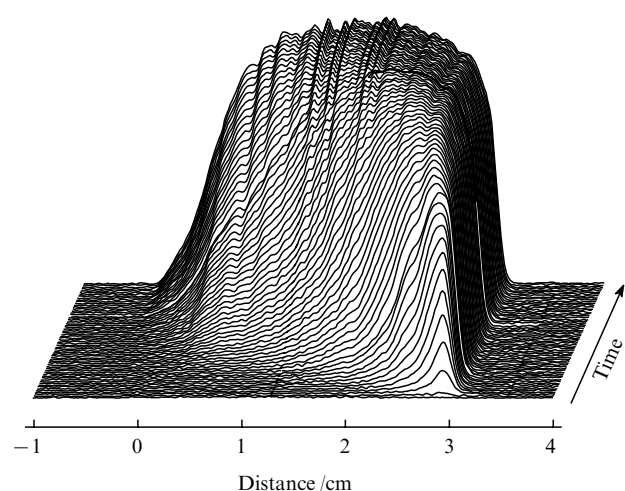


Figure 2. One-dimensional water distribution profiles in the axial direction of the cylindrical bead pack (internal cylinder diameter was 21 mm) comprised of small adsorbent granules (2–3 mm) recorded during the pumping of moist air through initially dry adsorbent. Recording each profile took 260 s. A total of 64 profiles were collected within 4 h 40 min. Air flow direction from right to left.

Practical implementation of such a 1D experiment is based on recording the temporal evolution of the transverse magnetisation of the sample (in the form of the free induction decay or the spin, stimulated or gradient echo) in the presence of a field gradient. In this case, the spin precession frequencies are different during the acquisition time; therefore, this technique is called the frequency encoding of spatial information. The angle of rotation, or the phase, of the magnetisation vector precessing in the xy plane continuously changes during the signal acquisition time $0 \leq t \leq T_{\text{reg}}$

$$\varphi = \omega t = \gamma \mathbf{B}_z t = \gamma \mathbf{B}_{0z} t + \gamma \mathbf{G}_x x t. \quad (3)$$

The MRI experiments can be conveniently described using the concept of the k -space. Let us define the components of the wave vector $\mathbf{k}$ as follows:

$$k_x = \frac{\gamma G_x t}{2\pi}; \quad (4)$$

The components k_y and k_z are defined analogously. During the recording of a signal in the presence of the gradient G_x , the k_x

value is continuously changed, so the detection process is equivalent to a discrete sampling of the NMR signal intensity at a discrete set of equidistant time or k_x values. Thus, in contrast to some other imaging techniques,²¹ the MRI experiments involve scanning the space of the wave vector $\mathbf{k}$ rather than real space. Therefore, n -dimensional imaging of an object requires scanning the k -space of the same dimension n with the centre at $\mathbf{k} = 0$. Image reconstruction in the real coordinate space is possible using, *e.g.*, the n -dimensional Fourier transform

$$S(\mathbf{k}) = \int \rho(\mathbf{r}) \exp(i 2\pi \mathbf{k} \mathbf{r}) d\mathbf{r}, \quad (5)$$

$$\rho(\mathbf{r}) = \int S(\mathbf{k}) \exp(-i 2\pi \mathbf{k} \mathbf{r}) d\mathbf{k}, \quad (6)$$

where $S(\mathbf{k})$ is the experimental NMR signal recorded by scanning the k -space and $\rho(\mathbf{r})$ is the spin density. The $\rho(\mathbf{r})$ value is proportional to the concentration of the substance under study.

The frequency encoding of the NMR signal (see above) allows the recording of a line in the k -space, *e.g.*, a line along the k_x direction if $k_y = k_z = 0$. Obtaining a two-dimensional (2D) image in, *e.g.*, the xy plane requires additional recording of the NMR signal at those points of the k -space for which $k_y \neq 0$. To this end, a pulsed gradient G_y is applied to the transverse magnetisation before the beginning of signal acquisition. As a result, the spin system is displaced in the k -space along the k_y direction by an increment

$$k_y = \frac{\gamma G_y \delta}{2\pi}, \quad (7)$$

where δ is the duration of the pulse gradient. Then, after recording the NMR signal in the presence of G_x , one gets a new line of points in the k -space, which is parallel to the preceding line. Multiple repetition of this procedure with step-by-step variation of the amplitude of the pulsed gradient G_y allows collecting the necessary 'two-dimensional' array of the signal amplitudes in the k -space. Since the pulsed gradient G_y is applied before recording the NMR signal, it changes the phases rather than the precession frequency of the magnetisation vectors contributing to the observed signal during the acquisition time. Therefore, this procedure is called the phase encoding of spatial information or signal.

A drawback of the phase encoding procedure is multiple repetition of experiments to obtain a complete set of k_y values. Prior to each repetition of the pulse sequence the spin system should return to thermal equilibrium. This takes time T_r of the order of $3T_1 - 5T_1$. For an analogue-to-digital converter with a maximum sampling rate of $1/(2.5 \mu\text{s})$, recording a line of 128 points in the k -space takes $128 \times 2.5 \mu\text{s} = 320 \mu\text{s}$. Obtaining a two-dimensional image of size 128×128 pixels requires 128 lines in the k -space to be recorded. For instance, in the case of bulk water ($T_1 = 2.7$ s) it would take $128 \times 3 \times T_1 \approx 17$ min. This way of scanning the k -space is inefficient since only 0.004% of the total duration of experiments is spent for recording the NMR signal. In addition, an increase in the image dimension leads to reduction of the size of the volume elements contributing to each image pixel, which in turn reduces the signal-to-noise ratio. Therefore, signal averaging is required which even greater extends the duration of experiments.

A three-dimensional (3D) image can be obtained by recording the signals from a set of planes in the k -space, corresponding to different k_z values ($k_z = \gamma G_z \delta / 2\pi$). This can be done using the phase encoding along the z axis, namely, the pulse sequence is augmented with the pulsed gradient G_z of duration δ . Clearly, such experiments take a very long time. Obtaining an image of size $128 \times 128 \times 128$ pixels requires 128×128 lines in the k -space to be recorded, which takes more than 36 h ($128 \times 128 \times 3 \times T_1$). However, an experiment with a sample with $T_1 = 10$ ms takes only

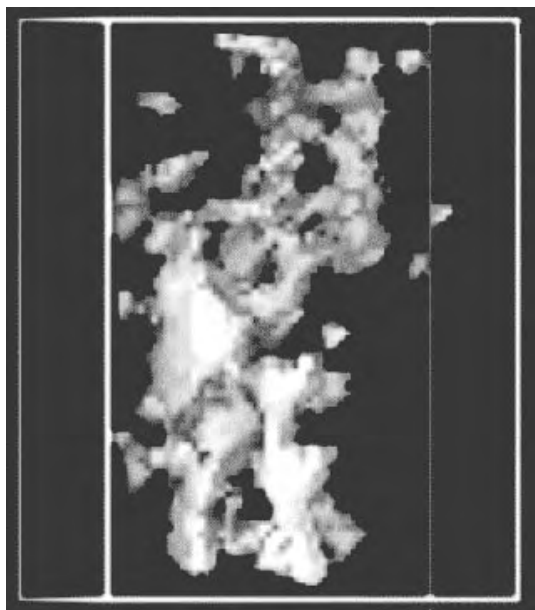


Figure 3. A reconstructed three-dimensional image of a cluster comprised of porous fine-grained (200 μm) alumina impregnated with Vaseline oil and filling out the interstices of a bead of large (5 mm) alumina granules. The latter contain no liquid and do not contribute to the NMR signal.

8 min. An example of a reconstructed three-dimensional image of an object is shown in Fig. 3.

Another approach to studies of three-dimensional objects involves recording two-dimensional images from one or several slices rather than the entire object (Fig. 4). Slice selection is most often achieved by using selective RF pulses. Any RF pulse has a limited excitation bandwidth, the bandshape being dependent on the parameters of the pulse. Many types of pulses nearly equally affect all spins in the frequency range $\omega_0 \pm \Delta\omega/2$ (ω_0 is the frequency of the RF pulse and $\Delta\omega$ is the bandwidth) while the spins with characteristic frequencies lying beyond this frequency range remain nearly unaffected. The $\Delta\omega$ value is inversely proportional to the duration of the RF pulse; therefore, a relatively long RF pulse range has a narrow excitation bandwidth. In the case of

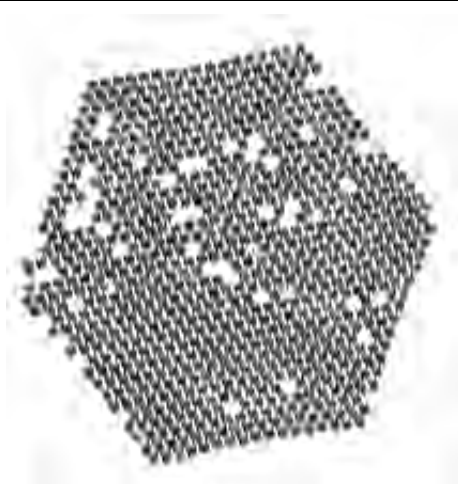


Figure 4. Two-dimensional image of a slice of a glass capillary-bundle column saturated with water.

The nominal in-plane spatial resolution was $5 \times 5 \mu\text{m}^2$ at a slice thickness of 15 mm. The diameter of individual capillaries was 40 μm . White spots in the image correspond to the blocked capillaries containing no water.

homogeneous magnetic field this can be used for, *e.g.*, selection of a particular signal in the entire NMR spectrum and obtaining a spatially resolved image for one of the components of a mixture. If the selective pulse is applied simultaneously with the field gradient G_z , this pulse becomes spatially selective and affects only those spins within a slice perpendicular to the axis along which the gradient is applied. As mentioned above, the time of the two-dimensional experiments is mainly spent for the recovery of the equilibrium magnetisation. Since selective pulses have no effect on the magnetisation outside the selected slice, one can scan lines in the k -space, corresponding to other slices of the sample while the magnetisation within a given layer relaxes to the equilibrium value. This allows imaging of a number of slices that do not intersect within the sample instead of one slice nearly without extension of the duration of the experiments. Since the directions of the gradients G_x , G_y and G_z are mutually orthogonal, the use of their linear combinations makes it possible to select a slice with arbitrary spatial orientation and to carry out a two-dimensional scan of a slice in the k -space without physical rotation of the sample. To obtain an excitation pattern with steeper transition regions at the edges of a slice, the so-called shaped RF pulses are employed.^{22–25}

Practical implementation of the frequency encoding of an NMR signal involves application of the gradient echo or a combination of the gradient echo and the spin echo. In the former case, rephasing of the spin precession is achieved by reversal of the gradients in the pulse sequence, while in the latter case this is achieved by rephasing using a 180° pulse. In contrast to the gradient echo, the spin echo also eliminates the effects caused by internal field gradients, differences in chemical shifts and heteronuclear spin-spin interaction.

In recording the echo signal an important parameter is the echo time T_e , *i.e.*, the effective time of the evolution of the transverse magnetisation, which is equal to the time interval between the instants of creation and rephasing of the transverse magnetisation and corresponds to the maximum spin echo signal. Often, the relaxation time of the transverse magnetisation, T_2 , is shorter than the shortest achievable T_e value. This leads to considerable loss of sensitivity of the experimental technique. The effective time of the transverse relaxation, T_2^* , of samples with large internal magnetic field gradients can be shorter than T_2 . In the latter case, it is more appropriate to use the spin echo technique, since the spin echo amplitude decays with the characteristic time T_2 , while the gradient echo signal decays with the time constant T_2^* . If T_2 is much shorter than the shortest achievable T_e , in some cases the free induction decay in the presence of the external field gradient is recorded instead of the echo signal, which corresponds to radial trajectories in the k -space. Subsequent image reconstruction can be performed by either interpolation of the signal at the nodes of a rectangular grid followed by multi-dimensional Fourier transformation²⁶ or from projections.^{27,28} A number of experimental techniques,²⁹ *e.g.*, single point imaging (SPI)^{30,31} and single point ramped imaging with T_1 enhancement (SPRITE)^{32–35} are based exclusively on the phase encoding (no frequency encoding is used).

Generally, the imaging time depends on the image dimension, imaging procedure, sensitivity, relaxation times of the nuclear spins used for recording the NMR signal and is to a great extent determined by the desired spatial resolution. Shortening the duration of the experiments is particularly important when dealing with fast dynamic processes. There is a number of approaches that were used as the basis for creation of fast imaging techniques for obtaining two- and three-dimensional NMR images.^{36–39} These techniques employ shortening the recovery time between the repetitions of the pulse sequences, recording more than one line in the k -space during each application of the pulse sequence, optimisation of the trajectories in the k -space, *etc.* For instance, each repetition of the pulse sequence in fast procedures based on acquisition of the gradient echo signal⁴⁰ uses only a small part of the longitudinal magnetisation of the sample due to the applica-

tion of the RF pulse with a small flip angle, $\alpha \ll 90^\circ$. As a result, the spin system is not fully saturated and there is no complete NMR signal loss even if the recovery time T_r is much shorter than T_1 . Yet another approach involves acquisition of a large set of the echo signals, each of them being corresponded to a different line in the k -space, during a single application of the pulse sequence.^{41–43} Recently, considerable attention has been given to spiral rather than linear scan of the k -space.^{44–46}

Magnetic resonance imaging can be used for mapping the RF field⁴⁷ and the static magnetic field^{48–50} within the sample giving the NMR signal. Therefore, shimming the magnetic field in the NMR experiments is now transformed from a kind of art⁵¹ into a field of exact science. This feature is used in MRI experiments for visualisation of the electromagnetic fields of the gradient coils and the fields created by eddy currents upon switching the external field gradients.^{52–54} Visualisation of the electric fields in a sample is used for the determination of the densities of the electric currents flowing within the sample.^{55–57}

Summing up, it should be mentioned that MRI experiments can be carried out using the gradients of the RF field B_1 (the so-called B_1 -imaging)^{58–61} instead of the gradients of the static field B_0 . The advantage of this technique is its insensitivity to internal inhomogeneities of the static magnetic field. One can use the RF field gradients to obtain images as well as to determine the relaxation times, diffusion coefficients and flow rates of fluids.^{62,63}

3. Spatial resolution of MRI method

Magnetic resonance imaging is characterised by a relatively low spatial resolution. Experiments with a resolution of the order of $(5\text{ }\mu\text{m})^3$ should be considered exceptions. In most cases, a spatial resolution is of the order of tens and even hundreds of micrometres. Often, the slice thickness ($\sim 1\text{--}10\text{ mm}$) in two-dimensional NMR imaging studies exceeds the in-plane spatial resolution. It should be noted that the experimentally achievable spatial resolution is not the major advantage of the MRI technique.

The spatial resolution that can be achieved in the experiment depends on several factors. In many instances, the major contribution comes from the relatively low sensitivity of NMR. Often, almost no information can be extracted from an image obtained with high (nominal) spatial resolution because of the noisiness of the image. This is due to the fact that enhancement of spatial resolution is associated with a decrease in the size of the volume element of the image (voxel), which in turn causes a proportional reduction of the signal-to-noise ratio for each image pixel.¹ This ratio can be improved by accumulating the NMR signal by means of multiple repetition of the experiments; however, the duration of the experiments becomes unacceptably long.

Another factor responsible for the spatial resolution is the spectral width of the NMR signal used in the imaging experiments. As mentioned above, the NMR images can be treated as multidimensional NMR spectra, namely, as the dependences of the signal amplitude on one or a number of frequency coordinates. The nominal resolution equals the actual one if two neighbouring pixels of an NMR image correspond to two non-overlapped spectral peaks, *i.e.*, if the NMR signal is narrower than the frequency difference between the centres of the neighbouring image pixels. In principle, this limitation can be surmounted by increasing the amplitude of the field gradient whereby the image is stretched in the frequency coordinates. In practice, the field gradient amplitudes are limited by the operating range of experimental equipment ($100\text{--}1000\text{ G cm}^{-1}$). Increasing the field gradient amplitudes is a challenge to MRI studies of solids,^{27,64–69} since the width of the NMR signals of solids (up to hundreds of kilohertz) much exceeds the values typical of liquids. Therefore, MRI studies of solids are often carried out using the field gradients of the order of 10^4 G cm^{-1} .

It should be emphasised that limitations associated with the linewidth of the NMR spectra are characteristic of the frequency

rather than phase encoding of the NMR signal. In addition, phase encoding excludes the appearance of artifacts in the NMR image originated from inhomogeneity of the magnetic field and differences in the chemical shifts.²⁹

Yet another factor that limits the spatial resolution is displacement of the nuclear spins in space (including molecular diffusion) during the acquisition time. The self-diffusion coefficient, D , of bulk water at 20°C is $2.0\text{ cm}^2\text{ s}^{-1}$. If the acquisition time of one echo signal, T_{reg} , is 1 ms, the characteristic displacement of water molecules along the direction of the magnetic field gradient is $(2DT_{\text{reg}})^{1/2} \approx 2\text{ }\mu\text{m}$. If the diffusion motion of the molecules is restrained, the diffusion-controlled resolution limit can be in principle reduced. In the case of motion of macroscopic parts of the object under study one should use another time scale and consider the motion (displacement) during a much longer time interval, that is, the acquisition time of the entire NMR image rather than the acquisition time of one echo signal. In particular, displacement of the entire object (*e.g.*, a patient undergoing an MRI evaluation) during the time interval needed to perform all measurements should not be larger than the desired spatial resolution. In the case of periodic motions of the object under study (cardiac muscle contractions, pulsatory blood flow, *etc.*), imaging is often controlled by the period of the motion (*e.g.*, synchronisation with the electrocardiogram signal).

Currently, there has been intensive research aimed at enhancing the spatial resolution of the MRI technique.⁷⁰ An avenue of biomedical research is based on the possibility of using MRM with a spatial resolution of the order of $1\text{ }\mu\text{m}$ in studies of plant cells and in animal experiments. Miniaturisation of the receiver RF coils allows improvement of the signal-to-noise ratio. However, further enhancement of spatial resolution using this approach faces severe difficulties. Much more promising seem to be other strategies (in particular, the use of magnetic resonance force microscopy which combines NMR imaging and atomic force microscopy).^{71–74}

4. Specific features, advantages and drawbacks of MRI techniques

An unquestionable advantage of MRI is the possibility of non-destructive (non-invasive) investigation of the internal structure and properties of various (including opaque) objects, which is of particular importance in medical research. Another advantage of the method is the lack of preferential direction, which allows obtaining spatial information along any direction or simultaneously along the three spatial coordinates.

Magnetic resonance imaging requires no probes or molecular tracers to be introduced into the object under study. Here, the nuclear spins of the molecules constituting the object under study are employed as inherent tracers. In principle, any nucleus with nonzero spin can give an NMR signal. The prospects for the MRI applications of a particular nucleus are first of all determined by the sensitivity of this nucleus and by the characteristic relaxation times. In practice, the number of different nuclei used in MRI experiments is limited and most of studies utilise the ^1H NMR signals.

In addition, in the case of multicomponent systems combining the NMR spectroscopy and MRI allow one to obtain separate images for each type of molecules or even each group of atomic nuclei in the molecules. Both approaches can also be used to obtain spatially resolved NMR spectra including those of a preselected volume element of arbitrary shape inside the sample (localised spectroscopy).^{75–79} The capabilities of spatially localised MRI are illustrated in Fig. 5.

As mentioned above, the major drawback of MRI consists in relatively low spatial resolution. Besides, NMR in general and MRI in particular can be used to study a large number but not all kinds of materials. Operation with electromagnetic radiation in RF range ($100\text{--}1000\text{ MHz}$) imposes severe restrictions on the possibilities of studying metals and other conducting materials, since in this frequency range the skin layer is thin and the RF



Figure 5. An image of the logo of the International Tomography Centre of the Siberian Branch, Russian Academy of Sciences. The image was obtained by spatial selection of the NMR signal using a simple 10-mm cylindrical tube filled with water as the sample.

radiation does not penetrate into the interior of the entire sample. Placing a conducting object into a RF coil causes a considerable loss of the energy stored in the resonant circuit, which reduces its Q -factor and affects the sensitivity of the method employed. In addition, MRI utilises pulsed magnetic field gradients which induce eddy currents responsible for the loss of signal and image distortion in studies of conducting materials. Dielectric losses in samples with high dielectric constant also reduce the Q -factor of the RF circuit. Investigations of magnetic materials in static magnetic fields of strength less than 20 T are also impossible.

Often, some limitations are also imposed on the size of sample under study. Magnetic resonance microimaging allows one to achieve the highest spatial resolution and the signal-to-noise ratio; however, the size of the sample usually does not exceed several centimetres. Using biomedical MRI instruments, one can investigate objects of size from ~ 10 cm up to a human body size. Currently, devices with open configuration are finding increasing application. They allow studies of objects of any size; this is achieved by moving the object under study or the device itself. In medicine, this type of systems is used for, *e.g.*, visualisation of internal organs during surgical operations^{80,81} and diagnosis.⁸² The NMR logging systems, a 'hydroscope' device designed for the exploration and characterisation of the underground pools of water and other fluids (see below), a GARfield device⁸³ for laboratory investigations of samples tens or hundreds of micrometres thick and the 'NMR Mouse', or a mobile explorer of the near-surface regions of large objects⁸⁴ can serve as examples of open design applications in other fields.

5. Image contrast mechanisms and informativity of the method

All things being equal, an n -fold increase in the spin density (concentration of the nuclear spins) causes an n -fold increase in the amplitude of the NMR signal. However, it is not necessarily true that if two signal amplitudes differ by a factor of n , the corresponding spin densities also exhibit the n -fold difference. This is due to the fact that the signal amplitude is a complex function of many parameters and first of all the spin relaxation times T_1 and T_2 . As a result, in practice the value $\rho(\mathbf{r})F(P)$ is measured instead of the spin density $\rho(\mathbf{r})$ [see expression (6)]. The function F determines the degree of image contrast due to parameters P that are different from $\rho(\mathbf{r})$. Therefore, sometimes quantitative MRM measurements of the spatial distribution of, *e.g.*, water in an object under study are difficult or even impossible since the influence of other factors on the NMR signal cannot be avoided completely. It is this apparent disadvantage that makes magnetic resonance imaging a powerful tool which is much more versatile compared to other modern spatial imaging methods.²¹

Spin density measurements (by, *e.g.*, integrating signals in an NMR spectrum) provide no way for discriminating the liquid and frozen water. However, the relaxation times of water in the liquid and solid state are appreciably different, which creates a contrast



Figure 6. Image of a pine bar of a square cross section of $(1.7 \text{ cm})^2$ and 5 cm in height. The bar was initially frozen and was melting during the MRI experiments.

The two-dimensional image was obtained in the horizontal plane without slice selection. Brighter gradations of gray correspond to more intense NMR signal. The early and late zones of the growth rings are clearly visualised as bright and dark stripes, respectively. The dark spot at the centre of the image corresponds to the frozen liquid.

in the NMR image of an object containing water in different states of aggregation (Fig. 6). The molecular spin relaxation times are rather sensitive to the environment, which allows this feature to be used in medical diagnosis. Often, pathological changes in tissues have virtually no effect on the spin density; however, they affect the T_1 and T_2 values, which leads to changes in contrast of corresponding regions in the NMR image. Sometimes contrast between the healthy and malignant tissues can be improved by introducing a contrast agent, *i.e.*, a paramagnetic compound that is capable of changing the relaxation times of the spin systems of water or lipids in tissues. The relaxation times are also sensitive to the concentration of oxygen, which allows studies of, *e.g.*, the dynamics of changes in the oxygen concentration in blood and tissues. In particular, this is used for visualisation of the brain regions responding to a particular external stimulus (functional MRI).⁸⁵

A broad spectrum of applications of NMR imaging is to a great extent due to the fact that the nature of contrast of the NMR image depends on the experimental conditions and can be chosen by researchers in a targeted manner depending on particular problems. For instance, by shortening the time delay between repetitions of the pulse sequence one can obtain NMR images with T_1 -contrast — $\rho(\mathbf{r})F(T_1)$, — *i.e.*, the images in which the colour of a particular pixel characterises not only the local concentration of the resonance spins, but also their local spin-lattice relaxation time. This is due to the fact that the amplitude of the NMR signal of the nuclear spins with $T_1 \ll T_r$, which have time to return to thermal equilibrium during the time interval between successive repetitions of the pulse sequence, is maximum and independent of T_r , whereas the NMR signal of the spins with $T_1 \geq T_r$ is partially suppressed and its amplitude is a function of the T_1/T_r ratio. This is the case of the so-called T_1 -weighted image.

Clearly, by varying the image contrast in a targeted manner one can obtain information not only on the time T_1 but also many other parameters characterising the spin system. However, the relaxation times (T_1 , T_2 , T_2^* , $T_{1\rho}$) occupy a special position among all these parameters. Nuclear spin relaxation is due to the fluctuating local magnetic interactions of the nuclear spins with their environment. The efficiency of the nuclear spin relaxation depends on the frequency spectrum corresponding to a particular type of interactions. The spectrum is to a great extent determined by both the motion of the probe molecule (and its fragments) and the motions of the molecular environment. The relaxation time T_1

is sensitive to components of the motion occurring at frequencies of the order of hundreds of megahertz, whereas the times T_2 and $T_{1\rho}$ are sensitive to the motions occurring in the kilohertz range. Therefore, by measuring the relaxation times one can study the frequency spectra of the molecular and atomic group motions and determine the correlation times and activation energies of such motions as well as particular distances in the system under study at the molecular level.

In addition to the spin density and relaxation times, the chemical shift, local magnetic fields, spin polarisation and spin-spin interactions can be used as the basis for image contrast in MRI studies. These parameters are sensitive to many physico-chemical properties of objects under study (*e.g.*, temperature, viscosity, mechanical stress, diamagnetic susceptibility, *etc.*) and processes occurring in them (*e.g.*, interaction with the surface, chemical transformations, flow and other types of motion, ordering, filler distribution, cross-linking, vulcanisation, ageing of materials, *etc.*). Experiments are designed in such a way that the changes in a property (process) of interest be responsible for changes in a certain spin-system parameter related to changes in a particular parameter of the measured NMR signal (resonance frequencies, amplitude, linewidth or phase).

Thus, virtually any property (process) influencing a certain parameter of the NMR signal can provide image contrast in the NMR imaging experiments. This allows both qualitative and quantitative studies of the spatial distribution of a particular property of the object at hand. Since the NMR signal is sensitive to some properties (processes), often the major problem is to separate the contributions of the process under study or the property of the object to this signal. Often, creation of the pulse sequences for MRI experiments and interpretation of the results obtained are substantially simplified when using a modular approach. In this case, the pulse sequence is augmented with a module responsible for creation of a particular type of contrast, which is executed before the module designed for collecting spatial information.

III. Structure and properties of liquid-containing materials

1. General remarks

Magnetic resonance imaging studies of liquid-containing solid porous materials allow one to elucidate their structure and properties as well as the distribution of the fluid within the pore space without performing solid-state NMR experiments.

The amplitude of the NMR signal of an image pixel characterises the pore volume filled with the liquid within the corresponding volume element. If the size of the liquid-filled pores exceeds the spatial resolution of the experimental method ($> 10\ \mu\text{m}$), NMR imaging permits investigations of the morphology of porous materials. For instance, the pore size in most of rocks can be as large as $200\ \mu\text{m}$ and even greater (in limestone rocks).⁸⁶ For smaller pores, each pixel of an NMR image corresponds to the NMR signal averaged over the particular volume element of the sample. If the pore size is much smaller than the spatial resolution, each image pixel characterises the local porosity of the sample and the presence of large non-porous inclusions and voids. If the pore size is comparable with the spatial resolution, the partial volume effects become of great importance for correct interpretation of experimental data.

As mentioned above, the amplitude of the NMR signal depends not only on the spin density (amount of liquid in the volume element) but also on some other parameters. By appropriately choosing the mechanism of image contrast formation one can obtain the distribution maps of various characteristics of the objects under study after processing the experimental data. Very often, investigations into porous materials involve mapping the nuclear spin relaxation times (T_1 , $T_{1\rho}$, T_2 , T_2^*). Relaxation-weighted NMR images are useful in revealing inhomogeneities of the properties of a porous medium,⁸⁷ while quantitative

relaxation time measurements allow one to determine the permeability,⁸⁸ wettability, pore saturation levels,⁸⁹ pore size and many other characteristics. Quantitative distribution maps of these parameters can be derived from the relaxation time distribution maps using appropriate models. Spatial inhomogeneity of a sample can be quantified by constructing histograms and evaluating the nonzero distribution moments for the maps obtained as well as by calculating the spatial correlation functions of the measured parameters.⁸⁶

Usually, the spin relaxation times of the liquids filling the pore system are shorter than those of bulk liquids. Because of the shortening of the time T_2 the amplitude of the NMR signal in the magnetic resonance images is often out of proportion to the content of the liquid (spin density) in a porous sample. Therefore, quantitative information is often extracted from a set of NMR images characterised by different degree of relaxation weighting. Computer simulation of the relaxation curves for each image pixel can then be used for deriving separate spin density and relaxation time maps.^{86,90}

In practice, studies of systems containing a number of immiscible and miscible liquids are not infrequent. For instance, the distribution of water and hydrocarbons in rocks is of considerable interest for the gas and petroleum extraction industry, while the reagent-to-product ratio is an important parameter in studies of chemical reactions. In the case of multicomponent systems selective NMR imaging is possible. This can be achieved using a number of methods. If the NMR signals of the liquids differ in chemical shifts, selective pulsed excitation of a particular line in the NMR spectrum allows one to carry out imaging studies using the signal of this spectral line (chemical shift selective imaging, CSSI).^{91,92} Selective pulses can also be used to suppress (saturate) all spectral lines except for that involved in the imaging procedure.⁹¹ However, it should be noted that shortening of the spin relaxation times can lead to appreciable line broadening in the NMR spectra of the liquids in the pores (up to hundreds of Hz and more), which precludes separation of the contributions of particular spectral lines to the NMR signal based on differences in chemical shifts.⁸⁶

Another approach is based on recording the free induction decay or the spin echo signal in the absence of external field gradients, which preserves the spectral information (chemical shift imaging, CSI).^{93–95} Having aimed at extracting spatial information, in this case one should reject the frequency encoding of the NMR signal. Low-resolution spectral information can also be obtained using the phase encoding of the signal. In such a case it is convenient to reconstruct spectral information by, *e.g.*, simulating the temporal evolution of the signal by the sum of several exponentially decaying sine curves rather than using the Fourier transformation.⁹⁶

If resonances are overlapped, chemical shift selective NMR imaging is impossible. In this case one should use distinctions between other parameters of the NMR signal. The contributions of different components of the system under study can be separated using differences in the spin relaxation times.^{97–99} For instance, by choosing an appropriate echo time, T_e , one can observe the contribution of the liquid characterised by the longest time T_2 . If the times T_1 differ appreciably, the pulse sequence can be augmented with an inversion pulse and a time delay that are applied prior to image readout. The time delay is chosen in such a way that the signal be recorded at a time instant corresponding to zero magnetisation of a particular liquid in a binary mixture during the spin-lattice relaxation process.^{92,100} Collecting a set of images with different degree of relaxation weighting followed by computer simulation of the relaxation curves for each image pixel allows one to obtain separate relaxation time and spin density maps. If the relaxation times of the liquids in the mixture are substantially different, this feature can be used to obtain the separate spin density maps for the individual components of the mixture.¹⁰¹ Scalar interactions occurring between inequivalent nuclei can also be used for separation of the contributions of

different liquids to the NMR signal by, *e.g.*, creating and detecting two-quantum coherence.^{97, 102}

Doping water with paramagnetic ions makes it possible to 'hide' its NMR signal owing to the short T_2 time. This can be used for selective observation of the NMR signal of a hydrocarbon in pores containing both liquids.¹⁰³

Yet another experimental technique involves the use of different magnetic nuclei¹⁰⁴ and their isotopes. For instance, saturation of porous rocks with D₂O/hydrocarbon or H₂O/fluorocarbon mixtures allows selective acquisition of the signal of a particular liquid.^{94, 103} The possibility of recording NMR signals from other nuclei extends the range of useful chemical substances.

Porous materials are characterised by the presence of numerous interfaces between phases with substantially different magnetic susceptibilities. Placing samples of porous materials in a strong magnetic field of the NMR spectrometer produces large field gradients near the interfaces. In this case, the decay time of the transverse magnetisation, T_2^* , becomes much shorter than the spin-spin relaxation time, T_2 . The reasons are the dephasing of the spin precession since all spins experience different magnetic fields and incoherence of the spin motion (owing to, *e.g.*, diffusion) in non-uniform magnetic field. As a result, gradient echo imaging allows better visualisation of structural defects. The NMR images obtained by the spin echo technique often exhibit artifacts in the form of bright spots near structural defects (due to difference in magnetic susceptibilities).¹⁰⁵ On the other hand, for many systems with T_2^* values in the submillisecond range, the gradient-echo technique produces no NMR signals at all. To prevent substantial shortening of the time T_2^* , experiments are usually carried out in relatively low fields and/or using multiple rephasing of the magnetisation by applying the sequence of 180° pulses¹⁰ (the so-called Carr–Purcell–Meiboom–Gill, or CPMG, pulse sequence). It should be noted that the magnitudes of local field gradients allow assessment of the pore shape and evaluation of the pore sizes.¹⁰⁶ Using the relaxation time of the transverse magnetisation of a system of immobile spins, one can extract information on the distribution of the square of the strength of local field gradients, which serves as a measure of the difference between the actual pore shape and an ellipsoid.¹⁰⁷ The values obtained from comparison of the calculated and experimental parameters can serve as semiempirical characteristics of the pore space (in particular, the shape and size of pores and inter-pore channels).

In addition to the aforesaid, diffusion in external field gradients applied to encode spatial information also causes shortening of the time T_2^* . Obtaining high spatial resolution requires application of large external gradients; however, this can be accompanied by substantial shortening of the times T_2^* . When studying samples with the T_2 (T_2^*) values lying in the sub-millisecond range it is appropriate to use experimental methods based on the phase encoding of spatial information (SPI, SPRITE)^{30–35} or on recording and collecting the free induction decay signals followed by image reconstruction from projections.²⁷ The relaxation times can also depend on the mechanical prehistory of the sample.¹⁰⁸

Magnetic resonance imaging studies should be carried out taking into account specific features of systems of different nature. For instance, in most of biological objects the spin systems do not exhibit a single-exponential relaxation due to structural inhomogeneity at the cell and tissue level.¹⁰⁹ Plant tissues are saturated with air bubbles; therefore, the magnetic field can be strongly inhomogeneous. Some liquid-containing porous materials (*e.g.*, rocks) possess electrical conductivity. This reduces the signal-to-noise ratio as a result of reduction of the Q -factor of the resonant RF circuit, changes its resonance frequency and can lead to a limited penetration depth of the RF field into the sample due to the skin effect.⁸⁶ In this case, experiments are carried out in relatively weak magnetic fields (*i.e.*, at lower frequencies). Rocks and synthetic porous materials can contain paramagnetic impurities that are responsible for appreciable shortening of the T_2 times

of liquids in pores, which can result in partial or complete loss of the NMR signal.

2. Model and synthetic porous materials

The internal structure of catalyst granules determines their efficiency in heterogeneous catalysis, service life and other properties. Rigby¹¹⁰ has reported a more accurate structural representation of a porous medium (catalyst granules) which was based on complementary information obtained from the results of NMR imaging experiments (visualisation of the pores of size greater than 10 μm) and low-temperature nitrogen adsorption (pores of size less than 10 μm) and mercury porosimetry measurements. Then, he modelled the void space of a porous solid by separate representations of both the macroscopic and mesoscopic length scale properties of the material.¹¹⁰ Nuclear magnetic resonance images (more correctly, spin density maps) of fluid-saturated solid granules can be used for determination of the local concentration of the fluid, *i.e.*, inhomogeneity of the sample porosity. The NMR images of alumina spheres saturated with an ethanol–water mixture revealed¹¹¹ a uniform structure with spherically layered solid material and voids, which is consistent with the manufacturing process of these particles. The spin density and T_1 time distributions of water in alumina were mapped.¹¹²

The T_1 maps allow one to reveal spatial inhomogeneities of the pore size distribution, while the effective diffusivity maps show inhomogeneities of the transport properties.¹¹³ Experiments with water-saturated alumina and silica granules showed that these types of inhomogeneities are not necessarily correlated.^{114, 115} Mention may be made that the case in point is structural inhomogeneities with a characteristic size exceeding the spatial resolution of the experimental technique. Microscopic structural inhomogeneities are averaged in the imaging experiments. It should be noted that if for porosity there is a simple statistical averaging, the dynamic averaging of the T_1 and diffusivity values is nontrivial. Gladden *et al.*¹¹⁶ proposed quantitative characterisation of the sample inhomogeneity in terms of a fractal dimension of two-dimensional NMR images of the sample. Water-saturated cylindrical alumina granules placed in a tube filled with D₂O exhibited different effective diffusivity and, hence, tortuosity of the pore space in the radial and axial directions. This is in agreement with different fractal dimensions of the two-dimensional NMR images of the same granules, whereas the fractal dimensions of two-dimensional T_1 maps obtained in the axial and radial directions were identical.

Different diffusivity measurement techniques are 'sensitive' to the structure of the pore space at different length scales. An assumption was made¹¹⁷ that the ratio of the pore space tortuosity determined in the experiments with H₂O/D₂O exchange to the tortuosity determined from the pulsed field gradient studies^{8, 25, 118, 119} provides an estimate of the tortuosity associated with the sample inhomogeneity at a length scale of the order of the sample size. This assumption was confirmed by calculations of the tortuosity coefficient carried out with construction of the pore space grid using the NMR images of water-saturated porous granules. This allowed one to represent the tortuosity coefficient of the pore space as product of several tortuosity coefficients obtained for different length scales. Based on these concepts, an attempt has been undertaken at constructing a correct model of a porous medium taking into account the structural hierarchy, that is, the micro(meso)scopic and macroscopic length scales.¹²⁰ A mathematical model for prediction of the properties of porous media at the micro(meso)scopic length scale was constructed using information on porosity and the average pore size obtained from conventional porosimetry measurements. Reliability of the model constructed at the length scale less than 10 μm was evaluated by comparing the calculated and experimental T_1 values of water filling the pores. The model for description of the macroscopic structure at the length scale spanning the range from 40 μm (typical spatial resolution of NMR images) to the size of the object (several millimetres) was constructed in such a

way that the fractal dimensions of the calculated two-dimensional NMR images (and/or T_1 maps) be in agreement with the experimental fractal dimensions. A complete hierarchical model was validated by comparing the calculated and experimental values of the effective diffusivities and pore space tortuosity coefficients.

A study of a porous Pyrex glass filter containing cyclohexane (average pore diameter was 160 μm) has been reported.¹²¹ The 1D NMR profiles obtained with a spatial resolution of 26 μm exhibited rather large signal amplitude fluctuations indicating some structural disorder at this length scale. From the distances between the neighbouring amplitude peaks one can extract statistically averaged information on the pore size and inter-pore distances. Both statistical analysis of the distribution histogram of the distances between the neighbouring peaks and calculations gave close values of the estimates of the average inter-pore distance. At distances from zero to 2–4 mm, the spatial correlation function of the signal amplitude fluctuations has a constant value while it rapidly decreases at longer distances. The results obtained are in good agreement with the data of the scanning electron microscopy (SEM) studies which, in contrast to MRI experiments, require a labour-consuming pre-treatment of the sample.

Signal amplitude fluctuations can also be due to a low signal-to-noise ratio. Lengthening the signal accumulation time allows the defects in a water-saturated, disk-shaped porous glass sample to be identified with ease.¹⁰⁵ If the in-plane spatial resolution is comparable with the average pore size, it is convenient to use thick-slice NMR imaging of the samples of relatively low porosity. At higher in-plane resolution, the best image contrast is achieved in the experiments carried out with the same resolution along the three spatial dimensions. The NMR images of different disk-shaped samples (average pore size varied from 5 to 200 μm) obtained with an isotropic spatial resolution of 100 μm exhibited only minor distinctions. Experiments revealed shortening of the relaxation times of water filling the pores of sizes 5 to 200 μm with a decrease in the pore size.¹⁰⁵ Magnetic resonance images of water in a glass bead pack have also been obtained.¹²² Studies of porous systems in packed bed reactors by MRI technique have been reported.¹²³

To determine the fractal properties of porous systems, two-dimensional and three-dimensional model porous structures obtained by computer simulation were fabricated on polystyrene layers using a plotter to construct two-dimensional or three-dimensional percolation clusters. Three-dimensional objects were composed as stacks of two-dimensional layers. Then water was allowed to fill the clusters to visualise the pore space. The measured fractal dimension was found to be in good agreement with that of the model. Based on the possibility of distinguishing the liquid in motion and at rest^{25, 124–127} when analysing the flow pattern along the percolation cluster, the dead ends were excluded from consideration and the fractal dimension of the percolation backbone was determined. For model objects, this parameter was found to be lower than that of the entire cluster dimension. Experiments with natural porous systems (natural sponge, pumice stone, quartz sand and glass bead agglomeration) showed that the pore space is much more highly interconnected and the backbone can hardly be distinguished from the total pore space in terms of the fractal dimension.¹²⁸

Relaxation times of the fluids contacting solid surfaces are strongly dependent on the surface properties. In particular, the relaxation times of fluid filling the pore system are shortened in the presence of paramagnetic atoms or molecules adsorbed on the surface. Catalyst poisoning with weakly paramagnetic coke formed in the pore space can change the relaxation times of fluids and cause partial blocking of pores. This feature was used for obtaining the NMR profiles of macroscopic distributions of coke formed in the reaction of ethanol dehydrogenation in alumina pellets.¹²⁹ After reduction of conversion degree to a particular value in the range from 100% to 50% the alumina pellets were removed from the reactor and saturated with water. MRI-studies

revealed high inhomogeneity of coke formation in the pellets and strong dependence of coke profiles on the pellet position in the reactor. Analogous studies of zeolite HY were carried out using 2,3-dimethylpentane or xenon as the probe molecules.¹³⁰ Contacting coke causes a change in the chemical shift of xenon. Relaxation time measurements of 2,3-dimethylpentane showed an inhomogeneous composition of coke within the sample.

Diamagnetic adsorbates can also change the relaxation times of the fluids filling the pore system due to, *e.g.*, steric shielding of paramagnetic ions adsorbed on the pore walls from the fluid molecules.¹³¹ For instance, adsorption of platinum hexachloride (PtCl_6^{2-}) on the developed surface of a porous support causes an increase in the nuclear spin relaxation times of protons of the liquids that fill the pore space of the support.^{131, 132} This fact was used¹³² for determining the type of macroscopic spatial distribution of the active component over the surface of the support, which is an important characteristic of supported catalysts. Experiments were carried out using $\gamma\text{-Al}_2\text{O}_3$ pellets with different types of spatial distribution of platinum hexachloride. The NMR images confirmed good agreement between the T_1 maps of the fluids filling the pore space and the platinum distribution profiles obtained using conventional visualisation techniques. Magnetic resonance microimaging studies allowed the real-time redistribution dynamics of adsorbed platinum hexachloride to be traced for the first time during competing adsorption of PtCl_6^{2-} and oxalic acid from solution on a single $\gamma\text{-Al}_2\text{O}_3$ pellet.¹³² Analogous experiments were carried out with palladium (PdCl_4^{2-}) and it was found that adsorption of PdCl_4^{2-} on $\gamma\text{-Al}_2\text{O}_3$ also causes an increase in the relaxation times of the fluids filling the pore system.¹³³

The opposite influence of diamagnetic and paramagnetic adsorbates on the relaxation times of fluids in pores was used for studying the redistribution dynamics of PtCl_6^{2-} and Cu^{2+} upon their simultaneous adsorption on the same alumina pellet. The results obtained showed that copper is gradually displaced inward from the surface of the pellet.^{133, 134}

3. Rocks

Magnetic resonance imaging of brine-saturated sandstone rock cores and mapping the spin density and relaxation times of the spin systems in them has been reported.^{86, 112, 135} The experiments revealed the presence of shale interlayers with small pore sizes and high content of clay, which appreciably suppress the amplitude of the water signal. Bedding planes ~ 1 mm thick were also clearly seen in the images.¹³⁵ Analogous magnetic resonance images of limestone rock samples exhibited large voids and porosity variations. The signal amplitude and relaxation times distribution histograms of partially dried samples showed a much more inhomogeneous structure of limestone rock compared to the alumina structure.⁸⁶ Three-dimensional images of water or brine in rock cores revealed inhomogeneity of the porous structure or inhomogeneous saturation of the samples with water.¹³⁶ The results of the MRI studies of brine-saturated sandstone rock cores were compared with the data obtained by X-ray computerised tomography.¹⁰³

The difference in the chemical shifts of water and dodecane was used for separation of their images in a sample comprised of two sandstone rock plugs placed one on top of the other, one of them being saturated with water and the other with n-dodecane,⁹⁵ and in a core saturated with a mixture of these fluids.⁹⁶ Two-dimensional chemical shift selective imaging of water and hydrocarbon in limestone rocks has also been reported.⁹⁴ In this case, a specified amount of hydrocarbon (water) was injected into the sample saturated with water (hydrocarbon). No complete displacement of one fluid by the other occurred. Experiments on displacement of H_2O by heavy water revealed the presence of a clearly seen interface between the two fluids. Two-dimensional images of kerosene distribution in a kerosene-saturated core are shown in Fig. 7.

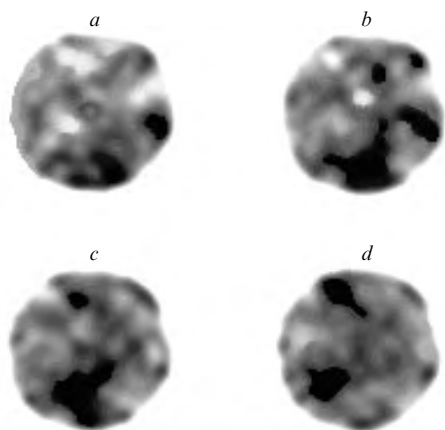


Figure 7. Sequential two-dimensional MRI images of adjacent slices of a kerosene-containing core. Darker regions in the image correspond to more intense NMR signal.

Each slice was 1.2 mm thick and the in-plane spatial resolution was $0.16 \times 0.16 \text{ mm}^2$.

Separate three-dimensional images of water and motor oil in sandstone rock samples have been obtained on the basis of the differences in relaxation times.¹⁰⁰ Biexponential analysis of the relaxation decay curves obtained for each image pixel was used in studies of a chalk core saturated with water and petroleum crude.¹⁰¹ The T_1 histograms exhibited two well-resolved peaks of finite width corresponding to the spin-lattice relaxation of water and petroleum. This allowed one to perform separate two-dimensional image reconstruction of water and petroleum, to establish that the regions with high concentration of water correspond to low content of petroleum (and *vice versa*) and to find cracks filled with water inside the core. Chemical shift selective imaging experiments were also carried out. The relaxation time histogram of the sample saturated only with water had one peak shifted towards longer times T_1 compared to the water peak of the preceding sample. This was explained by higher pore filling with water (assuming the same surface area of water contacting the pore surface) as a result of the removal of petroleum.

Magnetic resonance imaging studies of the dolomite cores dried under mild conditions and then saturated with oil⁹² revealed the presence of cracks, voids and microporous domains. Experiments carried out taking into account the differences in the chemical shifts and relaxation times of water and oil revealed large amounts of residual water in the sample. The results were compared with those obtained by X-ray computerised tomography.

Multinuclear NMR has been investigated as a method for discriminating the contributions of the organic and aqueous phases to the NMR signal in studies of flooded petroleum crude cores.¹⁰⁴ To this end, a sandstone rock plug with four openings 0.5 to 2.9 mm in diameter was sequentially saturated with aqueous LiCl solution and pure trifluorotoluene and the three-dimensional images were recorded using the ^7Li and ^{19}F NMR signals.

The Earth is the largest sample that can be studied by NMR imaging technique. Simultaneously, this is the least effective magnet that is used in the NMR studies. To carry out the NMR imaging experiments in the geomagnetic field,^{61, 137, 138} a 'hydro-scope' device was created, which has been used in search for and the determination of the depths of occurrence and evaluation of the field volumes of proton-containing fluids at depths up to 200 m. A wire loop ~ 100 m in diameter placed on the terrestrial surface is used for generation of the RF pulses and reception of the NMR signal. Very low signal-to-noise ratio is compensated by multiple accumulation of the NMR signal.

4. Polymers and gels

From the NMR standpoint, the properties of polymeric materials are intermediate between those of liquids and solids. This feature determines the choice of experimental techniques that can be used for studying this specific class of substances. Swelling of polymers in solvents allows imaging using the NMR signal of the solvent. Swelling also enhances the mobility of the polymer macromolecules, which sometimes permits a number of conventional liquid-state NMR techniques to be implemented to obtain the images of the polymer itself.^{139, 140} In addition, an increase in size due to swelling allows better visualisation of the sample morphology.

The NMR images of a sample of a water-saturated polymeric composite reinforced with carbon fibre exhibited well-resolved structural defects filled with water.¹⁴¹ These results were confirmed by sectioning the sample. If the size of structural defects and microcracks is smaller than the spatial resolution of the image, the amplitude of the NMR signal of the image pixel can be used for evaluating the defect size. Clearly, imaging of voids using the NMR signal of water is impossible; this can be done based on the NMR signal of the polymer itself.

Spin relaxation time measurements of polymers and gels allow one to obtain particularly valuable information. The time T_1 is sensitive to fast motions of atomic groups in the megahertz frequency range, while the times T_2 and $T_{1\rho}$ characterise slow, cooperative low-frequency motions and depend on the cross-link density and chain entanglement.^{139, 140, 142} Useful information can also be extracted from the relaxation times of solvents since the behavior of the solvent molecules is to a great extent determined by their interactions with the polymer molecules.

Magnetic resonance imaging studies of swollen butadiene rubber¹⁴⁰ and *cis*-1,4-polyisoprene¹⁴² of different initial compositions and cross-link density were carried out by detecting the NMR signal of the solvent (cyclohexane) or polymer (when cyclohexane- d_{12} was used).^{139, 140} The images obtained exhibited clearly seen spatial inhomogeneities of the samples as well as structural defects and voids and allowed one to establish structural changes as function of the rubber vulcanisation time. Lower solvent concentration corresponded to the regions with higher cross-link density. The regions near the surface contacting the mould were characterised by higher cross-link density and by a decrease in the cross-link density as a result of reversion effects (at long vulcanisation times).¹⁴⁰ The signal intensity histograms constructed using the images obtained by solvent imaging technique can be used for characterisation of the cross-link density and sample homogeneity. The results of the T_2 measurements allowed one to assess changes in the molecular mobility. Analysis of the T_2 maps of the solvent showed¹³⁹ that the T_2 value is determined by the polymer-solvent interactions and the cross-link density. As the cross-link density increases during vulcanisation, the molecular motions slow down and the relaxation time T_2 of the polymer is shortened, thus weakening the NMR signal of the polymer. This revealed spatial inhomogeneity of the cross-link density distribution over the sample. The T_2 maps were converted into corresponding histograms. Analysis of the histograms showed that the T_2 distributions become narrower and their maxima shift towards shorter T_2 values as the vulcanisation time increases. There are in fact two T_2 values corresponding to the monomer units of the polymer chain located at long and short distances to the cross-link points.^{139, 142} If triallyl cyanurate is used as vulcanising agent (at the vulcanisation temperature, this is a liquid whose mobility is sufficiently high for the domain formation), the polymers obtained are less homogeneous compared to those containing zinc diacrylate.

External perturbations can cause specific changes in the state of polymers and gels, *e.g.*, a temperature-induced volume-phase-transition. For instance, poly(*N*-isopropylacrylamide) gel swollen in water is in the equilibrium state at temperatures below the lower critical solution temperature (31–32 °C) and in the collapsed state above this temperature, the phase transition being reversible. The NMR images of this gel in different states, obtained using the

relaxation and diffusion contrast techniques provided an insight into the changes in the state of water and the mobility of the polymer molecules.¹⁴³

Two-dimensional spin density and T_2 maps of water in a cross-linked poly(methacrylic acid) hydrogel were obtained.¹⁴⁴ Analysis of these maps revealed a uniform distribution and high mobility of the water molecules in the gel.¹⁴⁴ Applying mechanical stress causes a decrease in the content of water within the compressed region of the gel due to migration of water molecules to the surrounding uncompressed regions. The molecular motion of water in the compressed region of the gel becomes lower, which leads to shortening of the time T_2 . Therefore, NMR imaging allows one to obtain information on the propagation of the strain induced by mechanical stress within the sample. Hydropolyelectrolyte gels can shrink in response to electric field. Imposing a voltage of 3 V across two platinum electrodes placed in contact with a gel led to its shrinkage which was larger near the positive electrode.¹⁴⁵ Using the two-dimensional gel images and T_2 maps, one can trace the changes in the shape of an initially cylindrical sample and determine the content and mobility of water in different regions of the gel sample. Analogous experiments were performed with the sample prepared using aqueous MnSO_4 solution and consisting of two parts with a different degree of cross-linking of the polymer.¹⁴⁶ The T_2 maps of water were converted into the Mn^{2+} ion concentration maps which showed that manganese ions migrate towards the negative electrode and this is responsible for the appearance of Mn^{2+} ion concentration gradients.

Nuclear magnetic resonance imaging has been used for quantitative studies of the properties of polysaccharide solutions and gels.¹⁴⁷ Gels were prepared by dialysing sodium alginate solutions against a solution containing calcium ions. The NMR images of the samples showed that the gels were inhomogeneous, that is, the gel concentration increased towards the centre of the sample. More homogeneous samples were obtained when NaCl was present in both solutions. The effect of the gel concentration (1%–4%) and degree of O-acetylation on the relaxation times, diffusion coefficient and magnetisation transfer parameters was studied taking into account the exchange of water molecules between bulk water and the chemisorbed water.

Freshly prepared agarose gels are characterised by a single-exponential transverse relaxation and direct proportionality of the relaxation rate to the agarose concentration. This is associated with small sizes of structural inhomogeneities of the gel ($< 0.3 \mu\text{m}$). However, relaxation measurements performed after the 'slow freeze–thaw' cycle revealed a multiexponential behaviour. Crystal growth under conditions of slow freezing causes essential changes in the gel morphology, namely, the formation of structural inhomogeneities with a characteristic size of several micrometres, which are retained after thaw. Multiexponential behaviour of the transverse relaxation is due to the fact that diffusion of water cannot induce averaging at this length scale. On the other hand, the longitudinal relaxation is single-exponential for all samples. The results of experiments are in agreement with the data of calculations carried out based on a model which includes the relaxation due to proton exchange with hydroxyl groups and the physical interaction between water molecules and agarose spiral aggregates.¹⁴⁸ The T_1 , T_2 and T_2^* maps of an Mn(II) -doped agarose gel and polyethylene have also been obtained.¹⁴⁹

5. Suspensions, emulsions and compacts

Magnetic resonance imaging can be useful in nondestructive studies of fabrication of ceramics, *e.g.*, slip casting. For instance, cross-sectional two-dimensional images of a plaster of Paris mould filled with an aqueous Al_2O_3 suspension (initial content of water was 30 mass %) were obtained.¹⁵⁰ The images exhibited clearly showed suspension, and solid deposits on the mould walls and the mould walls themselves, through which water was removed. The suspension and the solid deposits were character-

ised by the same content of water; however, the relaxation times of water in these regions were appreciably different. Growth of the deposit layer with time was observed.

Ceramics can also be fabricated by pressure moulding. In this case, it is possible to study the distribution of organic components (binder, plastifier, anti-adhesives) within the sample, which has a strong effect on quality of the ceramic materials. Visualisation of the distribution of the polymeric binder in green ceramics allows sorting out substandard articles before reaching the dewaxing and sintering stages. Different strategies of magnetic resonance imaging and recording spatially resolved NMR spectra of a polymeric binder were compared taking the compacts prepared by compacting alumina powder mixed with polymeric binder (2.5 mass % or 15 mass %) as examples.^{108, 151} No effect of the average particle size on the binder distribution was found; however, a decrease in the length-to-diameter ratio of the compact down to 0.17 led to increased concentration of the polymer around the periphery of the sample, which was associated with features of the pressing mechanics. The signal intensity histograms constructed based on the two-dimensional images of the compacts can be used for controlling the binder distribution homogeneity.¹⁰⁸ An NMR imaging study of a Si_3N_4 sample pressed in the form of a disk with openings of different diameters containing organic binder (15 mass %) has been reported.¹⁵¹ The relaxation times of low-molecular-mass poly(ethylene oxide), polyvinyl alcohol and poly(ethylene terephthalate) used as binders in fabrication of ceramics are $\sim 1 \text{ ms}$ (T_2) and $\sim 300 \mu\text{s}$ (T_2^*).¹⁰⁸

When growing large zeolite crystals, it is important to know the mixing degree of the starting components. Nuclear magnetic resonance was used for the determination of the mixing quality of two starting solutions in a batch mixer.¹⁵² The process was investigated under laboratory conditions. Zeolite A was synthesised from a sodium aluminate solution with triethanolamine (TEA) additives (TEA is an inhibitor of nucleation) and a silica suspension or sodium silicate solution. The NMR signal of the TEA protons was recorded; all other reagents were used in deuterated form. Analysis of the magnetic resonance images revealed the appearance of a large gradient of the TEA concentration after the first mixing cycle in the reaction with silica suspension. The concentration of TEA increased in a downward direction because of the higher density of the TEA–sodium aluminate mixture compared to the silica suspension density. Further mixing led to homogenisation of the TEA distribution in the mixture and after eleven cycles the mixture was almost homogeneous. The NMR images of the samples of the mixture exhibited clearly seen air bubbles trapped by the viscous medium. When the reaction was carried out with sodium silicate as the second component, homogenisation of the reaction mixture was even more complicated due to an increase in the viscosity of the mixture caused by gelation that started several seconds after placing the components in contact. Further mixing[§] led to the formation of aluminosilicate hydrogel clots. Clots of different compositions are clearly seen in the magnetic resonance images. Analogous studies were also carried out during the synthesis of zeolite X. Attempts at using this approach to study the synthesis of mordenite failed. In this case, tetraethylammonium bromide (cross-linking agent) was used instead of TEA. Unlike TEA, this compound is not involved in complexation with aluminium or silicon and, hence, one cannot use its distribution for evaluating the mixing degree of the reagents.

The size and distribution of voids and gas bubbles in secondary explosives have strong effect on the initiation and propaga-

[§] The efficiency of mixing strongly depends on the batch mixer design. The best batch mixer design was chosen based on analysis of the images of the samples obtained using four different types of batch mixers that were specially developed for the on-board synthesis of zeolites during space shuttle missions.

tion of detonation wave. The shock wave causes an adiabatic 'collapse' of voids, thus initiating a burst-like combustion. Void-containing samples can be obtained by mixing the explosives with hollow particles or by conducting a chemical reaction involving ammonium nitrate and sodium nitrite followed by liberation of dinitrogen. Concentrated oil-in-water emulsions can serve as examples of the secondary explosives. Two samples of the oil-in-water emulsions have been investigated.¹⁵³ One sample contained almost no voids while the other one was prepared using aqueous sodium nitrite solution to favour the formation of dinitrogen bubbles. Two-dimensional magnetic resonance images of the second sample exhibited voids of size up to 0.5 mm, whereas no voids were observed in the images of the first sample. These results are in agreement with the data of scanning electron microscopy studies.

Phase separation in the emulsion of sunflower oil in D₂O has been studied¹⁵⁴ taking a number of bulk samples and a sample prepared in the form of a film less than 600 μm thick as examples. Experiments revealed gravimetric separation of the dispersed phase from the continuous emulsion phase with time (creaming). An oil concentration gradient in the near-surface layer and an increase in the oil concentration with time were observed for all samples. Both facts seem to be associated with polydispersity of the sizes of the oil drops that become more 'close-packed' as a result of the action of the underlying layers.

6. Food products and plants

The potentialities of the MRI method in revealing the internal structure of and water distribution in the food systems containing small amounts of liquids was demonstrated¹⁵⁵ taking studies of the morphology of cookies, soft caramel with chocolate cream filler and a mixture of corn starch and water as examples.

Two-dimensional images and maps of the water spin density and T_2 distribution in plant tissues (Fig. 8) have been reported.¹⁰⁹ The relaxation time distribution maps give an accurate account of the peculiarities of the sample morphologies. For apples, the width of the NMR signal in a 4.7 T field is twice as large as that determined in the 2.35 T field. This is indicative of the local magnetic field gradients due to the difference in magnetic susceptibilities between the tissues and microscopic air bubbles.¹⁵⁶ Two-dimensional mapping of the distribution of the diffusion coefficient ($1.08\text{--}1.66 \times 10^{-5} \text{ cm}^2 \text{ s}^{-1}$) and the RMS local magnetic field gradient ($8.6\text{--}17.9 \text{ G cm}^{-1}$ in the 2.35 T field) was also performed. Mealiness in apples and peaches stored under various conditions was assessed using MRI techniques.¹⁵⁷ Spatially



Figure 8. Two-dimensional MRI image of a fragment of a cucumber.

resolved T_2 distribution maps were converted into corresponding T_2 histograms. Development of mealiness in apples leads to more pronounced asymmetry of the T_2 histograms. Analogous process in peaches causes transition from a Gaussian to a broad distribution with a flat top. This points to different physiological processes. The results of the MRI experiments were compared with the data obtained by conventional (mechanical) methods of fruit quality determination.

A MRI study of voidage in watermelons¹⁵⁸ involved recording the profiles of corresponding 1D projections on two orthogonal directions in the plane of a slice 20 mm thick. Then, these profiles were compared with analogous profiles expected for an ideal sphere. Out of 30 samples, 28 watermelons were correctly identified, which was confirmed by two-dimensional imaging.

Heat stress can retard the ripening of many fruits. Studies of tomato fruits kept at 42 °C revealed no changes in the size and overall content of water.¹⁵⁹ After 36 h the relaxation times T_1 and T_2 of water remained unchanged in the pericarp and became shorter for all other plant tissues. Then, the fruits were kept at 25 °C for 24 h; however, no lengthening of the relaxation time T_2 up to the initial value was observed. Probably, heat stress causes the formation of associates of some unbound water molecules with denatured proteins. No complete regeneration of the structure occurred during 24 h after heat stress, which seems to be responsible for a 120 h delay of change in colour, though the rate of ethylene and carbon dioxide production recovered virtually immediately after return to ambient temperature.

Bulk analysis of tobacco and cigarettes by magnetic resonance imaging was performed to map the spin density and relaxation time distributions.¹⁶⁰ The more mobile components (water and tobacco wax) were spin echo imaged while the solid components (cell wall polymers) were observed using the SPI technique. More dense packing of tobacco and lower content of water at the cigarette tip was pointed out. The region near the lateral surface of the cigarette is characterised by higher content of water in tobacco. Partial redistribution of water from tobacco to the filter region was also observed.

Knowledge of the internal morphology of wood is of great importance for wood-working industry. For instance, the possibility of revealing internal (hidden) defects of a log allows one to determine an optimum strategy of sawing beforehand. Cross-sectional two-dimensional images of white oak and black cherry samples 15 to 25 cm in diameter exhibited clearly seen heart-wood and sap-wood regions, the pith, the medullary rays and the growth rings.¹⁶¹ Besides, the eccentricity of the growth rings in the image pointed to the presence of the tension wood which is indistinguishable by the naked eye. The wet-wood region, which is hard to dry, looks as a bright strip in the image. Some water is evaporated through the cracks in the bark during long-term bulk storage of wood. As a result, the sap-wood contains regions characterised by the NMR signals of low intensity. For black cherry, the pith and the medullary rays are indistinguishable in the image owing to their small size; however, one can see gum spots, which are hard to polish when working, as well as hidden knots and scars, worm-holes and wood decay regions. The bark cannot be seen in the images because of the low content of water. Magnetic resonance imaging studies of plant roots have also been reported.^{162, 163}

7. Other materials

Three-dimensional images of the distribution of mobile components in coal were obtained in the temperature range from 25 to 475 °C.¹⁶⁴ It was found that this distribution is inhomogeneous and different for different sorts of coal. The fraction and homogeneity of distribution of the mobile proton-containing component increase as the temperature increases up to 450 °C and then dramatically decrease at higher temperatures as a result of sintering and coking.

Ice coated with gas hydrate melts at room temperature. The process involves the formation of liquid water encapsulated into a solid shell and the sample looks as a white powder-like solid. The

gas hydrate coating is formed in the reaction of ice crystals with CD_4 or xenon at high pressure.^{165, 166} Hyperpolarised xenon^{167–170} was used in studies of the formation of clathrate hydrates and in measurements of the rate constant for this process. Confirmation of the fact that the activation energy is negative¹⁷¹ was also obtained in the experiments with hyperpolarised Xe.

The distribution of water in foam churned from egg white and water has been studied.¹⁷² As time passes, the content of water increases in the lower part and decreases in the upper part of the sample (the liquid flows down under the action of the gravity force). This is accompanied by an increase in the relaxation time T_2 , which can be associated with growth of the foam bubbles. For the foam prepared by shaking water with additives (surfactants, polymer and alcohols), the upper part of the sample was characterised by a reduced spin density; this visually corresponded to much larger bubbles compared to those in the other regions of the sample.¹⁷³ Transformation of essentially non-rectangular water distribution profiles with time was compared with the results of model calculations carried out with inclusion of the downward flow of the liquid under the action of the gravity force. It was found that the model incorrectly describes the early stages of the process; however, it provides an adequate description at long times.

The 1D MRI profiles were also obtained, which illustrated the phase separation in the critical binary mixture aniline–cyclohexane after cooling below the upper critical equilibrium temperature.¹²¹

IV. NMR porosimetry

1. General remarks

In this Section we will consider some methods of the pore size determination based on the effect of the pore sizes on the nuclear spin relaxation times or on the freezing points of liquids in porous media. Besides, many other NMR measurements are to some extent sensitive to the pore size and other characteristics of the pore space. If pores are larger than 10 μm , their exact sizes can be determined by direct visualisation of the liquid that fills the pore space. Information on the pore sizes and tortuosity of the pore space can be extracted from, *e.g.*, the results of measurements of the diffusion coefficients of fluids that fill the pores.^{25, 174–179} The chemical shifts of the substances adsorbed from solution on the surface¹⁸⁰ and of the adsorbed gases (first of all, xenon^{181–185}) are sensitive to the pore size. The pore size distribution determines the shape of the water distribution profiles recorded during drying of liquid-saturated porous materials.^{186–188} The local magnetic field gradients can also reflect the shape and sizes of pores.^{189, 190}

The properties of the molecules of a liquid contacting a solid can be substantially different from the properties of bulk liquid. For instance, the properties of water adsorbed on the surface of silica glass are strongly different from those of bulk water due to the formation of hydrogen bonds with the surface hydroxyl groups.¹⁹¹ This leads to, *e.g.*, reduction of the density of the surface water layer, considerable reduction of rotational mobility of the molecules, anisotropy of the molecular mobility and to the freezing point depression. The NMR properties of the molecules that interact with the surface also change.

Most of the experiments on the NMR porosimetry were carried out without spatial resolution; however, this method can also be used in combination with the MRI technique. In the latter case, it is possible to determine the average pore size (or even the pore size distribution) and the pore volume (this parameter correlates with the local porosity of the sample) for each image pixel.¹¹⁰ It should be mentioned that the changes in the T_1 and T_2 values caused by the interaction with the surface can lead to relative enhancement or suppression of the NMR signal near the macroscopic interfaces when using relaxation-weighted imaging

and that the liquid in the smallest pores can have very short relaxation times T_2 and make no contribution to the NMR signal.

2. Relaxation porosimetry

Often, the spin relaxation (T_1 , T_2 , T_2^* , $T_{1\rho}$) in a liquid or gas contacting the surface of a solid occurs much faster than in the bulk. Detailed NMR investigations of the surface relaxation have been carried out for long. The results of the early studies of the relaxation of the liquids contacting solid silica (silica gel), alumina, coal and zeolite surfaces were generalised by Packer.¹⁹²

One of the reasons for higher relaxation rate of the nuclear spins of the fluid molecules contacting the surface is a substantial change in the correlation time of molecular motions caused by changes in the mobility of the molecules located on the wall or in the near-wall region. Besides, either the interaction between protons of the liquid and the spins of hydrogen atoms of the surface hydroxyl groups or proton exchange can produce additional fluctuating magnetic fields.^{148, 193} Paramagnetic ions or other paramagnetic centres that can exist on the surface or in the near-surface layer of the solid have the strongest effect on the relaxation of fluids.

The relaxation of liquids in silica-based rocks (sandstone rocks) is mostly associated with the presence of paramagnetic ions (*e.g.*, iron or manganese ions).^{194, 195} Their concentration can be as high as several per cent, the iron ions being more abundant.¹⁹⁶ In this case, relaxation is due to the dipole and scalar interactions between the electron and nuclear spins. These interactions are frequency modulated by the relaxation flips of the electron spin and by finite residence time of the molecule on the surface of the solid. The latter reason seems to be insignificant since no pronounced temperature effect was observed.¹⁹⁴ In addition, sandstone rocks sometimes contain particles of magnetic minerals, such as magnetite (Fe_3O_4), which favour an increase in the relaxation rate.¹⁹⁷ Often, sandstone rocks contain clays that possess a rather large specific surface area but have weaker effect on the relaxation parameters.¹⁹⁶ Carbonates are characterised by longer relaxation times compared to sandstone rocks.¹⁹⁷

The relaxation times of systems containing several liquids can strongly depend on the wettability of the pore surface and on the procedure for sample preparation (*e.g.*, on the order in which the pores are filled with different liquids). For instance, experiments with hydrocarbons and water contained in the pores of rock samples showed that the former have longer relaxation times than the latter. This is presumably due to the presence of a monolayer of water on the pore surfaces even in the initially dried samples.¹⁹⁴

Exchange between the surface layer and the bulk of the liquid or gas in the pore is responsible for a finite residence time of the molecules on the surface. The exchange rate strongly affects the results of measurements. The evolution of the magnetisation of a liquid in an isolated pore was studied in detail earlier.^{198, 199} In the case of slow exchange the amplitude of the relaxing magnetisation is different at different distances from the pore surface and the relaxation behaviour is a multiexponential superposition of the amplitudes of the magnetisation of different pore regions. At moderate exchange rates, interpretation of the relaxation behaviour is complicated. For a binary system with two times T_1 , the magnetisation relaxation is described by a sum of two exponents; however, the T_1 values and the contributions of the two components can be substantially different from true values. Moreover, at $T_1 > T_2$ the T_2 -relaxation can exhibit a biexponential behaviour while the T_1 -relaxation can remain single-exponential.¹⁹² The times T_1 and T_2 of the molecules in the surface layer can mainly be determined by different motions (*e.g.*, molecular rotation and reorientation of the axis of rotation).

The simplest case is fast molecular exchange between the near-wall layer and the volume of the pore (fast diffusion or slow surface relaxation). In this case the liquid in the pore exhibits a single-exponential relaxation behaviour even provided a non-

exponential temporal dependence of the relaxation of the molecule located on the pore wall. This holds if²⁰⁰

$$T_1 > \frac{r^2}{6D}, \quad (8)$$

where r is the pore radius and D is the diffusion coefficient of the molecules of the liquid. This condition is met if $r < 10\text{--}100\text{ }\mu\text{m}$ (e.g., for many sandstone rocks). In this case, the simplest model of relaxation of the liquid in the pore is a two-site model with fast exchange, according to which²⁰¹

$$\frac{1}{T_1} = \frac{a}{T_{1v}} + \frac{b}{T_{1p}}, \quad (9)$$

where a and b are the fractions of the liquid in the bulk and on the surface, respectively; and T_{1v} and T_{1p} are the corresponding relaxation times T_1 . The volume of the surface layer is often assumed to be equal to the product of the pore surface area, S , and the layer thickness, λ , though this can be not universally true for the smallest pores owing to high curvature of their surfaces.²⁰² Then one gets¹⁹⁴

$$\frac{1}{T_1} = \left(1 - \frac{\lambda S}{V}\right) \frac{1}{T_{1v}} + \frac{\lambda S}{V} \frac{1}{T_{1p}} \approx \frac{1}{T_{1v}} + \rho_1 \frac{S}{V}, \quad (10)$$

where V is the pore volume and ρ_1 is the surface relaxivity of the nuclear spins.

The reasons responsible for shortening of the times T_1 also cause shortening of the times T_2 of the liquid in pores. In addition, the rate of the transverse relaxation also increases due to molecular diffusion in the presence of local field gradients that can be produced owing to inhomogeneity of the external magnetic field near the boundary between the phases with different magnetic susceptibilities.^{86,203} Therefore, the T_2 time distribution allows characterisation of the pore sizes only if the experiments are carried out in relatively weak fields ($< 500\text{ G}$) and/or with multiple refocussing of the NMR signal using the CPMG pulse sequence. In this case, one can write for T_2 an expression analogous to Eqn (10):

$$\frac{1}{T_2} = \frac{1}{T_{2v}} + \rho_2 \frac{S}{V}. \quad (11)$$

Often, the first term in the right side of expressions (10) and (11) is small and can be neglected.¹⁹⁴

Interpreting the T_2 values is a challenge;²⁰⁴ nevertheless, relaxation porosimetry based on the T_2 measurements has found a number of practical applications. To take into account the effect of the local magnetic field gradients on the T_2 values, the parameter ρ_2 is sometimes assumed to be a function of the applied magnetic field. This implies a non-spherical shape of the pore; otherwise, application of external magnetic field cannot produce local field gradients. However, the pore surface is not ideally smooth; therefore, even for a spherical pore one should expect rather large local field gradients in the immediate vicinity of the surface.²⁰⁵

If all pores have an identical shape, the V/S ratio is a measure of the pore size. In the case of non-spherical pores (long cylindrical pores or slit-like pores) the relaxation porosimetry measurements are sensitive to the smaller size.²⁰⁴ Determination of the pore size requires knowledge of the surface relaxivity which can be found from calibrations which utilise sample-independent techniques of pore size measurements. In practice, the surface of the pore space has fractal character (that is, the measured value of the surface area is a function of the length scale that is used for measurements). Therefore, the surface relaxivity values strongly depend on the type of the sample-independent calibration technique. In particular, the V/S ratio and the surface relaxation parameters can be extracted from an analysis of the results of the effective diffusion coefficient measurements of the gas or liquid molecules

in the pores, as it was done in, e.g., studies of some natural rocks.¹⁷⁴ Another procedure for determining the ρ_1 and ρ_2 values involves measurements of the relaxation times using the samples characterised by a monolayer coverage of the surface of the pore space.²⁰⁶ For the model media (e.g., bead packs), the V/S ratio can be calculated.²⁰⁷

The surface relaxivity values vary over a wide range from 10^{-7} to 10^{-3} m s^{-1} . For water in synthetic materials the ρ_1 values usually span the range from 1×10^{-4} to $20 \times 10^{-4}\text{ m s}^{-1}$ (see Ref. 196). Typical of water in sandstone rocks are the values $\rho_1 \sim 2.5 \times 10^{-6}\text{ m s}^{-1}$ and $\rho_2 \sim 5 \times 10^{-6}\text{ m s}^{-1}$, while water in carbonate rocks is characterised by the parameters $\rho_1 \sim 0.8 \times 10^{-6}\text{ m s}^{-1}$ and $\rho_2 \sim 1.7 \times 10^{-6}\text{ m s}^{-1}$. Experiments with different samples of natural rocks showed that the ρ_1 value varies only slightly despite the fact that the concentration and type of paramagnetic impurities can vary over a wide range from one sample to another (see below). The ρ_1 parameter of water in limestone rock, chalk and sandstone rock cores was reported to vary from $\sim 7 \times 10^{-6}$ to $23 \times 10^{-6}\text{ m s}^{-1}$.²⁰⁷

The effect of paramagnetic ions on the relaxation times of liquids has been studied in detail. For instance, calcite powder packs with known concentration of manganese were prepared by centrifuging the suspension of calcite particles (10 or $30\text{ }\mu\text{m}$) in water with addition of aqueous MnCl_2 solution.¹⁹⁵ Then, the surface layer of the liquid was removed. For all samples, the spin-lattice relaxation was found to be single-exponential. The specific surface areas of the powder packs were measured using low-temperature adsorption of nitrogen. It was found that high concentrations of adsorbed manganese increased the parameter ρ_1 by a factor of ~ 50 (up to a value of $2.4 \times 10^{-5}\text{ m s}^{-1}$) and that an increase in the initial concentration of manganese led to saturation of this parameter. This can be the reason why various natural rock samples are characterised by similar ρ_1 values. Moreover, long contact times of calcite with manganese caused a decrease in the ρ_1 value despite an increase in the amount of the adsorbed manganese. Presumably, some adsorbed manganese becomes buried by freshly precipitated calcite. NMR experiments revealed that only the ions in the outermost atomic layer affect the relaxation. Analogous experiments with Co^{2+} ions showed that these ions have virtually no effect on the relaxation times of water, whereas adsorbed iron ions shorten the T_1 value of water (however, to much lesser extent compared to Mn^{2+} ions). Thus, relaxation owing to the presence of manganese predominates for limestone rocks and possibly plays an important role for sandstone rocks. Flowing a $4\text{ }\mu\text{M}$ aqueous solution of a Mn^{2+} salt through a sample of natural limestone rock led to a decrease in the T_1 value of water by a factor of ~ 6 due to adsorption of Mn^{2+} ions on the surface. Partial desorption of manganese and dissolution of the sample under the action of an aqueous solution of ethylenediaminetetraacetic acid caused partial recovery of the initial T_1 value of water.

Kleinberg *et al.*¹⁹⁶ prepared powder packs of the α -modification of calcium silicate with known concentrations of iron or manganese paramagnetic ions by centrifuging suspensions in water and measured the relaxation times T_1 and T_2 of the samples with different content of Mn and Fe. It was found that the T_1 and T_2 values are virtually temperature independent in the range between 25 and $175\text{ }^\circ\text{C}$. Hence, diffusion, molecular motions and the residence time play an insignificant role and the surface relaxation cannot be due to thermally activated processes such as adsorption and translational and rotational motions. The parameters ρ_1 and ρ_2 were found to be linearly proportional to the manganese and iron concentration, the slopes of the corresponding plots constructed for Fe and Mn being comparable in magnitude. In the limit of zero concentration of these elements, the ρ_1 and ρ_2 values can be determined by the concentration of point defects on the crystal surfaces. Clay-bound water does not mix with water filling the pores and gives a separate peak in the T_2 distribution.

Clearly, in real porous media the pores are interconnected and voids are not filled with fluid. Therefore, the model of the evolution of the magnetisation in isolated pores^{198, 199} is a particular case of a more general model that treats a system of pores filled with a fluid and interconnected by narrow channels.²⁰⁸ If no fluid transport occurs in the system of pores, the relaxation time distribution corresponds to a superposition of the relaxation times of the fluid in individual pores. If the connectivity of the system of pores is low, the relaxation time distribution is broadened and shifted towards shorter times. If the connectivity of the system of pores is high, the relaxation time distribution again becomes narrower and exhibits a maximum at a value determined by the ratio of the total surface area to the total volume of the pores in the sample. If the pores are connected by very narrow channels, the latter can act as efficient relaxation sinks. From the standpoint of the fluid relaxation measurements, this allows one to treat the pores as isolated.^{201, 209} It should be emphasised that if the surface relaxation dominates, the rate of the change in the magnetisation at short times is proportional to the ratio of the total surface area to the total volume of the pore space irrespective of the pore system connectivity.

Samples of synthetic porous materials are characterised by relatively small structural inhomogeneities. Therefore, the molecules have time to 'explore' the pores of all sizes during the NMR experiment; this often leads to single-exponential relaxation. On the other hand, relaxation of fluids in rocks is non-exponential since the observation time is too short for the molecules to travel the distances comparable with the length scales of structural inhomogeneities.

Thus, if pores can be considered isolated in the time scale of the NMR experiments, the magnetisation relaxation is a superposition of the contributions of pores of different sizes and the relaxation time distribution correlates with the pore size distribution. The results of relaxation measurements are analysed using the average T_1 value or a number of models that represent the experimental data by the sum of several (from 1 to 3) exponents or as stretched exponential functions

$$M_{xy}(t) = M_0 \exp \left[- \left(\frac{t}{T_2} \right)^\alpha \right], \quad (12a)$$

$$M_z(t) = M_0 \left\{ 1 - 2 \exp \left[- \left(\frac{t}{T_1} \right)^\alpha \right] \right\}. \quad (12b)$$

Computer simulation of the magnetisation relaxation by the random walk method showed that expressions of the type (12) are physically substantiated. However, this model has a significant drawback consisting in the impossibility of back extrapolating the experimental data to time zero at $\alpha < 1$, which precludes a correct estimation of the spin density (amount of fluid). To overcome this problem, a modified model²¹⁰ has been suggested

$$M_{xy}(t) = M_0 \exp \left[- \frac{t}{\tau_0} \left(1 + \frac{t}{\tau_c} \right)^{\beta-1} \right], \quad (13)$$

where τ_0 , τ_c and β are empirical parameters.

At short times, this function describes a single-exponential decay corresponding to the weighted sum of the initial rates for each relaxation time in the entire distribution of relaxation times. At long times, the function is transformed into expression (12a). Using this model, relaxation measurements of a total of 50 rock samples saturated with different fluids were carried out in different magnetic fields. The model (13) exhibited some advantages in determining the amount of fluid by back extrapolation of the experimental data to time zero, especially for partially saturated samples after centrifuging. Correlation between the parameters of the model and the petrophysical properties of the samples has been discussed. Applicability of the model for representing the T_1 -relaxation data has been pointed out.²¹⁰ The virtue of the models (12) and (13) is their compactness.

Theoretical approaches involving either discrete or continuous distributions, $f(T_1)$, have been widely used in fluid relaxation studies. In this case, the magnetisation relaxation is described by the following expression

$$M(t) = M_0 \left[1 - 2 \int_0^\infty f(T_1) \exp \left(- \frac{t}{T_1} \right) dT_1 \right]. \quad (14)$$

Using appropriate models, the $f(T_1)$ distributions can be converted into the pore size distributions. For rocks, the T_1 values usually span the range from 1.5 to 3 orders of magnitude. Reconstruction of the relaxation time distribution function from experimental data is an ill-posed problem. Solving this problem requires specific theoretical approaches (*e.g.*, regularisation).^{203, 207}

Typical of many samples is fast diffusion within pores. This is confirmed by, *e.g.*, the lack of strong temperature dependence of the relaxation times in the range between 25 and 75 °C, which indicates that diffusive motion is not a rate-limiting process.¹⁹⁴ In this case, each pore of a particular size is characterised by exponential relaxation with its own time constant T_1 . More sophisticated models involve a multisite exchange and a number of T_1 values for arbitrary rate of exchange between the components within each pore. This is significant for mesoscopic and macroscopic pores in which the fast diffusion limit cannot be reached. For instance, relaxation of the longitudinal magnetisation was simulated with a pore size distribution in the form of a sum of three log-normal distributions. The procedure was evaluated using a model data set with known pore size distribution and the factors affecting the reliability of the reconstructed pore size distribution were analysed.²⁰¹ The results of computer simulation of the experimental T_1 measurements allowed one to obtain the pore size distributions for brine-saturated sandstone rock and limestone rock samples.²⁰⁹ The ρ_1 value was assumed to be 10^{-4} m s^{-1} . Inapplicability of this technique to large pores (hundreds of micrometres) due to the loss of sensitivity to the exact shape of the pore size distribution was pointed out.

In the case of (quasi-)continuous distributions the values of the function $f(T_1)$ are often reconstructed²¹¹ using a discrete set of argument values (~ 100 points). This is an ill-posed problem complicated by noisiness of the experimental data. Considerable attention has been given to solving this problem.²¹² The major drawbacks of most of algorithms consist in broadening sharp $f(T_1)$ peaks and replacing broad $f(T_1)$ distributions by a set of narrower peaks. An algorithm has been proposed, which is free from these drawbacks.^{212, 213} The procedure was evaluated taking a model data set as an example and then used for reconstruction of the function $f(T_1)$ for a number of samples of water-containing ceramics and brine-saturated sandstone rock cores.

The nuclear spin relaxation times of water in crushed porous glass of different pore sizes and amounts of the adsorbed fluid were studied.^{191, 214} Nearly single-exponential relaxation (T_1 , $T_{1\rho}$, T_2) was observed in all the experiments. The measured relaxation times were analysed in the framework of the model of fast proton exchange between the surface layer and bulk water. The relaxation times of water in the first monolayer were found to be $T_1 = 150$ and $T_2 = 0.5 \text{ ms}$.²¹⁴ Relaxation (at least, the T_1 relaxation) is due to modulation of the dipole–dipole interaction of the nuclear spins, which allowed one to estimate the correlation times, τ , of rotational molecular motion. It was found that $\tau \sim 20\tau_0$ for water in the first monolayer, $\tau \sim (6-10)\tau_0$ for water in the second monolayer and $\tau \sim \tau_0$ for the rest of adsorbed water, where τ_0 is the correlation time of bulk water (of the order of 10^{-11} s), the lifetime of the water molecules in each state being no longer than 0.5 ms .²¹⁴ According to the results of $T_{1\rho}$ dispersion measurements (dependence on the amplitude of the RF field in the spin-locking experiments), fast rotational motions with a characteristic correlation time of 10^{-8} s are accompanied by much slower motions, namely, reorientations of the rotation axis of the molecule after every 10^{-5} s .¹⁹¹

Correctness of the relaxation model was confirmed by the results of relaxation studies with controlled variation of pore saturation level which was achieved either by adsorption of a known amount of liquid by a dry sample or by centrifuging a saturated sample.^{194, 204} In the latter case, an increase in the centrifugation rate led to removal of the liquid from progressively smaller pores. Experiments with water in porous glass showed that smaller pores have a stronger effect on the relaxation times¹⁹¹ that are shortened as the pore saturation level decreases,^{191, 214} which is consistent with the relaxation model.

Gradual increase in the content of water in silica samples with different pore sizes revealed the biexponential T_2 relaxation.²⁰² A model of the pore filling with water, which takes into account the dependence of the contributions and the individual relaxation times of the two water components, is as follows. Initially, an increase in the pore saturation level leads to an increase in the surface area covered by the water monolayer and to an increase in the number of the smallest water droplets at the pore corners. Then the surface is covered by the second monolayer of water molecules while water droplets begin to grow and merge until complete filling of the pores. Another picture was observed for cyclohexane in conventional silica and for water in hydrophobic silica with methyl groups attached to its surface. In these cases the pore filling occurred uniformly starting from the smallest pores. Analysis of the experimental data allowed determination of the surface-area-to-volume ratio for water and of the number of water droplets at the pore corners at different saturation levels.²⁰²

Various rock cores saturated with water or brine have been studied using controlled variation of the saturation level. Computer simulation of the relaxation data was carried out with the sum of three exponents,²⁰⁰ expressions of the types (12a) and (12b)²⁰⁶ or with continuous relaxation time and pore size distributions.^{92, 207} In all cases, the measured relaxation times agreed with the assumption that during the saturation process the smallest unoccupied pores are filled out first, while during the drainage the largest occupied pores are first to be emptied. The pore size distribution peaks also shifted towards smaller pore sizes, which can be associated with the presence of partially filled pores.²⁰⁷ It was found that the relaxation times of water in sandstone rock²⁰⁶ are temperature independent in the range between 13 and 60 °C and that the T_1/T_2 ratio lies between 1.4 and 3.2. The longest-to-shortest T_1 ratio is 1800, which is in satisfactory agreement with the largest-to-smallest pore radius ratio in the sample.²⁰⁰ Analysis of results of measurements at different saturations allowed extraction of the pore size range without determining the S/V ratio for the entire sample with completely filled pores. It was found that the relationship between the average relaxation time and the saturation level (C) has the form

$$\langle T_1 \rangle = 1.29 C^{1.26}. \quad (15)$$

This correlation can be useful when determining the absolute values of saturation levels of the sample from relaxation measurements.

Agreement between the calculated and experimental data can be substantially improved by using a model with inclusion of narrow inter-pore channels that are filled first, thus determining the relaxation properties at low saturations.²⁰⁶ This allowed one to estimate the volume ($\sim 4.5\%$) and diameter (0.75 μm) of these channels. The channel size is in agreement with the observed water–vapour percolation threshold occurring when the thickness of the adsorbed layer becomes equal to the radius of the channel. The pore sizes obtained from mercury porosimetry studies are by an order of magnitude smaller since this technique is mostly sensitive to the sizes of the inter-pore throats.²⁰⁷ Mass transport can alter the NMR signal from the liquid in small pores. The residual saturation is due to the presence of capillary-bound water and, probably, water in isolated cavities.⁹²

Spatially resolved relaxation porosimetry experiments are also possible. This allows mapping the pore saturation level and pore sizes for each pixel of the image. For instance, catalyst granules¹¹⁰

and water-saturated sandstone rock cores were studied using this technique. Some samples were modified by attaching a silane chain to the surface of the pore space.⁹⁰ The experimental porosity values of these samples were found to be in agreement with the results of mercury porosimetry measurements. It was found that modification of the surface causes a twofold increase in the T_1 and T_2 values of water in pores, which permits wettability studies of the surface of the pore space. The modified sample was characterised by equal T_1 values of the surface water and bulk water, which means that the surface has no effect on the spin-lattice relaxation.

Relaxation porosimetry can also be applied to studies of other materials. In particular, the sizes of the pores left in the food systems and gels after freeze-drying at a reduced pressure characterise the sizes of initial ice crystals. Knowledge of the size distribution allows optimisation of sublimation conditions to improve, *e.g.*, quality of food after thaw. For instance, starch gel was freeze-dried at a reduced pressure and then filled with acetone.²⁰⁵ Samples of different compositions were studied at different freezing rates and the T_2 distributions were determined (T_2 values varied from 55 ms to 2.5 s). Measurements in different magnetic fields revealed rather large local field gradients. Freezing of a cylindrical sample caused the formation of ice crystals (pores), whose sizes increased in the radial direction from the centre to the surface of the sample. The pore sizes in the samples of 10% and 15% gels were different. Calculations performed assuming spherical pores led to the ρ_2 values spanning the range from 1.2×10^{-5} to $4.2 \times 10^{-5} \text{ m s}^{-1}$, which is of the same order of magnitude with the surface relaxation coefficient at the water/glass interface ($3.5 \times 10^{-5} \text{ m s}^{-1}$). The results of these experiments were compared with those of the scanning electron microscopy studies.

Nuclear magnetic resonance logging is one of the most prominent examples of practical implementation of the NMR porosimetry. Borehole logging is used in studies of the deep-earth properties of rocks. One of the most important applications of this method is investigation of the properties of the petroleum and gas fields (in particular, determination of the content of petroleum, gas and water and studies of the interactions of these fluids with rocks). The NMR logging experiments involve lowering a device containing the source of the magnetic field (a magnet or a coil) and a RF coil for creation of the RF field and reception of the NMR signal down a borehole. In this case, the NMR signal comes from the region that is outside the device (within the thickness of the rock mass)^{197, 215–218} at a depth up to several centimetres from the borehole wall. (For comparison, in an NMR spectrometer the sample is located inside the probe). There is a number of different designs of the NMR logging devices.¹⁹⁷ All of them use relatively low magnetic fields; therefore, only the ^1H NMR measurements provide sufficiently high sensitivity. Weak non-uniform magnetic field precludes separation of the contributions of the hydrocarbons and water to the NMR signal based on the chemical shifts.¹⁹⁷ On the other hand, the amplitude of the NMR signal characterises the content of the fluid while the relaxation times correlate with the pore sizes and the types of the fluids filling the pores. This allows determination of such borehole characteristics as the free fluid index, porosity and rock permeability.²¹⁹ Because of the low sensitivity of the method, the T_2 measurements are most often used since they can be performed much faster compared to the T_1 measurements. The relaxation times T_2 of unbound fluid are usually much longer than those of the bound fluid; therefore, analysis of the results of measurements of the T_2 distributions permits separation of the contributions of the unbound and capillary-bound fluid.^{197, 219} Most of rocks possess hydrophilic properties; therefore, the hydrocarbon is at the centre of the pore and does not contact the surface. In this case, the relaxation times of the hydrocarbons of low viscosity are much longer than those of water, which makes it possible to separate their contributions to the NMR signal.¹⁹⁷ Using empirical correlations between the viscosity and the T_2 values of hydrocarbons, one can determine the properties of the hydrocarbon pools and the hydrocarbon

type.²¹⁹ Based on the knowledge of the pore size distribution, the permeability of and the capillary pressure in porous media can be estimated. It was empirically found that the permeability of water-saturated sandstone rocks is proportional to the square of the relaxation time.¹⁹⁷ This is in agreement with expressions (10) and (11) assuming the rock permeability to be proportional to the $(S/V)^{-2}$ ratio.

The contributions of water and hydrocarbons to the NMR signal can be separated even at equal relaxation times.²¹⁹ To avoid explosive outbursts, drilling is carried out under excessive pressure which causes permeation of the fluid from the borehole into the rock. Therefore, the near-wall region used for the NMR measurements contains a mixture of the formation and borehole fluids. By doping the fluid injected in the borehole with water-soluble paramagnetic additives one can substantially shorten the relaxation times of water in the rock without changing the relaxation rates of hydrocarbons. In practice, a number of different types of the logging devices is simultaneously lowered down the borehole. Comparison of the results obtained by different methods allows better characterisation of the borehole.

3. Cryoporosimetry

Using the NMR technique, one can easily distinguish between the fluid and the solid based on considerably different relaxation times. For instance, freezing of water leads to shortening of the time T_2 from 1.8 s to 6 μ s (see Ref. 220). A short time T_2 means that the transverse magnetisation (the NMR signal) experiences a rapid decay. Therefore, the use of a time delay of the order of 20 μ s before recording the free induction decay or the recording of the spin echo signal allows one to exclude the contribution of the frozen fluid to the NMR signal. In addition, the T_1 value of ice (~ 900 s at 263 K in a 7.05 T field)²²¹ much exceeds the T_1 value of liquid water (2.7 s). Hence, the NMR signal of ice is additionally suppressed due to saturation. This permits selective detection of the signal of the liquid phase (see Fig. 6).

The pore liquid has a lower temperature of the liquid–solid phase transition. This effect is analogous to the capillary effect and is a result of a change in the free energy caused by the curved surface of the liquid. Reduction of the temperature of the liquid–solid phase transition can be described by the Gibbs–Thomson (Kelvin) equation written in the form^{222, 223}

$$\Delta T = T_0 - T_c = \frac{2\sigma T_0}{R\Delta H\rho} = \frac{K}{R}, \quad (16a)$$

or as follows²²¹

$$\Delta T = T_0 - T_c = \frac{K}{R - d}, \quad (16b)$$

where T_0 is the phase transition temperature for the bulk liquid; T_c is the phase transition temperature for the pore liquid; σ is the surface energy at the liquid–solid interface; R is the radius of ice crystal; ΔH is the molar heat of fusion; ρ is the density of the solid; and d is the thickness of the surface layer which freezes at a lower temperature compared to the rest of the liquid in the pore of radius R . The parameters K and d depend on the nature of the system under study. The surface layer behaves as part of the pore surface;²²⁴ therefore, the pore radius is $R - d$. Sometimes, calculations give negative values of the parameter d and this interpretation loses its meaning. After rewriting²²⁵ expression (16b) in another form

$$\Delta T = T_0 - T_c = K^* \frac{R}{R - d} \frac{1}{R}. \quad (16c)$$

one gets a new physical interpretation, namely, the molar heat of fusion that appears in the expression for K becomes pore size dependent.

The parameter K can be found by comparing the results of the NMR experiments with the data obtained by conventional methods, e.g., low-temperature adsorption of nitrogen. The

parameters for water were found to be $K_w = 495$ K $\text{\AA}$, $d_w = 3.5$ $\text{\AA}$,²²⁴ and $K_w \approx 515$ K $\text{\AA}$ and $d_w \approx 3$ $\text{\AA}$.²²⁵ Benzene ($T_0 = 278.5$ K) or cyclohexane ($T_0 = 279.5$ K), which are more sensitive to small variations of temperature, are used instead of water in the case of large pore sizes. The parameters for cyclohexane are $K_c \approx 1800$ K $\text{\AA}$ (see Refs 222 and 226) and $K_c \approx 870$ K $\text{\AA}$, $d_c \approx -1.4$ $\text{\AA}$ ²²⁵ while those for benzene are $K_b \approx 1100$ K $\text{\AA}$ and $d_b \approx 7$ $\text{\AA}$.²²⁵ For all liquids, the parameter K was found to be only slightly dependent on the nature of the porous material.²²⁴ Formulae (16b) and (16c) lose their meaning at $R \leq d$; in addition, the filling of micropores is strongly affected by the properties of the fluid and the microporous material. Therefore, the application of this method to microporous objects is still to be clarified. Nevertheless, the technique allows experimental determination of the volume fraction of micropores.²²⁴

Nuclear magnetic resonance porosimetry experiments with slow cooling of the pore fluid or heating of a preliminarily frozen sample are used to obtain the plots of the dependences of the integrated amplitude of the NMR signal on temperature (IT -curves) or on the inverse temperature $I(1000/T) = I(X)$. For some samples the cooling–heating cycles exhibit hysteresis effects of the order of several degrees. Often, measurements are carried out only during heating the sample to avoid supercooling of the fluid. The experimental data should be processed taking into account the temperature dependences of other parameters affecting the NMR signal, such as the Boltzmann factor (Curie law), the Q -factor of the RF coil and the relaxation times. Usually, the integrated intensity of the NMR signal is determined to an accuracy of several per cent.

Often, experiments are carried out with excess amount of fluid to ensure a complete pore filling. The fluid on the outer surface of the material freezes at the normal freezing temperature and is readily distinguishable in the IT -curves, which allows determination of the S/V ratio for the sample under study.

The $I(X)$ curve is given by the following expression²²⁴

$$I(X) = \sum_{i=1}^N \frac{I_{0i}}{\sqrt{\pi}} \int_0^{(X-X_{ci})/\sqrt{2\Delta_i}} \exp(-u^2) du. \quad (17)$$

The derivative,

$$\frac{dI}{dX} = \sum_{i=1}^N \frac{I_{0i}}{\sqrt{\pi}} \exp\left(-\frac{X-X_{ci}}{\sqrt{2\Delta_i}}\right)^2 \quad (18)$$

is the sum of Gaussian functions with the transition temperatures $T_{ci} = 1/X_{ci}$, widths Δ_i and weights I_{0i} . The correlation time distribution of molecular motions is assumed to be log-normal.

Taking into account Eqn (16a), the differential pore size distribution can be represented as follows:²²⁵

$$\frac{dI}{dR} = -\frac{K}{R^2} \frac{dI}{dR}. \quad (19)$$

The pore sizes that can be measured using the NMR cryoporosimetry technique span the range from ~ 10 to 2000 $\text{\AA}$.^{221–223, 225}

The IT -curves of water in silica were measured.^{224, 225} The broad component corresponding to the largest X value ($T = 210$ K) was attributed to the phase transition at the interface between the pore surface and the rest of the solid ice within the pore.²²⁴ Simultaneous fitting of the data obtained for samples with different pore sizes allowed one to avoid the necessity of independent determination of the parameters K and d . The silanol groups were found to contribute to the NMR signal.²²⁵ The NMR spectrum of benzene in silica and zeolite Y (pore size 7.4 $\text{\AA}$) at 227 K comprises several broad overlapped lines. Assuming fast proton exchange between the fluid at the pore wall and the rest of the fluid in the pore, the average chemical shift value was found to be dependent on the thickness, d , of the surface layer. Estimations from positions of the NMR signals give the same value as that obtained from analysis of the IT -curves. The chemical shift

appreciably changes as the pore radius R changes in the mesopore range (at $R > 10$ Å) while it remains virtually unchanged for micropores ($R < 10$ Å). This can be used for the determination of the volume fraction of micropores in the sample. The results obtained were found to be in good agreement with those found by low-temperature adsorption of nitrogen.

It is convenient to perform model experiments using the mesoporous material MCM-41 which possesses a hexagonal array of identical one-dimensional mesopores of size in the range from 18 to 100 Å. Some of the IT -curves of water exhibited characteristic hysteresis effects between cooling and heating processes, while the results of several cooling–heating cycles were identical, which means that the phase transition causes no mechanical damages to the pore space.²²⁴ The IT -curves of MCM-41 with a pore size of 26 Å exhibited¹⁹³ a narrow phase transition at 226 K. In addition, a broad (without hysteresis) transition was observed^{193,227} in the temperature range 200–207 K, which corresponds²²⁷ to a total of more than 60% of the overall amount of water and cannot be attributed to the fluid in micropores due to their lack. It was assumed²²⁷ that the pore contains a layer of the fluid ~ 5 Å thick, which gradually freezes at a lower temperature compared to the rest of the fluid in the pore. This is in agreement with substantial broadening of the NMR signal on cooling due to a decrease in the molecular mobility and to enhancement of the effects associated with differences in the magnetic susceptibilities.²²⁷

At the same time, it is possible that the low-temperature phase transition is only an apparent transition. Mention has been made¹⁹² that if the correlation time distribution of the molecular motions is broad, cooling can lead to observation of an apparent phase transition when performing the T_2 NMR measurements. This transition is associated with reduction of the molecular mobility and with passage from exponential relaxation to the rigid lattice regime with a Gaussian relaxation decay. Such a transition is not accompanied by changes in the phase state and is manifested only in the NMR experiments. For instance, studies of water adsorbed on silica gel and on porous glass with the pore sizes 60 to 240 Å revealed not only the phase transitions at 273 K for the excess water and at 265 K (with hysteresis) for the pore water but also an apparent transition in the temperature range 120–255 K, which occurs smoothly without hysteresis.²²⁰ Only a water layer two or three monolayers thick is involved in the apparent transition. The corresponding distribution of correlation times is shifted towards longer times as the temperature decreases. This is accompanied by retardation of proton exchange between the molecules with different T_2 values. Studies of the samples with controlled pore filling showed that initially the amount of non-freezing water increases as the amount of adsorbed water increases and then is saturated at a level corresponding to coverage of the surface of the pore space by two or three monolayers of water. The ‘non-freezing water’ does not assume the structure of ice on cooling below the freezing point and differs from liquid water at high temperatures.

Combining the results of analysis of the temperature dependences of the parameters ΔT and $1/T_1$ allowed determination of the enthalpy of freezing of bound water and of the width of the correlation time distribution of water molecules.^{193,220} The ΔT and $1/T_1$ values are inversely proportional to the pore sizes; because of this, a linear correlation between ΔT and $1/T_1$ was observed²²⁸ for water in MCM-41 with the pore sizes ranging from 19 to 38 Å at 263 K.

The results obtained for water in MCM-41 are in good agreement with the data obtained by low-temperature adsorption of nitrogen and by high resolution electron microscopy.²²⁴ However, expression (18) cannot describe the experimental data for the microporous material (aluminophosphate molecular sieves VPI-5).

By varying the pore saturation level one can study the process of filling of porous materials with fluids. Controlled saturation (10%–100%) studies of porous silica (silica gel with 60 Å pores)

with water or cyclohexane have been reported.²²⁶ The samples were initially cooled down to 173 K (cyclohexane) or 223 K (water) and the measurements were carried out during heating. It was found that cyclohexane fills out the entire pores starting from the smallest ones, whereas water initially forms droplets whose size is much smaller than that of the smallest pores in the sample. The size of the water droplets increases as the saturation level of the sample increases. The freeze–thaw cycles have no effect on the characteristics of the pore space. The character of the relaxation time distribution of cyclohexane is such that the pore size distributions exhibit false peaks.²²⁶ In addition, solid cyclohexane undergoes a phase transition from a monoclinic crystal structure to a plastic f.c.c. crystal at 186 K.²²⁹ Measurements of the relaxation times T_2 and $T_{1\rho}$ in the temperature range 77–295 K for cyclohexane in silica gel with pores of size 60, 200 and 500 Å revealed a phase transition in solid cyclohexane in the two last-named samples.

Spatially resolved (1D, 2D and 3D) IT -curves of water and cyclohexane in porous silica of different pore sizes have been reported.^{222,223} The NMR signal was calibrated against that of isopentane which has a low freezing point. The results obtained allowed determination of the pore size distribution at any point of the sample²²³ and imaging of those regions of the object that contained pores of preset sizes.²²² The relaxation time T_2 of solid cyclohexane was ≤ 2 ms.

Spatially resolved NMR cryoporosimetry was used for determination of the size of filled pores in partially dried concrete prepared from white Portland cement and quartz filler.^{230,231} On cooling, freezing began at the centre of the sample (this region is characterised by larger amount of water and by filling of larger pores).²³⁰ Further cooling led to uniform freezing of water along length of the sample. No freezing of water occurred in the gel pores even at -53 °C. The apparent phase transition in the form of a slow (without hysteresis) change in the amplitude of the NMR signal was also observed. The 1D moisture profiles of cylindrical concrete and mortar samples were obtained simultaneously and their changes were traced during cooling down to 223 K. This experiment allowed one to determine the size of the filled pores along the length of a cylindrical sample.²³² The sample completely saturated with water exhibited a phase transition at ~ 273 K corresponding to a wide range of mesopores. The samples of partially water-saturated concrete and mortar exhibited identical distributions of the filled pore sizes. It was found that most of the water resides in the pores of size less than 6 nm. Characteristic of all samples was a dramatic decrease in the NMR signal amplitude at ~ 223 K. This is associated with desorption of water followed by the formation of ice in another regions of the sample. At 218 K, nearly 50%–55% of water exists in the form of ice. The relaxation times (T_1 , T_2 and T_2^*) were mapped and it was shown that the times T_2 and T_2^* are shortened while the time T_1 is lengthened as temperature decreases.

* * *

The features of NMR image contrast formation allows the use of the NMR imaging technique for obtaining a vast variety of information on the objects under study. The authors of this review tried to emphasise some salient features and to illustrate potential applications of this method. Additional information on the studies of the structure and properties of liquid-containing materials is presented in the Supplement.

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V. Supplement

Additional information on the studies of the structure and properties of liquid-containing materials is given in Table S.1.

Table S.1. Applications of the MRI technique based on the ^1H NMR signals.

Magnetic field /T	Object, process	Technique	Dimension	Spatial resolution characteristics ^a	Recording time	Ref.
1.4	Water + 0.1% CuSO_4 in a pipe with abrupt contraction (expansion)	spin echo + PRI	2D	64×64 , a slice 0.33 mm thick	—	19
0.73	Plastic or rubber articles	gradient echo with oscillating gradients	3D	$64 \times 64 \times 64$, (0.5 mm) ³	3 h 38 min	26
4.7	Vulcanised rubber impregnated with aluminium and sodium sulfate crystals; filled phenol-formaldehyde resin; a 72-h <i>Manduca sexta</i> caterpillar	spin echo or PRI	2D	180° FIDs, (35 μm) ² for PRI 128×128 , a slice 1 mm thick or without slice selection	from 2 to 17 h	27
0.7	Sandwich-type layered model sample; alkyd resin film coated with cobalt catalyst	spin echo	1D	256, 512; 13, 6.5 μm	17 min	83
0.4	Various solid materials	the same	—	WSR	—	84
2.0	Water in Al_2O_3 , water + NaCl in sandstone rock or limestone rock cores	"	2D, 3D	128×128 , (200 μm) ² , a slice 5 mm thick (2D); $128 \times 128 \times 256$, (300 μm) ³ (3D)		86
0.1	Water in sandstone rock plugs	"	1D, 3D	1 mm (1D); $2.4 \times 2.4 \times 7$ mm (3D)	3 min (1D); 1 h (3D)	90
2.0	Oil + water or brine in dolomite plugs	—	2D	—	—	92
4.7	$\text{H}_2\text{O}/\text{D}_2\text{O}$ or H_2O /hydrocarbon mixture in limestone rock sample	spin echo	2D	128×128 , (0.94 mm) ² , a slice 5 mm thick	35 min	94
1.9	Water or n-dodecane in sandstone rock cores	the same	2D	256×256	—	95
2.0	Aqueous KCl solution and dodecane in sandstone rock core	"	2D	128×128 , (0.44 mm) ² , a slice 5 mm thick	43 min	96
2.0	Water, sunflower oil or sunflower oil-in-water emulsion flowing in a pipe	gradient echo	2D, 3D	64×64 , (850 μm) ² , (780 μm) ² , a slice 2 mm or 2.5 mm thick (2D); $64 \times 64 \times 64$, (710 μm) ³ (3D)	20–60 s (2D); 23 min (3D)	97
0.5	Decane in peroxide vulcanised natural rubber	gradient echo with oscillating field gradients	2D	250 (400) μm for decane, 600 μm for rubber, a slice 5 mm thick	20 min	98, 99
1.89	Water or motor oil/ $\text{H}_2\text{O}/\text{D}_2\text{O}$ mixture in sandstone rock sample	spin echo with inversion–recovery	3D	$256 \times 256 \times 256$, $20 \times 19 \times 930$ μm	—	100
2.0	Water + salt and petroleum in chalk core	—	2D	(800 μm) ² , a slice 3 or 5 mm thick	—	101
2.0	Acetone + benzene in vulcanised rubber cylinder	chemical shift selective spin echo	2D	a slice 4 mm thick	2 min	102
2.0	Isooctane in vulcanised rubber cylinder saturated with cyclohexane	gradient echo for two-quantum coherence	2D	a slice 8 mm thick	8 min	102
	Salt solution in sandstone rock sample	—	2M	—	—	103
4.7	LiCl brine or trifluorotoluene in sandstone rock samples ^b	—	3D	$64 \times 64 \times 16$, $1 \times 1 \times 5$ mm (^7Li); $128 \times 128 \times 16$, $0.4 \times 0.4 \times 3$ mm (^1H , ^{19}F)	546 min (^7Li); 273 min (^{19}F); 17 min (water); 273 min (^1H of trifluorotoluene)	104
1.5, 4.7	Water in porous glass disk-shaped pellets	spin echo or gradient echo	2D, 3D	256×128 , 128×128 , (0.1–1 mm) ² , a slice 80 μm to 3 mm thick (2D)	from 4 min to 9 h	105
9.4	Methane in zirconia bead pack	FID or spin echo	—	WSR	—	107

Table S.1 (continued).

Magnetic field /T	Object, process	Technique	Dimension	Spatial resolution characteristics ^a	Recording time	Ref.
2.0	Alumina powder compacts prepared with polymeric binder	spin echo	2D	128 × 128, (552 μm) ² , 64 × 64, (652 μm) ² , 128 × 128, (326 μm) ²	from 3.5 to 28 min	108
0.47	Aqueous MnCl ₂ solution (1.5–25 mM), water in plant tissues	the same	2D	128 × 128, (0.23 mm) ² , 256 × 256, (0.1 mm) ² , a slice 2 or 5 mm thick	—	109
4.7	Water in alumina or silica	"	2D	128 × 128, (40 μm) ² , a slice 0.3 to 1 mm thick	—	110
7.05, 9.4	Water + ethanol in alumina granules	"	2D, 3D	256 × 256, (39 μm) ² , a slice 200 μm thick; 128 × 128 × 128 (3D)	30 min (2D)	111
2.0	Water in alumina, salt solution in sandstone rock samples	"	2D	128 × 128, (0.5 mm) ² , a slice 5 mm thick	2.5 h	112
4.7	Water in alumina or silica	stimulated echo	—	WSR	—	113
		spin echo or gradient echo	2D	128 × 128, 64 × 64, (30–100 μm) ² , a slice 0.2 to 1 mm thick	< 30 min	114
4.7	Water or H ₂ O/D ₂ O mixture in alumina or silica	the same	2D	128 × 128, 64 × 64, (30–190 μm) ² , a slice 0.2 to 1 mm thick	1.7 or 3.4 min	115
4.7	H ₂ O/D ₂ O mixture in alumina	spin echo	1D, 2D	128 × 128, (100 μm) ² , a slice 1 mm thick (2D)	40 s (1D), 3.4 min (2D)	116
4.7	Water or H ₂ O/D ₂ O mixture in alumina or silica	the same	2D	128 × 128, (40 μm) ² , a slice 0.3 to 1 mm thick	—	117
4.7	Water or H ₂ O/D ₂ O mixture in alumina or silica gel	"	2D	128 × 128, (40 μm) ² , —	—	120
7.05	Cyclohexane or aniline + cyclohexane in glass filter	"	1D	2048; 26 μm	—	121
4.7	Water in glass bead pack	spin echo (EPI or PEPI)	2D, 3D	128 × 128, (94 μm) ² , a slice 0.5 mm thick (2D); 128 × 128 × 128, (117 μm) ³ (3D)	51 min or 24 s (2D); 9 h or 15 min (3D)	122
—	Water in latex microsphere bead pack	spin echo	2D	128 × 128, (31.5 μm) ² , a slice 200 μm thick 64 × 64, (63.5 μm) ² , a slice 1 mm thick	—	125
—	Water in porous polystyrene, natural sponge, pumice stone or glass bead pack	spin echo or gradient echo	3D	—	—	128
4.7	Water in alumina pellets with coke	gradient echo	2D	128 × 128, (40 μm) ² , a slice 0.5 mm thick	4 h	129
7.05, 9.4	Benzene (+ Xe) in zeolite powder; 2,3-dimethylpentane or Xe in zeolite pellets with coke ^c	spin echo	1D, 2D	—	—	130
0.84	Aqueous NaCl solution in sandstone rock samples	spin echo + PRI	2D	256 × 256, a slice 1.5 cm thick	5 min	135
0.5	Water or 3% aqueous NaCl solution in dolomite, sandstone rock and petroleum well plug	spin echo (PEPI)	2D, 3D	64 × 64 × 128, (1.5 mm) ³	1.5 min	136
7.05	Vulcanised <i>cis</i> -1,4-polybutadiene + cyclohexane-d ₁₂	spin echo	2D	256 × 256, (37 μm) ² , (58 μm) ² , a slice 1 mm thick	—	139
7.05	Vulcanised polybutadiene rubber + deuterocyclohexane or cyclohexane-d ₁₂	the same	2D	256 × 256, (39 μm) ² , (32 μm) ²	—	140
2.0	Water in a polymeric composite reinforced with carbon fibre		3D	256 × 256 × 16, 0.25 × 0.25 × 7 mm	2.5 h	141

Table S.1 (continued).

Magnetic field /T	Object, process	Technique	Dimension	Spatial resolution characteristics ^a	Recording time	Ref.
7.05	Cyclohexane in cross-linked <i>cis</i> -1,4-polyisoprene + triaryl cyanurate + zinc diacrylate	spin echo	2D	256 × 256, (78 μm) ² , a slice 1 mm thick	—	142
7.05	Water + poly- <i>N</i> -isopropylacrylamide gel	the same	1D, 2D	a slice 1 mm thick	—	143
6.34	Water or water + MnSO ₄ mixture in cross-linked polymethacrylic acid gel	"	2D	a slice 2 mm thick	—	144, 145, 146
2.35	Sodium alginate + NaCl + water, dialysis against aqueous CaCl ₂ solution	"	2D	256 × 128 (135 μm) ² , a slice 3 mm thick	—	147
0.47	Agar gel	"	—	WSR	—	148
2.35	Agar gel doped with Mn(II), mortar, concrete, polyethylene	SPRITE	2D	64 × 64, (1.25–1.5 mm) ²	—	149
1.0	Aqueous Al ₂ O ₃ + CuSO ₄ suspension in plaster of Paris mould	spin echo	2D	128 × 128, (200 μm) ² , a slice 8 mm thick	64 s	150
	Organic components in Si ₃ N ₄ or Al ₂ O ₃	the same	2D	128 × 128, (640 μm) ² 310 × 340 μm	29 min 17 h	151
2.0	Aluminosilicate mixture + triethanolamine or tetraethylammonium bromide in batch mixer	"	2D	128 × 128, (470 μm) ² , a slice 2 mm or 4 mm thick	—	152
7.05	Emulsion explosives	"	2D	128 × 128 (63 μm) ² , a slice 3 mm thick	—	153
5.3	Emulsion of sunflower oil in D ₂ O	STRAFI	1D	—	1, 7 min	154
0.35	Water in food systems	SPRITE, spin echo	1D, 2D; 2D	64 × 64 (2D)	4 min, 15 min	155
2.35, 4.7	Apple	spin echo	2D	128 × 128, a slice 2 mm thick	—	156
—	Apple, peach	the same	2D	128 × 128 (0.78 mm) ² , 64 × 64 (1.56 mm) ² , a slice 5 mm thick	0.9 s	157
0.5	Watermelon	"	1D, 2D	256, a slice 20 mm thick (1D)	—	158
7.05	Tomato	"	2D	128 × 128 (0.2 mm) ² , a slice 1 mm thick	—	159
4.7 2.4	Cigarettes	spin echo, SPI, SPRITE	1D, 2D, 3D	32 × 32, (300 μm) ²	—	160
0.5	White oak or black cherry logs	spin echo	2D	(1.2 mm) ² , (1.95 mm) ²	7.5 min	161
9.45	Coal or coal + pyridine-d ₅	SPI, spin echo	2D, 3D	128 × 128, (50 μm) ² (2D); 128 × 128 × 128, (50 μm) ³ (3D)	8 min (2D); 16 h (3D)	164
9.4	Water inside the CD ₄ + ice gas hydrate	spin echo	2D	128 × 128 (80 μm) ² , a slice 0.5 mm thick	—	165
4.3	Xe (80% ¹²⁹ Xe) (1–3 atm) in nested tubes or capillary bundle ^d	gradient echo (FLASH)	2D	128 × 64, 0.1 mm	—	168
4.3	Xe (80% ¹²⁹ Xe) (1–3 atm) in aerogel ^d	the same	1D	0.1 mm	—	168
9.4	Xe (70% ¹²⁹ Xe) in mice lungs <i>in vitro</i> (in ampoule) ^d	"	2D	128 × 128, (0.37 mm) ²	600 ms	169
2.0	Foam churned from egg white and water	spin echo	1D	—	—	172
1.89	Foam churned from water with surfactant, polymer and alcohol additives	the same	1D	—	—	173
2.0	Salt solution in sandstone rock or limestone rock samples	stimulated echo	—	WSR	7 h	174

Table S.1 (continued).

Magnetic field /T	Object, process	Technique	Dimension	Spatial resolution characteristics ^a	Recording time	Ref.
1.9	C ₂ F ₆ or C ₄ F ₈ in ceramics (Y-stabilised zirconia) ^c	spin echo	3D	—	2 h	175
2.0	Water in a gap between glass plates	the same	—	WSR	—	176
178	Various liquids in rock or alumina samples	stimulated echo	—	"	—	178
7.05	Acetonitrile, benzene, dichloromethane and CCl ₄ in carbonaceous adsorbent	FID	—	"	—	180
0.7	Water in porous glass	"	—	"	—	191
7.05	Water in MCM-41	"	—	"	—	193
0.23	Water in calcium carbonate packs in the presence of Mn, Fe or Co ions	—	—	"	—	195
0.05	Water in calcium silicate packs in the presence of Mn or Fe ions	spin echo	—	"	7 min, 2 h	196
2.0	Water in sandstone rock samples	—	1D	"	—	200
0.47	Water or cyclohexane in silica	spin echo	—	WSR	—	202
2.0	Bentonite + water + NaOH + lignosulfonate dispersant (+ barite) in sandstone rock or limestone rock cores	the same	1D	128	—	203
7.05, 0.55	Acetone in corn starch gel	"	—	WSR	—	205
0.7	Water in sandstone rock plugs	FID, gradient echo or spin echo	1D	WSR, 0.2 mm	—	206
2.0	Water in glass bead pack or in limestone rock, chalk or sandstone rock samples	inversion—recovery, stimulated echo	—	WSR	—	207
1.0	3% Aqueous NaCl solution in sandstone rock or limestone rock cores	FID	—	"	45–60 min	209
0.66, 2.35	Aqueous salt solution, dodecane or cyclooctane in sandstone rock and carbonate rock plugs	FID, spin echo	—	"	—	210
0.78	Water in crushed porous glass	the same	—	"	—	214
2.1	Water in silica gel, porous glass, activated charcoal	FID	—	"	—	220
7.05	Water in silica (amorphous silicate)	the same	—	"	—	221
0.5, 2.5	Water or cyclohexane in porous silica	spin echo	1D, 2D, 3D	64 × 64 (2D), 64 × 64 × 32 (3D)	4.3 min (2D), 1 h (3D)	222
0.5, 2.5	The same	the same	1D, 2D, 3D	64 × 64, a slice 20 mm thick (2D); 64 × 64 × 32 (3D)	4.3 min (2D); 60 min (3D)	223
7.05	Water in MCM-41, aluminophosphate molecular sieves (VPI-5) and amorphous silicate	FID	—	WSR	—	224
7.05	Water, benzene, cyclohexane in porous silica	spin echo or FID	—	"	—	225
	Water, cyclohexane in porous silica	spin echo	—	"	—	226
7.05	Water in MCM-41, silica, zeolite Y and industrial catalyst	FID	—	"	—	227
7.05	Water in MCM-41	"	—	"	—	228
0.5	Cyclohexane in porous silica	FID or spin echo	—	"	—	229

Table S.1 (continued).

Magnetic field /T	Object, process	Technique	Dimension	Spatial resolution characteristics ^a	Recording time	Ref.
2.35	Water in concrete (white Portland cement + quartz filler)	SPRITE	1D	64; 1.6 mm	—	230
2.4	Water in mortar or concrete	"	1D	64; 2.2 mm		231, 232

Notations: PRI is Projection Reconstructed Imaging, WSR is Without Spatial Resolution, FID is Free Induction Decay, EPI is Echo-Planar Imaging, PEPI is Echo-Planar Imaging with Pi-pulses; STRAFI is Stray Field Imaging and FLASH is Fast Low-Angle Shot.

^a Listed are the image dimension (in pixels), spatial resolution and slice thickness. ^b Imaging using the ¹H, ⁷Li and ¹⁹F NMR signals. ^c Imaging using the ¹H and ¹²⁹Xe NMR signals. ^d Imaging using the ¹²⁹Xe NMR signals. ^e Imaging using the ¹⁹F NMR signals.

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Complex phosphates containing mono- and trivalent cations

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Abstract. The review surveys the data on the synthesis, structures, thermal stability and physical properties of complex phosphates containing M^I and M^{III} cations generated from double phosphates by the partial replacement $M^I \rightarrow H^+$ or $PO_4^{3-} \rightarrow X^{n-}$ [$X^{n-} = F^-, OH^-, EO_4^{n-}$ (VO_4^{3-} , MoO_4^{2-}) or $S_2O_3^{2-}$]. The sizes of the M^I and M^{III} cations and their ratio have a dominant role in the structure formation of complex phosphates. The prospects of the use of complex phosphates as polyfunctional materials are discussed. The bibliography includes 161 references.

I. Introduction

In the last two decades, an extensive search has been carried out for new ferroelectric, piezoelectric, laser, luminescent and other materials, which can be applied in quantum electronics and fibre optics and used as sorbents and catalysts. In this connection, complex phosphates containing mono- and trivalent cations, in particular, compounds of the $M_3^I M^{III}(PO_4)_2$ and $M_3^I M_2^{III}(PO_4)_3$ types (M^I are alkali metals), attract considerable interest.¹ These compounds exhibit ionic conductivity as well as nonlinear optical and other interesting properties. Numerous luminophores possessing excellent technical characteristics have been already prepared on the basis of inorganic phosphates.^{2,3}

The classical approach to the design of new materials involves the construction of more compositionally complex compounds and composites. Presently, new methods for the preparation of phosphates containing different combinations of mono- and polyvalent cations as well as procedures for the synthesis of complex phosphates in which the PO_4^{3-} anions are combined

with the F^- , OH^- , VO_4^{3-} , MoO_4^{2-} or $S_2O_3^{2-}$ anions attract considerable attention.

Purposeful changes in the compositions of the cationic and anionic components of complex phosphates allow one to vary the dimensional characteristics of framework structures and inter-layer spaces in layered phases thus influencing various properties of complex phosphates containing M^I and M^{III} cations, in particular, the ionic mobility, ion-exchange processes, catalytic properties and sensor characteristics (gas detection). Complex hydrogen phosphates containing the H^+ ions and polyvalent cations are of obvious interest. The data on these types of complex phosphates have not been generalised. Such complex orthophosphates involving the H^+ ions and anions of different nature along with M^I and M^{III} cations are the subject of the present review. Both the data published in the literature and the results of our studies are surveyed. The review also surveys the data on double orthophosphates containing mono- and trivalent cations. The latter compounds along with hydrogen orthophosphates with trivalent cations are parent compounds of complex phosphates under consideration.

Each group of complex phosphates containing M^I and M^{III} cations is characterised by different compositions. The targeted synthesis of new complex phosphates containing variable combinations of cations and anions and predictions of their physico-chemical characteristics require revealing the composition–structure–property relationships for different types of compounds, in particular, for complex double and hydrogen phosphates containing M^I and M^{III} cations, fluoride phosphates, hydroxide phosphates and phosphates containing other tetrahedral groups.

II. Double phosphates containing mono- and trivalent cations

Studies of the phase formation in the $M_3^I PO_4 - M^{III} PO_4$ systems ($M^I = Na, K$; $M^{III} = REE, Y, In, Sc$)^{4–8} were started in 1970s in connection with a search for new laser, luminescent and other materials. Two types of compounds, viz., $M_3^I M^{III}(PO_4)_2$ (**1**) and $M_3^I M_2^{III}(PO_4)_3$ (**2**), were found.[†] Compounds **1** are known for all rare-earth ($Y, La-Lu$) and some other (Sc, In, Fe) elements,

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[†]Data on double phosphates with more complex compositions, viz., $Na_6 M_3^{III}(PO_4)_5$ (**3**), where $M^{III} = Dy, Ho$ or Tm , are limited to the conditions of their formation in the $Na_3 PO_4 - M^{III} PO_4$ binary systems.⁴

whereas compounds **2** are typical only of trivalent cations with the ionic radii $r_{M^{III}} \leq 0.85 \text{ \AA}$. In studies of these compounds, primary attention has been given to their structures, polymorphic transformations, ionic conductivity and luminescent properties.

1. Synthesis

Phosphates with compositions $M_3^I M^{III}(PO_4)_2$ and $M_3^I M^{III}(PO_4)_3$ are generally prepared by the solid-phase synthesis from stoichiometric amounts of oxide $M_2^{III}O_3$, carbonate $M_2^I CO_3$ and alkali-metal and ammonium hydrogen orthophosphates characterised by different degrees of replacement at temperatures from 400 to 1100 °C.^{9–11} Different types of dielectric ceramics with such compositions are produced by hot pressing.¹² The synthesis from aqueous solutions of the corresponding salts at normal¹³ or high¹⁴ pressure (hydrothermal method) is used more rarely. There are also procedures, which, strictly speaking, cannot be considered as preparative. As an example we refer to the reactions of cerium(IV) oxide with sodium and potassium hydrogen phosphates or diphosphates¹⁵ accompanied by oxygen liberation. Another procedure for the preparation of double phosphates involves calcination of mixtures of REE hydrogen phosphates with composition $H_3 M^{III}(PO_4)_2 \cdot 2 H_2O$ with alkali-metal hydroxides or carbonates.¹⁶ Single crystals of $M_3^I M^{III}(PO_4)_2$ were grown under the hydrothermal conditions at high temperatures ($T = 600\text{--}900 \text{ }^\circ\text{C}$)¹⁴ or prepared by crystallisation from flux using an excess of alkali-metal halides (for example, KF).¹⁷

2. Structures and properties

Compounds with composition $M_3^I M^{III}(PO_4)_2$ containing different metal cations are similar in structure and physicochemical characteristics. The main structural feature common to all com-

pounds of this group is the fact that they belong to the glaserite [$K_3Na(SO_4)_2$], arcanite ($\beta\text{-K}_2SO_4$), sodium chromate (Na_2CrO_4) or NASICON $\ddagger$ [$NaZr_2(PO_4)_3$] structural types (Fig. 1).

The $K_3Na(SO_4)_2$ (space group $P3m1$, $a_1 = b_1 = 5.680$, $c_1 = 7.309 \text{ \AA}$),¹⁸ $\beta\text{-K}_2SO_4$ (space group $Pnam$, $a_2 = 7.456$, $b_2 = 10.080$, $c_2 = 5.776 \text{ \AA}$)¹⁹ and Na_2CrO_4 (space group $Cmcm$, $a_3 = 5.862$, $b_3 = 9.251$, $c_3 = 7.145 \text{ \AA}$)²⁰ structural types are widespread among inorganic salts with the PO_4^{3-} tetrahedral anions.^{1,21,22} All these salts belong to layered structures. In the crystals of these salts, the PO_4 tetrahedra have different orientations with respect to the cation positions (denoted as M , X and Y , see Fig. 1)²¹ and can combine with each other to form numerous subtypes. The relationship between the parent structural types can be represented as the relation between the unit cell parameters of glaserite (a_1, b_1, c_1) and those of arcanite (a_2, b_2, c_2) and sodium chromate (a_3, b_3, c_3): $a_2 \approx c_1$, $b_2 \approx a_1\sqrt{3}$, $c_2 \approx a_1$ and $a_3 \approx a_1$, $b_3 \approx a_1\sqrt{3}$, $c_3 \approx c_1$.

It is assumed that the ratio between the radii of the cations is the governing factor responsible for the formation of glaserite- or arcanite-like structures.²¹ The glaserite-like structures are stable for compounds in which the difference between the radii of the M^+ and M^{3+} cations [$\Delta r_{(M^+ - M^{3+})}$]²³ occupying the M , X and Y positions is in the range $0.59 \leq \Delta r_{(M^+ - M^{3+})} \leq 0.89 \text{ \AA}$.^{21,24–27} However, compounds that are characterised by $\Delta r_{(M^+ - M^{3+})} < 0.59 \text{ \AA}$ and have glaserite-like structures are also known. Thus, $\Delta r_{(M^+ - M^{3+})}$ for $Na_3Fe(PO_4)_2$ (glaserite structural type) is $0.38 \text{ \AA}$.²⁴ At $\Delta r_{(M^+ - M^{3+})} < 0.59 \text{ \AA}$, compounds generally crystallise in the arcanite structural type.^{19–22}

$\ddagger$ NASICON stands for Na Super Ionic Conductors.

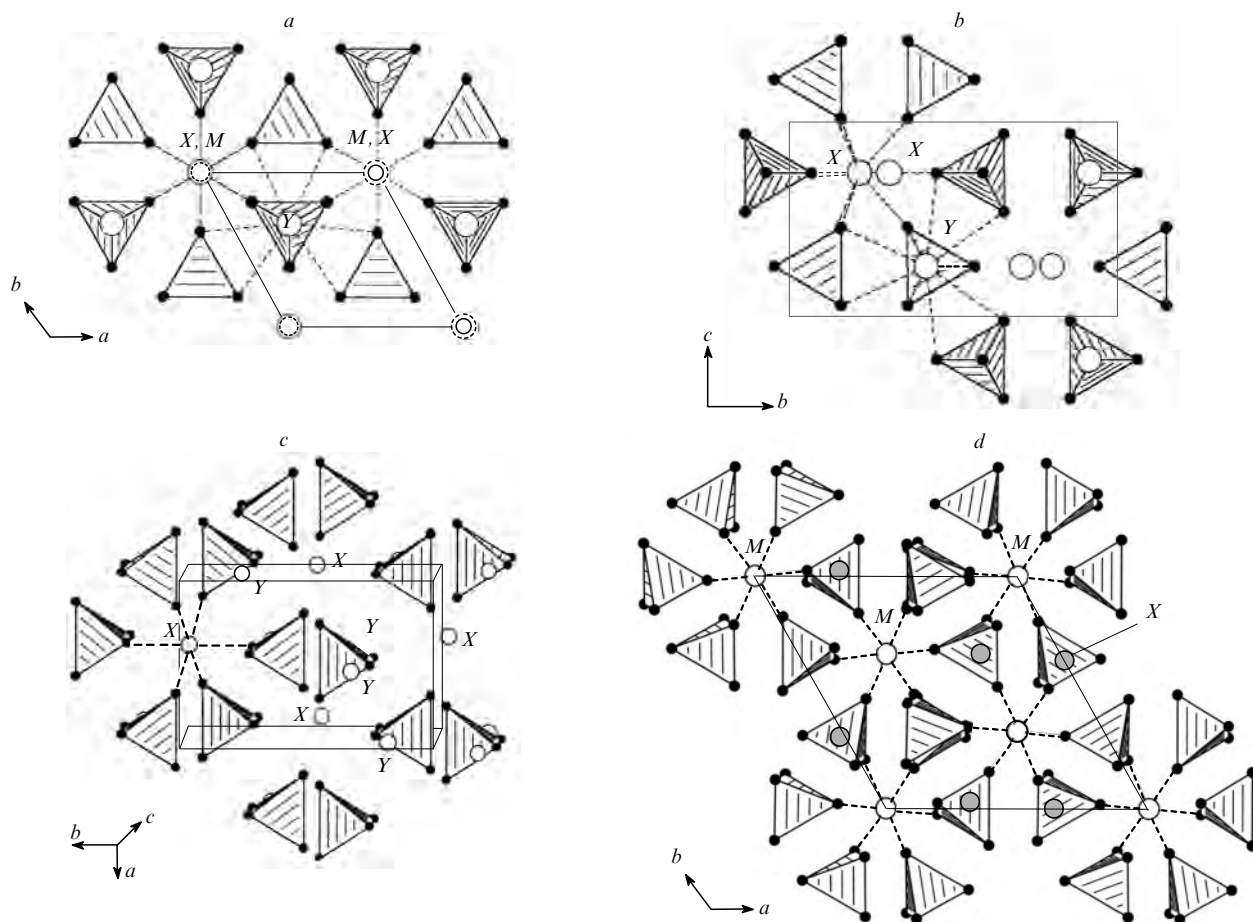


Figure 1. Projections of the $K_3Na(SO_4)_2$ (a), $\beta\text{-K}_2SO_4$ (b), Na_2CrO_4 (c), and $NaZr_2(PO_4)_3$ (NASICON) (d) structures. Hereinafter, the structures are drawn using the atomic coordinates published in the original studies.

The majority of representatives of the $M_3M^{III}(PO_4)_2$ group have structures of arcanite (β - K_2SO_4) or structures of an intermediate type (combinations of the β - K_2SO_4 and Na_2CrO_4 structures). In particular, the former structural type is typical of $K_3M^{III}(PO_4)_2$ ($M^{III} = La-Yb$)^{1,17,28} and the latter type is characteristic of $K_3In(PO_4)_2$ (see Ref. 29) and β - $Na_3M^{III}(PO_4)_2$ ($M^{III} = La-Lu, In$).^{13,14,30-33} These compounds belong to 'arcanite-like phosphates'.

In the structures of glaserite- and arcanite-like phosphates $M_3M^{III}(PO_4)_2$, the M^I and M^{III} cations occupy the X positions in an ordered fashion. The Y positions are occupied only by monovalent cations. However, the coordination polyhedra of the cations in the structures of $M_3M^{III}(PO_4)_2$ differ from those in the parent structural types due to distortions of the ideal β - K_2SO_4 - and Na_2CrO_4 -type crystal structures caused by displacements of the cations from the ideal positions and rotation of the PO_4 tetrahedra. For example, the coordination sphere about potassium in the structures of $K_3M^{III}(PO_4)_2$ ($M^{III} = Y, La-Yb$) involves nine or ten oxygen atoms, whereas the coordination spheres about the REE atoms are formed by seven oxygen atoms. In $Na_3M^{III}(PO_4)_2$, the coordination numbers of both Na^+ and M^{III} vary from 6 to 8–12.

The NASICON structural type can be described as the $\{[M_{2-x}^{III} \square_x(PO_4)_3]^{3-}\}_{3\infty}$ framework whose channels are occupied by alkali-metal cations.²¹ The $NaZr_2(PO_4)_3$ (NASICON) structural type is widespread among superionic conductors, whereas double phosphates with composition $Na_3M^{III}(PO_4)_2$ containing only REE of the end of the series ($M^{III} = Tm, Yb, Lu$) belong to this structural type. According to the stoichiometry of the framework, the structures of the latter compounds should be described by the $Na_{4.5}M_{1.5}^{III}(PO_4)_3$ formula.³⁴

Most of the sodium-containing phosphates $Na_3M^{III}(PO_4)_2$ ($M^{III} = Y, La-Lu, In$) have two or three crystal modifications each (Fig. 2, Table 1), viz., monoclinic low-temperature β and γ modifications based on the arcanite structure (A type) or a combination of the β - K_2SO_4 and Na_2CrO_4 structures (arcanite-

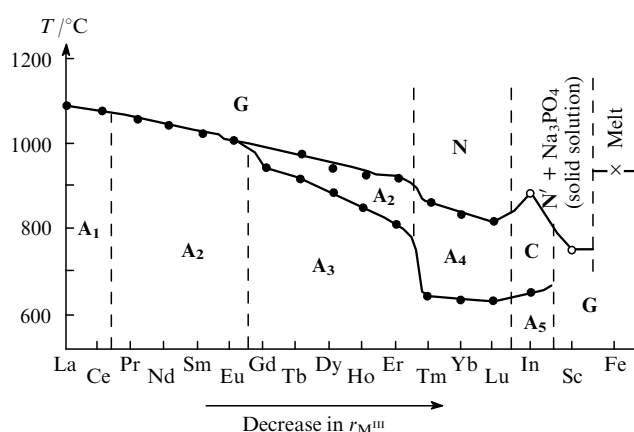


Figure 2. Occurrence of the structural types of the $Na_3M^{III}(PO_4)_2$ compounds depending on the temperature and nature of the M^{III} cation. **A₁–A₅**, arcanite-like subtypes (a combination of the β - K_2SO_4 and Na_2CrO_4 structures; **G**, **N** and **C**, the structural types of glaserite, NASICON and sodium chromate; **N'**, the NASICON-like phase with variable composition $Na_{3(1+x)}M_{(2-x)}^{III}(PO_4)_3$ ($0 \leq x \leq 0.2$). Solid and empty circles denote polymorphic transformations and decomposition, respectively; the cross indicates incongruent melting.

like structures, **A₁–A₅** subtypes) and high-temperature α modifications derived from the structures of glaserite (**G** type) or NASICON (**N** structural type).^{20,34}

The polymorphism of sodium-containing phosphates is, apparently, associated with a small difference in the ionic radii of sodium and trivalent REE. In arcanite-like structures of β - $Na_3M^{III}(PO_4)_2$, the proportion of the sodium-chromate structural motif in a combination of the β - K_2SO_4 and Na_2CrO_4 structures increases on going from lanthanum [$r_{VIII}(La^{3+}) = 1.18 \text{ \AA}$] to lutetium [$r_{VII}(Lu^{3+}) = 0.85 \text{ \AA}$] and indium

Table 1. Crystallographic characteristics of the $M_3M^{III}(PO_4)_2$ compounds.

Compound	M^{III}	Subtype (structural type)	Crystal system	Space group	Z^a	Unit cell parameters				Ref.
						$a/\text{\AA}$	$b/\text{\AA}$	$c/\text{\AA}$	β/deg	
β - $Na_3M^{III}(PO_4)_2$	La–Ce	$Na_3La(PO_4)_2$ (A₁)	ortho-rhombic	$Pc2_1b$	8	5.34 (Ce)	18.67 (Ce)	14.05 (Ce)	—	30
	Pr–Eu	$Na_3Nd(PO_4)_2$ (A₂)	"	$Pbc2_1$	24	15.89 (Pr)–15.88 (Eu)	13.97 (Pr)–13.96 (Eu)	18.51 (Pr)–18.47 (Eu)	—	33
	Y, Gd–Lu	$Na_3Nd(VO_4)_2$ (A₃)	monoclinic	Cc	12	27.59 (Gd)–27.27 (Lu)	5.35 (Gd)–5.28 (Lu)	13.92 (Gd)–13.88 (Lu)	91.2 (Gd)–91.3 (Lu)	13
	In	$Na_3In(PO_4)_2$ (A₅)	"	$P2_1/c$	4	7.127	18.220	8.616	143.36	14, 32
γ - $Na_3M^{III}(PO_4)_2$	Y, Nd–Er	$Na_3Nd(PO_4)_2$ (A₂)	ortho-rhombic	$Pbc2_1$	24	15.87 (Nd)–15.86 (Er)	13.95 (Nd)–13.93 (Er)	18.47 (Nd)–18.31 (Er)	—	33
	Tm–Lu	$Na_3Tm(PO_4)_2$ (A₄)	"	$Pnmm$ ($Pnm2_1$)	12	18.43 (Tm)–18.33 (Lu)	6.97 (Tm)–6.95 (Lu)	15.82 (Tm)–15.80 (Lu)	—	13
	La–Er	$K_3Na(SO_4)_2$ (G)	trigonal	$P\bar{3}m1$	1	5.47 (La)–5.37 (Er)	—	7.69 (La)–7.56 (Er)	—	27
α - $Na_3M^{III}(PO_4)_2$	Tm–Lu	$NaZr_2(PO_4)_3$ (N)	"	$R\bar{3}c$	6	9.15 (Tm)–9.11 (Lu)	—	21.88 (Tm)–21.80 (Lu)	—	34
	In	Na_2CrO_4 (C)	monoclinic	$P2_1/m$	2	8.634	5.455	7.048	90.30	32
	Fe	$K_3Na(CrO_4)_2$ (G)	"	$C2/c$	4	9.074	5.034	13.873	91.44	24
$K_3M^{III}(PO_4)_2$	Y, La–Yb	$K_3Nd(PO_4)_2$ (A)	"	$P2_1/m$	2	9.632 (La)–9.324 (Yb)	5.660 (La)–5.613 (Yb)	7.514 (La)–7.417 (Yb)	90.55 (Lu)–90.92 (Yb)	28
	Lu	$K_3Na(SO_4)_2$ (G)	trigonal	$P\bar{3}$	3	9.611	—	7.731	—	26
	In	$K_3In(PO_4)_2$ (A₆)	monoclinic	$C2/c$	8	15.643	11.193	9.700	91.44	29
	Sc	$K_3Na(SO_4)_2$ (G)	trigonal	$P\bar{3}$	3	9.424	—	7.619	—	25

^a Z is the number of formula units per unit cell.

[$r_{VI}(\text{In}^{3+}) = 0.76 \text{ \AA}$] to form new subtypes in the temperature range $T < 700\text{--}900^\circ\text{C}$. This is in agreement with the general principle consisting in the fact that trivalent cations in arcanite-like structures [for example, in $\beta\text{-Na}_3\text{La}(\text{PO}_4)_2$] occupy the XO_8 polyhedra corresponding to the XO_9 polyhedra in the structure of $\beta\text{-K}_2\text{SO}_4$, whereas these cations with smaller ionic radii tend to reduce their environment to octahedral, which corresponds to the XO_6 polyhedron in the structure of sodium chromate.^{30,33} The $\text{Na}_3\text{Sc}(\text{PO}_4)_2$ and $\text{Na}_3\text{Fe}(\text{PO}_4)_2$ compounds with the Sc^{3+} or Fe^{3+} cations possessing smaller ionic radii [$r_{VI}(\text{Sc}^{3+}) = 0.745 \text{ \AA}$, $r_{VI}(\text{Fe}^{3+}) = 0.645 \text{ \AA}$] than In^{3+} do not show polymorphism and crystallise in the glaserite structural type.²⁴

As the temperature is increased ($T > 900^\circ\text{C}$), sodium-containing phosphates $\text{Na}_3\text{M}^{\text{III}}(\text{PO}_4)_2$ ($\text{M}^{\text{III}} = \text{La} - \text{Er}$) are transformed from the β and γ modifications into the α modification corresponding to the higher-symmetry glaserite structural type. The high-temperature α modifications of $\text{Na}_3\text{M}^{\text{III}}(\text{PO}_4)_2$ ($\text{M}^{\text{III}} = \text{Tm} - \text{Lu}$) belong to the NASICON structural type.³⁴ At high temperatures, $\alpha\text{-Na}_3\text{In}(\text{PO}_4)_2$ would also be expected to transform into the NASICON-like modification. Instead, this compound decomposes at $T = 910^\circ\text{C}$ to give a NASICON-like phase with variable composition $\text{Na}_{3(1+x)}\text{In}_{(2-x)}(\text{PO}_4)_3$ ($0 \leq x \leq 0.2$) and a solid solution based on $\alpha\text{-Na}_3\text{PO}_4$. Analogous processes were observed upon heating of the $\text{Na}_3\text{Sc}(\text{PO}_4)_2$ and $\text{Na}_3\text{Fe}(\text{PO}_4)_2$ compounds above 790 and 975°C , respectively.^{24,31}

The nature and size of the REE ion have only a slight effect on the formation of a particular structural type of double potassium-containing phosphates $\text{K}_3\text{M}^{\text{III}}(\text{PO}_4)_2$.²⁸ However, a decrease in the ionic radius of the trivalent cation on going from ytterbium to lutetium also leads to the transformation from an arcanite-like to glaserite-like structure, which is accompanied by an increase in the symmetry of the crystal lattice from monoclinic [$\text{K}_3\text{M}^{\text{III}}(\text{PO}_4)_2$ compounds with large M^{III} cations (Y , $\text{La} - \text{Yb}$)^{27,28}] to trigonal [typical of $\text{K}_3\text{M}^{\text{III}}(\text{PO}_4)_2$, where $\text{M}^{\text{III}} = \text{Lu}$ or Sc].^{1,26}

In the structures of $\text{K}_3\text{M}^{\text{III}}(\text{PO}_4)_2$ ($\text{M}^{\text{III}} = \text{La} - \text{Yb}$), two of three potassium atoms are surrounded by ten oxygen atoms each, whereas the third potassium atom is surrounded by nine oxygen atoms. Due to distortion of the initial arcanite structure, the $\text{X}^{[6+3]}\text{O}_9$ polyhedra are transformed into $\text{M}^{\text{III}}\text{O}_7$ seven-vertex polyhedra, viz., trigonal monocapped prisms with the $\text{M}^{\text{III}} - \text{O}$ distances in the range of $2.20\text{--}2.60 \text{ \AA}$. In the virtually non-distorted glaserite-like structures of $\text{K}_3\text{M}^{\text{III}}(\text{PO}_4)_2$ ($\text{M}^{\text{III}} = \text{Lu}$, Sc), the M^{III} cations have an octahedral environment formed by oxygen atoms. Apparently, the transformation from an arcanite-like to glaserite-like structure is associated not only with an increase in the difference between the M^{III} and K^+ radii but also with the effect of the electronic structure of the M^{III} atom. Thus the $\text{K}_3\text{Lu}(\text{PO}_4)_2$ compounds [$\Delta r_{(\text{K}^+ - \text{Lu}^{3+})} = 0.58 \text{ \AA}$] would be expected to have arcanite-like structures stable at $\Delta r_{(\text{M}^+ - \text{M}^{3+})} < 0.59 \text{ \AA}$. However, $\Delta r_{(\text{K}^+ - \text{Lu}^{3+})}$ is actually equal to $0.69 \text{ \AA}$ and the glaserite-like structural type is realised. Because of the larger ionic radius of ytterbium [$\Delta r_{(\text{K}^+ - \text{Yb}^{3+})} = 0.57 \text{ \AA}$] as compared to that of lutetium and the more labile f shell, the ytterbium cation tends to expand the nearest environment. As a consequence, $\text{K}_3\text{Yb}(\text{PO}_4)_2$ crystallises in the $\beta\text{-K}_2\text{SO}_4$ structural type. However, the arcanite-like structure of $\text{K}_3\text{Yb}(\text{PO}_4)_2$ is unstable and is readily destabilised under the action of different factors, in particular, upon the partial replacement of the PO_4^{3-} ions by the bulkier VO_4^{3-} anions.²⁸

The $\text{K}_3\text{In}(\text{PO}_4)_2$ compound may be assigned to a new subtype of arcanite-like phosphates (A_6) characterised by a combination of the $\beta\text{-K}_2\text{SO}_4$ and Na_2CrO_4 structural motifs (Fig. 3).²⁹ Analysis of the crystal structure of $\text{K}_3\text{In}(\text{PO}_4)_2$ demonstrated that the potassium cations displace the indium cations from the X positions to the Y positions corresponding to the Y positions in the structure of sodium chromate (see Fig. 1c), as distinct from double phosphate $\text{Na}_3\text{In}(\text{PO}_4)_2$ in which the Y positions are occupied exclusively by the Na^+ cations. Hence, the larger potassium cation (compared to sodium) causes the indium ions to change an octahedral environment formed by the oxygen atoms

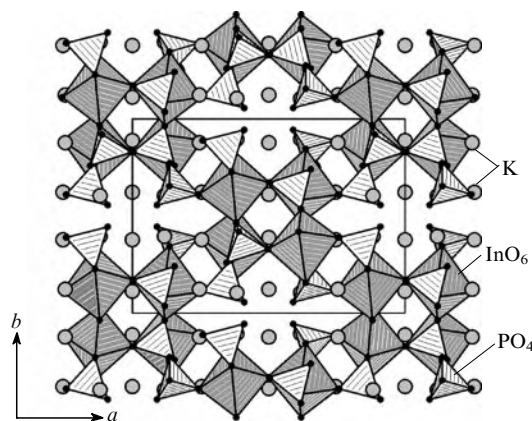


Figure 3. Structure of $\text{K}_3\text{In}(\text{PO}_4)_2$ projected onto the ab plane.

from six PO_4 tetrahedra for an octahedral environment formed by the oxygen atoms belonging to five PO_4 tetrahedra. In the structures of arcanite-like double phosphates $\text{Na}_3\text{M}^{\text{III}}(\text{PO}_4)_2$ ($\text{M}^{\text{III}} = \text{La} - \text{Lu}$), the co-existence of the $\beta\text{-K}_2\text{SO}_4$ and Na_2CrO_4 motifs is achieved due to the presence of REE with different coordination numbers (6–8), whereas the co-existence of these motifs in the $\text{K}_3\text{In}(\text{PO}_4)_2$ structure is, apparently, associated with a substantial distortion of the polyhedra about the potassium atoms. Like the $\text{K}_3\text{M}^{\text{III}}(\text{PO}_4)_2$ compounds ($\text{M}^{\text{III}} = \text{REE}$), $\text{K}_3\text{In}(\text{PO}_4)_2$ does not possess polymorphism below 1000°C . The only difference is that the REE compounds decompose prior to melting ($T = 800\text{--}1000^\circ\text{C}$), whereas $\text{K}_3\text{In}(\text{PO}_4)_2$ melts congruently at a temperature above 1200°C .³⁵ Taking into account the difference in the $\text{K}_3\text{In}(\text{PO}_4)_2$ and $\text{K}_3\text{M}^{\text{III}}(\text{PO}_4)_2$ structures ($\text{M}^{\text{III}} = \text{Lu}$, Sc) and considering that the radii of the M^{III} cations decrease in the series $\text{Lu} - \text{In} - \text{Sc}$, it can be assumed that the size of the M^{III} cation is of secondary importance in the formation of a particular structural type in the group of the $\text{M}_3^{\text{I}}\text{M}^{\text{III}}(\text{PO}_4)_2$ compounds.

Double phosphates with composition $\text{M}_3^{\text{I}}\text{M}_2^{\text{III}}(\text{PO}_4)_3$ (type 2, $\text{M}^{\text{I}} = \text{Li}$, Na , K ; $\text{M}^{\text{III}} = \text{Fe}$, Sc , In , Cr) (Table 2) are typical of small M^{III} cations ($r_{\text{M}^{3+}} < 0.8 \text{ \AA}$).^{36–48} The crystallographic characteristics of such compounds in which M^{III} is an REE atom ($\text{Ce} - \text{Gd}$) are available in the literature.^{10,11} For these compounds, the unit cell parameters were calculated assuming of trigonal system. However, these data are in doubt. Composites of the general formula $\text{M}_{3(1+x)}^{\text{I}}\text{M}_{2-x}^{\text{III}}(\text{PO}_4)_3$ ($0.07 \leq x \leq 0.5$) are known. These composites belong to the region of solid solutions on the basis of high-temperature α modifications of $\text{Na}_{4.5}\text{M}_{1.5}^{\text{III}}(\text{PO}_4)_3$ ($\text{M}^{\text{III}} = \text{Tm}$, Yb , Lu).³⁴

The crystal structures of most of the $\text{M}_3^{\text{I}}\text{M}_2^{\text{III}}(\text{PO}_4)_3$ compounds were established, which made it possible to assign these compounds to the NASICON type. Complex phosphates of the general formula $\text{M}_x\text{M}_2'(\text{PO}_4)_3$, where $\text{M} = \text{M}^+ (\text{Li}$, $\text{Na})$ or $\text{M}^{2+} (\text{Sr}$, $\text{Ba})$ and $\text{M}' = \text{M}^{2+} (\text{Mg})$, $\text{M}^{3+} (\text{Sc}$, In , $\text{Fe})$, $\text{M}^{4+} (\text{Zr}$, $\text{Ti})$ or $\text{M}^{5+} (\text{Ta}$, $\text{Nb})$, belong to this structural type. The occupancies of the M positions can vary over a wide range ($0 \leq x \leq 4$). The exception is the low-temperature β modification of $\text{Na}_3\text{In}_2(\text{PO}_4)_3$, which has an unusual structure.⁴⁵

Depending on the combination of the cations, the symmetry of the unit cell in the $\text{M}_3^{\text{I}}\text{M}_2^{\text{III}}(\text{PO}_4)_3$ compounds changes from trigonal to monoclinic. All structures have framework structures built from the $\text{M}^{\text{III}}\text{O}_6$ and PO_4 polyhedra in a ratio of 2 : 3. The cavities in the framework are occupied by alkali-metal cations (Li^+ , Na^+). The frameworks of the structures are penetrated by channels of two types, *I* and *II*, extended along the b axis of the unit cell (Fig. 4a). The channel of type *III* is perpendicular to the channels *I* and *II* and intersect these channels. The smallest cross-sections of the channels *I*, *II* and *III* are 1.0 , 1.1 and $0.9 \text{ \AA}$, respectively. The large cavities in these channels (at the intersections of the channels *I* and *III* and of the channels *II* and *III*) are

Table 2. Crystallographic characteristics of the $M_3M_2^{III}(PO_4)_3$ compounds.

Compound	M^{III}	Crystal system	Space group	Z	Unit cell parameters				Ref.
					$a/\text{\AA}$	$b/\text{\AA}$	$c/\text{\AA}$	β/deg	
$\beta\text{-Li}_3M_2^{III}(PO_4)_3$	Fe	monoclinic	$P2_1/n$	4	8.562	8.612	12.005	90.5	37
	Sc	"	$P2_1/n$	4	8.853	8.802	12.273	90.0	38
	In	"	$P2_1/n$	4	8.592	8.908	12.290	90.0	39
$\alpha\text{-Li}_3M_2^{III}(PO_4)_3$	Fe ^a	trigonal	$R\bar{3}c$	6	8.316	—	22.459	—	40
	Sc	orthorhombic	$Pbcn$	4	12.400	8.835	8.827	—	41
	In ^a	trigonal	$R\bar{3}c$	6	8.432	—	23.268	—	42
$\beta\text{-Na}_3M_2^{III}(PO_4)_3$	Fe ^a	"	$R\bar{3}c$	6	8.727	—	21.808	—	40
	Sc ^a	"	$R\bar{3}c$	6	8.927	—	22.340	—	47
	In	monoclinic	$C2/c$	4	12.439	12.772	6.583	114.16	31, 45
$\alpha\text{-Na}_3M_2^{III}(PO_4)_3$	Cr ^a	trigonal	$R\bar{3}c$	6	8.643	—	21.619	—	46
	Fe ^a	monoclinic	$C2/c$	4	15.070	8.740	8.724	125.1	43
	Sc ^a	"	Bb	4	16.100	9.109	8.928	127.2	44
	In ^a	trigonal	$R\bar{3}c$	6	8.966	—	22.100	—	31, 48
	Ce–Gd	"	see ^b	6	9.18 (Ce)– 8.86 (Gd)	—	14.44 (Ce)– 14.20 (Gd)	—	10, 11
$K_3M_2^{III}(PO_4)_3$	Ce–Gd	trigonal	see ^b	3	9.30 (Ce)– 8.86 (Gd)	—	14.41 (Ce)– 14.27 (Gd)	—	10, 11
	Fe	monoclinic	$C2/c$	8	16.303	9.463	16.691	118.4	36

^a The NASICON structural type. ^b The space groups were not unambiguously established.

occupied by alkali-metal cations located in two positions, *viz.*, $M(1)$ and $M(2)$ (Fig. 4*b*). The analysis of the number of the polyhedra and their coordination environments demonstrated that the general crystal-chemical formula of the NASICON structural type can be written as $[M(1), M(2)]_3M(3)_2(PO_4)_3$.

Taking the space group $R\bar{3}c$ (the highest symmetry for the compounds under consideration) as the basis, the $M(1)O_6$ polyhedron can be described as an elongated antiprism with the

$M(1)–O$ distances to the nearest six oxygen atoms equal to $\sim 2.6 \text{ \AA}$ (the other six O atoms are at considerable distances from the metal atom, *viz.*, at $\sim 3.7 \text{ \AA}$). The metal atom in the $M(2)$ position is surrounded by ten oxygen atoms eight of which are involved in the nearest environment, whereas the remaining two O atoms are somewhat remote. The analysis of the cross-sections of the channels showed that the cations with the radii of $\sim 1 \text{ \AA}$ (for example, Na^+) could migrate within these channels. The cations can also pass through narrower regions, *viz.*, through the ABC and ABD faces (see Fig. 4*b*),⁴⁷ due to thermal displacements of the oxygen atoms. This fact is responsible for superionic conductivity of the $M_3M_2^{III}(PO_4)_3$ compounds.⁴⁹ The cations can occupy the $M(1)$ and $M(2)$ positions in different fashions: (1) these positions are completely occupied [$Na_{4.5}M_{1.5}^{III}(PO_4)_3$ or $M_3M^{III}(PO_4)_3$, where $M^{III} = Tm, Yb, Lu$];³⁴ (2) only the $M(2)$ position is completely occupied (together with vacancies), for example, in $\beta\text{-Na}_3Sc_2(PO_4)_3$;⁴⁴ (3) the $M(1)$ and $M(2)$ positions are statistically occupied (together with vacancies), for example, in $\alpha\text{-Na}_3M_2^{III}(PO_4)_3$, where $M^{III} = Sc, In$.^{47, 48}

The low-temperature β modification of $Na_3In_2(PO_4)_3$ is described by the crystal-chemical formula $X(2)X(1)M(1).M(2)_2(PO_4)_3$. Alluaudite-like phosphates have analogous structures [the mineral alluaudite has the formula $Na_{0.6}Mn_{1.2}^{2+}Ca_{0.1}.Fe_2^{3+}Mg_{0.1}(PO_4)_3$]. The structures of indium compounds are characterised by the presence of the In_2O_{10} dimers (bioctahedra) (Fig. 5*a*), which form a framework structure together with the tetrahedral PO_4 groups (Fig. 5*b*). The analysis of the polyhedra in the crystal structure of $\beta\text{-Na}_3In_2(PO_4)_3$ led one to the conclusion that the complete occupancy of the $M(2)$ position by a double- or triple-charged cation according to the crystal-chemical formula $X(2)X(1)M(1)M(2)_2(PO_4)_3$ is a necessary condition for crystallisation of double phosphates in the alluaudite structural type. It should be noted that the ionic radius of the cation in the dimer [$M(2)$ position] must be in the strictly specified range $0.74 \leq r \leq 0.76 \text{ \AA}$. The radii r of the Fe^{2+} and In^{3+} cations fall within this range. Actually, the data on alluaudite-like phosphates $Na_2Fe^{3+}Fe_2^{2+}(PO_4)_3$, $NaCaMn^{2+}Fe_2^{2+}(PO_4)_3$ and $NaCd.In_2^{3+}(PO_4)_3$ are available in the literature.⁵⁰ The fact is that the occurrence of alluaudite-like structures is determined by the size of the PO_4 tetrahedron. Two of ten PO_4 groups in the dimer are bridging and fix the distances between the vertices of the octahedra [$d(O \cdots O) \approx 2.5 \text{ \AA}$], which are equal to the length of the edge of the tetrahedron. As a result, this distance $d[M(2) \cdots M(2)]$ in the

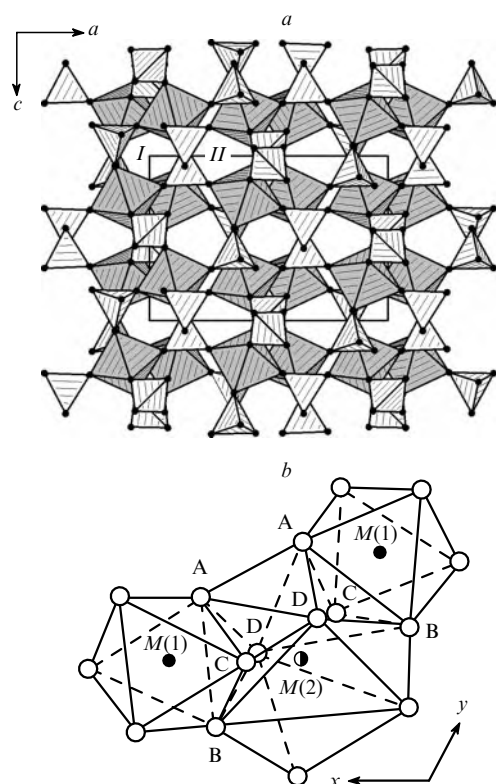


Figure 4. Structure of $M_3M_2^{III}(PO_4)_3$ projected onto the ac plane (*a*) and the oxygen environment about the $M(1)$ and $M(2)$ positions occupied by alkali-metal cations (*b*). The $M(3)$ position is omitted.

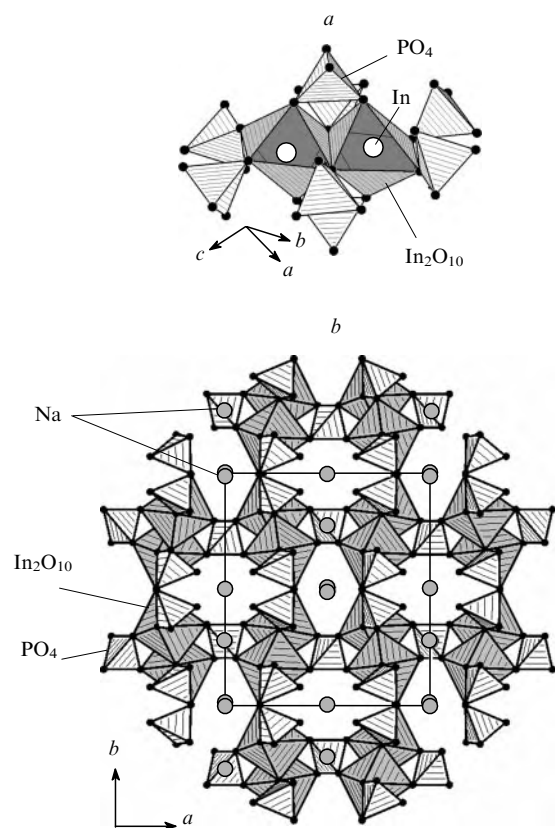


Figure 5. The In_2O_{10} biocahedron (a) and the structure of $\beta\text{-Na}_3\text{In}_2(\text{PO}_4)_3$ projected onto the ab plane (b).

dimer must be approximately equal to 3.0 Å. Due to repulsion between the cations, this distance increases to 3.19 Å in $\text{Na}_3\text{Fe}^{3+}\text{Fe}_2^{2+}(\text{PO}_4)_3$, 3.35 Å in $\beta\text{-Na}_3\text{In}_2(\text{PO}_4)_3$ and 3.38 Å in $\text{NaCdIn}_2(\text{PO}_4)_3$. The larger or smaller size of the cation as compared to In^{3+} and (*i.e.*, $r < 0.74$ and $r > 0.76$ Å) will lead to destruction of the dimer as the structural block, which is confirmed by the lack of information on alluaudite-like phases with composition $\text{M}_3^{\text{I}}\text{M}_2^{\text{III}}(\text{PO}_4)_3$, where $\text{M}^{\text{III}} = \text{REE}, \text{Sc}, \text{Fe}, \text{Cr}$.

From the crystal-chemical viewpoint, the transformation of the alluaudite-like β phase into the NASICON-like α phase [which was established from the analysis of the structures of both modifications of $\text{Na}_3\text{In}_2(\text{PO}_4)_3$] involves the radical rearrangement of the atoms. It was demonstrated that the transformation from the β phase to the α phase is accompanied by an increase in the distance between the indium atoms, destruction of the In_2O_{10}

dimers and formation of the isolated InO_6 octahedra. This rearrangement leads to an increase in 'porosity' [$\Delta(V/Z)_{\beta \rightarrow \alpha} = 8.1\%$] of the crystal structure due to the formation of rather large channels, which are statistically occupied by alkali-metal cations. The irreversibility of the polymorphic transformation $\beta\text{-Na}_3\text{In}_2(\text{PO}_4)_3 \rightarrow \alpha\text{-Na}_3\text{In}_2(\text{PO}_4)_3$ at $T = 820^\circ\text{C}$ was confirmed by the DTA data.

Hence, compounds with two compositions, *viz.*, $\text{M}_3^{\text{I}}\text{M}^{\text{III}}(\text{PO}_4)_2$ and $\text{M}_3^{\text{I}}\text{M}_2^{\text{III}}(\text{PO}_4)_3$, are most widespread among double phosphates containing mono- and trivalent cations. The structural types of these compounds are determined by the nature and size of the M^{III} cation as well as by the difference in the radii of the M^{I} and M^{III} cations, which is most pronounced for indium compounds (Table 3).

Investigations of the luminescence properties of REE phosphates showed that the $\text{M}_3^{\text{I}}\text{M}^{\text{III}}(\text{PO}_4)_2$ compounds ($\text{M}^{\text{I}} = \text{Na}, \text{K}$; $\text{M}^{\text{III}} = \text{Y}, \text{La}, \text{Nd}, \text{Gd}$) are promising laser materials.^{27, 51–54} Due to the unique luminescence properties (large absorption and luminescence cross-sections, rather large radiative lifetimes, weak concentration quenching of luminescence, low thresholds of generation, *etc.*), these crystals are quite competitive even with the recognised leader of this class of materials, *viz.*, yttrium–aluminium garnet $\text{YAG}:\text{Nd}^{3+}$, which is traditionally used in compact lasers. Luminophores based on $\text{M}_3^{\text{I}}\text{M}^{\text{III}}(\text{PO}_4)_2$ have the linear current characteristic of luminance at the cathode excitation in the current-density range of 0.1–50 $\mu\text{A cm}^{-2}$ (for the known $\text{Zn}_2\text{SiO}_4\text{–Mn}$ luminophore, the saturation of luminance takes place at the current load of 5–10 $\mu\text{A cm}^{-2}$). The introduction of the second M^{III} cation (diluent) into these materials leads to a noticeable increase in the line width resulting in deterioration of the optical characteristics. This was observed for the $\text{Na}_3\text{Nd}_{1-x}\text{M}_x^{\text{III}}(\text{PO}_4)_2$ ($\text{M}^{\text{III}} = \text{Gd}, \text{Lu}, \text{Y}$) solid solutions.⁵² The introduction of the Ce^{3+} and Tb^{3+} cations into a matrix of the $\beta\text{-K}_2\text{SO}_4$ type leads to an increase in the quantum yield due to the energy transfer from Ce^{3+} to Tb^{3+} .⁵³

The sizes of the polyhedra in the structures of NASICON-like phosphates allow one to predict the positions of the cations in the lattice and their mobility. Thus, a decrease in the size of the structure-forming M^{III} cation hinders the migration of mobile alkali-metal cations within the channels of the framework. It was experimentally found that the ionic conductivity of $\text{Na}_3\text{M}_2^{\text{III}}(\text{PO}_4)_3$ is weakened as the radius of the trivalent cation decreases. At 570 °C, σ is equal to 5.0×10^{-2} , 9.8×10^{-3} and $7.8 \times 10^{-3} \text{ S cm}^{-1}$ for $\text{Na}_3\text{Sc}_2(\text{PO}_4)_3$, $\text{Na}_3\text{Fe}_2(\text{PO}_4)_3$ and $\text{Na}_3\text{Cr}_2(\text{PO}_4)_3$, respectively.^{21, 51} The dependence of the ionic conductivity of NASICON-like REE-containing phases on the temperature and degree of replacement of Zr by M^{III} was studied only for mixed phosphates $\text{Na}_{1+x}\text{Zr}_{2-x}\text{M}_x^{\text{III}}(\text{PO}_4)_3$ ($\text{M}^{\text{III}} = \text{Gd}, \text{Tb}, \text{Dy}, \text{Y}, \text{Er}, \text{Yb}, \text{In}$; $0 \leq x \leq 2$).⁵⁵ For the $\text{Na}_{2.4}\text{In}_{1.4}\text{Zr}_{0.6}(\text{PO}_4)_3$ compound, the maximum σ value ($10^{-1} \text{ S cm}^{-1}$) was found at

Table 3. Characterisation of the structures of different types of double phosphates containing mono- and trivalent cations.

Compound	Ratio $\text{M}^{\text{I}} : \text{M}^{\text{III}}$	Ratio $\text{M}^{\text{III}} : \text{PO}_4^{3-}$	Crystal system	Space group	Building blocks	Structural type
$\text{M}_3^{\text{I}}\text{M}^{\text{III}}(\text{PO}_4)_2$ $\text{M}^{\text{I}} = \text{Na}; \text{M}^{\text{III}} = \text{REE},$ $\text{In}, \text{Ga}, \text{Sc}, \text{Al}, \text{Fe}, \text{Cr}$	3 : 1	1 : 2	trigonal orthorhombic monoclinic	$P\bar{3}m1$ $Pbc2_1, Pnmm$ Cc	$[\text{M}^{\text{III}}\text{O}_{8(7,6)}] + [\text{PO}_4]$ $[\text{M}^{\text{III}}\text{O}_6] + [\text{PO}_4]$	layered [$\text{M}^{\text{III}} = \text{La} - \text{Er},$ $\text{In} (\alpha \text{ phase}), \text{Sc}, \text{Al}, \text{Fe}, \text{Cr}]$ framework [$\text{M}^{\text{III}} = \text{Tm} - \text{Lu},$ $\text{In} (\beta \text{ phase})]$
$\text{M}^{\text{I}} = \text{K}; \text{M}^{\text{III}} = \text{REE},$ $\text{Sc}, \text{In}, \text{Fe}$			monoclinic	$P2_1/m, C2/c$	$[\text{M}^{\text{III}}\text{O}_{7(6)}] + [\text{PO}_4]$	layered ($\text{M}^{\text{III}} = \text{La} - \text{Er}, \text{Sc}, \text{Fe}$), framework ($\text{M}^{\text{III}} = \text{In}$)
$\text{M}_3^{\text{I}}\text{M}_2^{\text{III}}(\text{PO}_4)_3$ $\text{M}^{\text{I}} = \text{Li}, \text{Na}; \text{M}^{\text{III}} =$ $\text{Yb} - \text{Lu}, \text{Ga}, \text{Sc}, \text{Al}, \text{Fe}, \text{Cr}$	3 : 2	2 : 3	monoclinic trigonal orthorhombic monoclinic	$P2_1/n, C2/c, Bb$ $R\bar{3}c$ $Pbcn$ $C2/c$	$[\text{M}^{\text{III}}\text{O}_6] + [\text{PO}_4]$ $[\text{M}_2^{\text{III}}\text{O}_{10}] + [\text{PO}_4]$	framework framework [$\text{M}^{\text{III}} = \text{In} (\beta \text{ phase})]$
$\text{M}^{\text{I}} = \text{Na}, \text{M}^{\text{III}} = \text{In}$						

400 °C and the minimum value ($2 \times 10^{-5} \text{ S cm}^{-1}$) was observed at room temperature. Of REE-containing composites, the Yb-doped analogue $\text{Na}_{2.4}\text{Yb}_{1.4}\text{Zr}_{0.6}(\text{PO}_4)_3$ is the most competitive material (σ is $8.5 \times 10^{-2} \text{ S cm}^{-1}$ at 400 °C).

III. Hydrogen phosphates containing mono- and trivalent cations

Complex hydrogen phosphates containing mono- and trivalent cations are characterised by the presence of hydrogen bonds between the oxygen and hydrogen atoms of the HPO_4 groups. Although formally belonging to double phosphates containing mono- and trivalent cations, these compounds possess a series of specific features. Hence, it is reasonable to consider these compounds separately. Hydrogen phosphates containing mono- and trivalent cations are classified into four main types, viz., $\text{M}^{\text{I}}\text{M}^{\text{III}}(\text{HPO}_4)_2 \cdot n\text{H}_2\text{O}$, $\text{M}_x^{\text{I}}\text{M}_y^{\text{III}}(\text{HPO}_4)_z(\text{PO}_4)_u \cdot n\text{H}_2\text{O}$, $\text{M}_x^{\text{I}}\text{M}_y^{\text{III}}(\text{H}_2\text{PO}_4)_z(\text{HPO}_4)_u \cdot n\text{H}_2\text{O}$ and $\text{M}_x^{\text{I}}\text{M}_y^{\text{III}}(\text{H}_2\text{PO}_4)(\text{HPO}_4)_2 \cdot (\text{H}_3\text{PO}_4) \cdot n\text{H}_2\text{O}$, where $\text{M}^{\text{I}} = \text{Na, K, Rb, Cs, H}_3\text{O, NH}_4$ and $\text{M}^{\text{III}} = \text{Al, V, Fe, Ga, In}$.

Phosphates $\text{M}_3^{\text{I}}\text{M}^{\text{III}}(\text{OH})(\text{HPO}_4)(\text{PO}_4)$ containing the HPO_4 groups along with the OH groups, which serve as bridges linking the $\text{M}^{\text{III}}\text{O}_6$ polyhedra in infinite chains, are known only for Al and Ga in combination with Na. These compounds will be considered in Section V.

1. Synthesis

The hydrothermal synthesis is one of conventional procedures for the preparation of hydrogen phosphates containing the M^{I} and M^{III} cations.^{56–75} The problems associated with the preparation of compounds with specified compositions consist in choosing the optimum conditions of the synthesis. The compositions of the resulting compounds depend substantially on the parameters of the synthesis (the temperature, the degree of filling of an autoclave or a tube, the concentrations of the starting reagents, the aggregate state, pH of the medium, duration of the synthesis). General procedures for the preparation of this group of compounds are lacking. One of the criteria for the existence of complex hydrogen phosphates containing different cations and anions is the presence of a strongly acidic medium (pH is no higher than 2–2.5). All the aforesaid refer equally to the conditions of the hydrothermal synthesis of hydrogen phosphates with compositions $\text{M}^{\text{I}}\text{M}^{\text{III}}(\text{HPO}_4)_2 \cdot n\text{H}_2\text{O}$ ($\text{M}^{\text{I}} = \text{Na, K, Rb, Cs, H}_3\text{O, NH}_4$; $\text{M}^{\text{III}} = \text{Al, Fe, V, In}$; $n = 0–18$) and $\text{M}_x^{\text{I}}\text{M}_y^{\text{III}}(\text{HPO}_4)_z(\text{PO}_4)_u \cdot n\text{H}_2\text{O}$ ($\text{M}^{\text{I}} = \text{Rb, Cs}$; $\text{M}^{\text{III}} = \text{V, Ga, In}$; $n = 0.5–2$). The $\text{M}^{\text{I}}\text{M}^{\text{III}}(\text{HPO}_4)_2 \cdot n\text{H}_2\text{O}$ compounds are prepared under rather mild conditions (145–240 °C, see Table 4).

In studies of the phase formation in the $\text{In}_2\text{O}_3\text{--M}^{\text{I}}\text{H}_2\text{PO}_4\text{--H}_3\text{PO}_4\text{--HF}$ and $\text{In}_2\text{O}_3\text{--M}^{\text{I}}\text{Hal--H}_3\text{PO}_4$ systems under hydrothermal conditions ($T = 200$ °C), a series of indium hydrogen phosphates with composition $\text{M}^{\text{I}}\text{In}(\text{HPO}_4)_2$ ($\text{M}^{\text{I}} = \text{K, Rb, Cs, NH}_4$) were prepared. These compounds are stable at pH 0.5–1.5.⁵⁶ The $\text{RbIn}(\text{HPO}_4)_2$ compound was isolated as crystals of two forms (colourless prismatic and elongated bipyramidal) characterised by the same empirical formula. Crystals of hydrogen phosphate $\text{Na}_2\text{In}_2(\text{HPO}_4)_4 \cdot \text{H}_2\text{O}$ were prepared in the synthesis of microporous borophosphates.⁵⁷ Interestingly, the phosphate with the same composition was synthesised under analogous conditions in the absence of $\text{Na}_2\text{B}_4\text{O}_7 \cdot 10\text{H}_2\text{O}$. Attempts to prepare a gallium-containing analogue according to the same procedure failed and led to the formation of new borophosphate with composition $\text{NaGaBP}_2\text{O}_7(\text{OH})_3$.⁵⁷ Attempts to synthesise mixed rubidium gallium hydrogen phosphate were also unsuccessful in spite of the fact that the initial reagent ratio was varied over a wide range. Hydrogen phosphate $\text{Rb}_2\text{Ga}_4(\text{HPO}_4)(\text{PO}_4)_4 \cdot 0.5\text{H}_2\text{O}$ crystallised simultaneously with GaPO_4 (see Ref. 58) due, apparently, to high stability and low solubility of GaPO_4 (the solubility product is 1×10^{-21}).

The field of chemistry dealing with the synthesis of porous compounds has been extensively developed in recent years. These

compounds have inorganic frameworks built from the phosphate tetrahedra. The cavities in these frameworks can capture different positively charged groups, including organic groupings. The preparation of these compounds under hydrothermal conditions is often accompanied by the formation of complex hydrogen phosphates as by-products. For example, prismatic crystals of $\text{NH}_4(\text{Al}_{1-x}\text{Ga}_x)(\text{HPO}_4)_2$ ($x = 0.36$) comprising ~5%–10% of the total weight of the product were obtained under mild conditions ($T = 130$ °C) from a mixture consisting of aluminium and gallium chlorides, tetramethylammonium hydroxide and a cobalt complex with composition $[\Lambda\text{-Co(en)}_3(\text{H}_2\text{PO}_4)_3]$ (en is ethylenediamine).⁵⁹ Two types of crystals were isolated from a mixture of $\text{RbOH--FePO}_4 \cdot 2\text{H}_2\text{O--Me}_2\text{NH--MePO}(\text{OH})_2\text{--H}_3\text{PO}_4$ at 230 °C, viz., colourless elongated parallelepiped-shaped crystals of hydrogen phosphate $\text{RbFe}(\text{HPO}_4)_2$ (see Ref. 60) and prismatic crystals of unknown structure. It should be noted that a powdered product obtained in the course of the synthesis had the same nominal composition as that of the crystals of $\text{RbFe}(\text{HPO}_4)_2$ but was the low-symmetry modification.

Vanadium hydrogen phosphates $\text{M}^{\text{I}}\text{V}(\text{HPO}_4)_2$ ($\text{M}^{\text{I}} = \text{Rb, NH}_4$) were synthesised under slightly modified conditions ($T = 240$ °C).⁶¹ Only triclinic crystals of $\alpha\text{-RbV}(\text{HPO}_4)_2$ were isolated in pure form. Attempts to obtain their monoclinic analogues $\beta\text{-RbV}(\text{HPO}_4)_2$ and $\beta\text{-(NH}_4\text{)}\text{V}(\text{HPO}_4)_2$ in pure form failed even upon variation of the initial reagent ratio over a wide range. According to the results of chemical analysis, the composition of the impurity phase is identical to that of $\beta\text{-(NH}_4\text{)}\text{V}(\text{HPO}_4)_2$. This indicates that the phase formation of vanadium hydrogen phosphates, like that of indium hydrogen phosphates $\beta_1\text{-}$ and $\beta_2\text{-RbIn}(\text{HPO}_4)_2$, is a complex process resulting in co-crystallisation of different modifications of a compound under the same conditions. Attempts to prepare hydrogen phosphates $\text{M}^{\text{I}}\text{V}(\text{HPO}_4)_2$ ($\text{M}^{\text{I}} = \text{K or Cs}$) led to the formation of two phases, viz., $\text{K(V}^{\text{IV}}\text{O)V}^{\text{III}}(\text{HPO}_4)_3(\text{H}_2\text{O})_2$ and $\text{CsV}_2(\text{PO}_4) \cdot (\text{HPO}_4)_2(\text{H}_2\text{O})_2$.⁶² The caesium indium derivative $\text{CsIn}_2(\text{PO}_4) \cdot (\text{HPO}_4)_2(\text{H}_2\text{O})_2$ (see Ref. 63) was isolated from aqueous solutions containing InCl_3 , H_3PO_4 , CsVO_3 and Me_4NOH in a ratio of 2 : 6 : 1 : 1. It should be noted that mixed caesium indium hydrogen phosphate was not produced in the synthesis with the use of CsCl , CsOH and Cs_2CO_3 instead of CsVO_3 . Hydrogen phosphates containing the H_2PO_4^- and HPO_4^{2-} anions were prepared from solutions containing high concentrations of H_3PO_4 ($\geq 3 \text{ M}$). The synthesis with the use of $\text{CsGa}(\text{H}_2\text{PO}_4)_4$ as the starting compound in the presence of Cs_2CO_3 and an excess of H_3PO_4 afforded $\text{Cs}_2\text{Ga}(\text{H}_2\text{PO}_4)(\text{HPO}_4)_2 \cdot \text{H}_3\text{PO}_4 \cdot 0.5\text{H}_2\text{O}$.⁶⁴

2. Structures and properties

The $\text{M}^{\text{I}}\text{M}^{\text{III}}(\text{HPO}_4)_2$ compounds possess a series of interesting structural features. These compounds were prepared for the Al, V, Fe, Ga and In cations in combination with K, Rb and Cs^{56, 60, 61, 65} as well as with the single-charged NH_4^+ and H_3O^+ cations.^{56, 59, 61, 66–68} The composition of the unit cell of mixed indium sodium hydrogen phosphate does not correspond to the $\text{M}^{\text{I}}\text{M}^{\text{III}}(\text{HPO}_4)_2$ formula, which is associated with the incorporation of water molecules in the crystal lattice of this compound. Two compounds whose compositions correspond to the $\text{Na}_2\text{In}_2(\text{HPO}_4)_4 \cdot \text{H}_2\text{O}$ ⁵⁷ and $\text{Na}_4\text{In}_8(\text{HPO}_4)_{14}(\text{H}_2\text{O})_6 \cdot 12\text{H}_2\text{O}$ formulas were isolated.⁶⁹ The crystallographic characteristic of mixed-cation hydrogen orthophosphates $\text{M}^{\text{I}}\text{M}^{\text{III}}(\text{HPO}_4)_2$ and more complex sodium indium phosphates are given in Table 5.

All $\text{M}^{\text{I}}\text{M}^{\text{III}}(\text{HPO}_4)_2$ compounds have frameworks built from the vertex-sharing $\text{M}^{\text{III}}\text{O}_6$ octahedra and PO_4 tetrahedra. The cavities and channels of the frameworks are occupied by mono-valent cations. Variations in the sizes of the M^{I} and M^{III} cations give rise to different structural types. Thus, different types of frameworks can be formed, the polyhedra are distorted and the sizes of the channels and cavities are changed. As a consequence, the crystal lattice can incorporate water molecules, which participate in structure formation. It seems essential that in all structures, the protonated vertices of the PO_4 tetrahedra are directed

Table 4. Hydrothermal synthesis of complex hydrogen phosphates.

Compound	Characteristics of the crystals (colour)	Starting reagents (molar ratio)	Synthesis conditions			Ref.
			pH	$T/^{\circ}\text{C}$	τ/h	
$\text{KAl}(\text{HPO}_4)_2 \cdot \text{H}_2\text{O}$	colourless prismatic	$\text{Al}(\text{OH})_3$, 1M KH_2PO_4 , 1M H_3PO_4 (K : P = 0.5)	—	145 ^a	720	65
$\text{NH}_4(\text{Al}_{1-x}\text{Ga}_x)(\text{HPO}_4)_2$	the same	$\text{AlCl}_3 \cdot 6\text{H}_2\text{O}$, GaCl_3 , H_3PO_4 , $[\Lambda\text{-Co(en)}_3(\text{H}_2\text{PO}_4)_3]$, Me_4NOH , H_2O [Co(en) ₃ : Al : Ga : P : Me ₄ NOH : H ₂ O = 0.25 : 1 : 1 : 2.86 : 2 : 90]	—	130	96	59
$(\text{H}_3\text{O})\text{Fe}(\text{HPO}_4)_2$	pink needle-like	$\text{Fe}_3(\text{PO}_4)_2 \cdot 3\text{H}_2\text{O}$, FePO_4	2	227	168	67
$\text{RbFe}(\text{HPO}_4)_2$	colourless parallelepiped-shaped	RbOH , $\text{FePO}_4 \cdot 2\text{H}_2\text{O}$, Me_2NH , $\text{MePO}(\text{OH})_2$, H_3PO_4	—	230	96	60
$\beta\text{-(NH}_4\text{)V}(\text{HPO}_4)_2$	yellow-green	$[\text{V}_2\text{O}_5 : \text{V}_{\text{met}} : (\text{NH}_4)_2\text{HPO}_4 : \text{H}_3\text{PO}_4 : \text{H}_2\text{O} = 1 : 1 : 2 : 10 : 190]$	—	240	48	61
$\beta\text{-RbV}(\text{HPO}_4)_2$	pale-green platelet-like	$(\text{Rb}_2\text{V}_2\text{O}_6 : \text{V}_{\text{met}} : \text{Bu}_4\text{NBr} : \text{H}_3\text{PO}_4 : \text{H}_2\text{O} = 9 : 2 : 1 : 60 : 760)$	—	240	48	61
$\alpha\text{-RbV}(\text{HPO}_4)_2$	yellow-green	$(\text{Rb}_2\text{V}_2\text{O}_6 : \text{V}_{\text{met}} : \text{PhMe}_3\text{NBr} : \text{H}_3\text{PO}_4 : \text{H}_2\text{O} = 1 : 1 : 0.5 : 15 : 190)$	—	240	44	61
$\text{Na}_2\text{In}_2(\text{HPO}_4)_4 \cdot \text{H}_2\text{O}$	colourless platelet-like	$\text{Na}_2\text{B}_4\text{O}_7 \cdot 10\text{H}_2\text{O}$, $\text{Na}_2\text{HPO}_4 \cdot 12\text{H}_2\text{O}$, In_{met} , HCl (Na : In : P : B = 17 : 1 : 6 : 10) ^b	—	80	168	57
$\text{Na}_4\text{In}_8(\text{HPO}_4)_{14}(\text{H}_2\text{O})_6 \cdot 12\text{H}_2\text{O}$	colourless hexagonal-prismatic	$\text{Na}_2\text{HPO}_3 \cdot 5\text{H}_2\text{O}$, $\text{In}(\text{NO}_3)_3 \cdot 3\text{H}_2\text{O}$, H_3PO_3	—	130	336	57
$\text{KIn}(\text{HPO}_4)_2$	transparent colourless bipyramidal	In_2O_3 , KH_2PO_4 , H_3PO_4 , HF (K : In : P : F = 4.8 : 1 : 6.2 : 3) ^c	1.5	200	144	56
$(\text{NH}_4)\text{In}(\text{HPO}_4)_2$	white powder	In_2O_3 , NH_4Cl , H_3PO_4 (NH ₄ : In : P = 8 : 1 : 2) ^c	1	200	144	56
$\beta_2\text{-RbIn}(\text{HPO}_4)_2$	transparent colourless bipyramidal	In_2O_3 , RbH_2PO_4 , H_3PO_4 , HF (Rb : In : P : F = 4.65 : 1 : 6.15 : 3) ^c	0.5	200	144	56
$\text{CsIn}(\text{HPO}_4)_2$	colourless needle-like	In_2O_3 , CsF , H_3PO_4 (Cs : In : P = 3 : 1 : 6) ^c	1	200	96	56
$\text{Rb}_2\text{Ga}_4(\text{HPO}_4)(\text{PO}_4)_4 \cdot 0.5\text{H}_2\text{O}$	the same	Ga_2O_3 , 3M RbH_2PO_4 , 3M H_3PO_4 (Rb : P = 0.5)	—	600 ^d	40	58
$\text{CsV}_2(\text{PO}_4)(\text{HPO}_4)_2(\text{H}_2\text{O})_2$	green	$\text{Cs}_4\text{V}_2\text{O}_7$, V_{met} , H_3PO_4 , H_2O , PhMe_3NCl (1 : 2 : 46 : 800 : 1.1)	—	200	48	62
$\text{CsIn}_2(\text{PO}_4)(\text{HPO}_4)_2(\text{H}_2\text{O})_2$	pale-yellow	InCl_3 , H_3PO_4 , CsVO_3 , Me_4NOH , H_2O (2 : 6 : 1 : 1 : 125)	—	200	48	63
$\text{KFe}_3(\text{H}_2\text{PO}_4)_6(\text{HPO}_4)_2 \cdot 4\text{H}_2\text{O}$	colourless hexagonal-prismatic	Fe_2O_3 , H_3PO_4 , K_2CO_3 , H_2O (Fe : P : K = 1 : 4 : 1)	—	290 ^e	1	75
$\text{Cs}_2\text{Ga}(\text{H}_2\text{PO}_4)(\text{HPO}_4)_2 \cdot \text{H}_3\text{PO}_4 \cdot 0.5\text{H}_2\text{O}$	colourless needle-like	$\text{CsGa}(\text{H}_2\text{PO}_4)_4$, Cs_2CO_3 , H_3PO_4 ($\text{Cs}_2\text{O} : \text{Ga}_2\text{O}_3 = 7.5 : 1$)	—	—	1	64

^a Slow cooling to 25 °C for 24 h; ^b the degree of filling of the autoclave was 30%; ^c the degree of filling of the autoclave was 75%; ^d slow cooling to 275 °C for 65 h; ^e slow cooling with a rate of 20 °C per hour.

Table 5. Crystallographic characteristics of the $\text{M}^{\text{I}}\text{M}^{\text{III}}(\text{HPO}_4)_2$ compounds.

Compound	Crystal system	Space group	Z	Unit cell parameters				Ref.
				$a/\text{\AA}$	$b/\text{\AA}$	$c/\text{\AA}$	β (or α , β , γ) /deg	
$\text{KAl}(\text{HPO}_4)_2 \cdot \text{H}_2\text{O}$	monoclinic	$P2_1/c$	8	10.040	9.107	16.254	100.98	65
$\text{KAl}(\text{DPO}_4)_2 \cdot \text{D}_2\text{O}$	"	$P2_1/c$	8	10.037	9.105	16.223	100.97	65
$(\text{H}_3\text{O})\text{Fe}(\text{HPO}_4)_2$	"	$P2_1/c$	4	5.191	8.748	14.448	94.81	67
$\text{NH}_4(\text{Al}_{0.64}\text{Ga}_{0.36})(\text{HPO}_4)_2$	triclinic	$P\bar{1}$	3	7.109	8.695	9.252	$\alpha = 65.01$, $\beta = 70.25$, $\gamma = 69.01$	59
$\alpha\text{-(NH}_4\text{)Fe}(\text{HPO}_4)_2$	"	$P\bar{1}$	6	9.838	7.185	14.159	$\alpha = 93.46$, $\beta = 85.58$, $\gamma = 89.47$	68
$\text{RbFe}(\text{HPO}_4)_2$	trigonal	$R\bar{3}c$	6	8.160	—	52.75	—	60
$\beta\text{-(NH}_4\text{)V}(\text{HPO}_4)_2$	monoclinic	$P2_1/c$	4	5.201	8.738	14.398	94.8	61
$\alpha\text{-(NH}_4\text{)V}(\text{HPO}_4)_2$	triclinic	$P\bar{1}$	3	7.173	8.841	9.458	$\alpha = 65.1$, $\beta = 70.7$, $\gamma = 69.6$	66
$\beta\text{-RbV}(\text{HPO}_4)_2$	monoclinic	$P2_1/c$	4	5.210	8.789	14.330	94.4	61
$\alpha\text{-RbV}(\text{HPO}_4)_2$	triclinic	$P\bar{1}$	3	8.831	9.450	7.188	$\alpha = 109.6$, $\beta = 110.3$, $\gamma = 65.3$	61
$\text{KIn}(\text{HPO}_4)_2$	monoclinic	$P2_1/c$	4	9.623	8.257	9.457	115.72	56
$(\text{NH}_4)\text{In}(\text{HPO}_4)_2$	"	$P2_1/c$	4	9.665	8.276	9.596	116.15	56
$\beta_2\text{-RbIn}(\text{HPO}_4)_2$	"	$P2_1/c$	4	9.705	8.367	9.528	116.60	56
$\text{CsIn}(\text{HPO}_4)_2$	"	$P2_1/c$	4	5.330	9.157	14.796	93.81	56
$\text{Na}_2\text{In}_2(\text{HPO}_4)_4 \cdot \text{H}_2\text{O}$	triclinic	$P\bar{1}$	2	9.3013	9.4976	9.2685	$\alpha = 98.710$, $\beta = 98.953$, $\gamma = 60.228$	57
$\text{Na}_4\text{In}_8(\text{HPO}_4)_{14}(\text{H}_2\text{O})_6 \cdot 12\text{H}_2\text{O}$	trigonal	$P\bar{3}c1$	2	13.850	—	18.493	—	69

inside the channels. This arrangement of the protons has an effect on the shape of the channels and their presence compensates the negative charge of the frameworks of these compounds.

Two types of the AlO_6 octahedra and four crystallographically independent PO_4 tetrahedra are the main polyhedra in the structure of $\text{KAl}(\text{HPO}_4)_2 \cdot \text{H}_2\text{O}$.⁶⁵ The alternating AlO_6 and HPO_4 polyhedra are linked in chains along the a and c axis thus forming a framework (Fig. 6). The size and shape of the cavities in the framework are affected by the potassium cations and protons involved in the HPO_4 groups. The $\text{Al}(1)\text{O}_6$ octahedron, which is formed by four oxygen atoms belonging to four HPO_4 groups and two oxygen atoms of two *cis*-oriented water molecules, is strongly distorted. The $\text{Al}(2)\text{O}_6$ octahedron is less distorted and is formed only by the oxygen atoms of the HPO_4 groups. The $\text{Al}(1)\text{O}_6$ octahedra are arranged along the a axis, whereas the $\text{Al}(2)\text{O}_6$ octahedra are aligned along the c axis. The structure contains two types of the K cations. The coordination sphere about the $\text{K}(1)$ cation is formed by the oxygen atoms of only the HPO_4 groups, whereas the coordination sphere about the $\text{K}(2)$ cation involves the oxygen atom of the H_2O molecule along with the oxygen atoms of the HPO_4 groups. The coordination numbers of the potassium atoms in both polyhedra are equal to 9. In the structure of the deuterated analogue $\text{KAl}(\text{DPO}_4)_2 \cdot \text{D}_2\text{O}$,⁶⁵ seven types of hydrogen bonds were revealed.

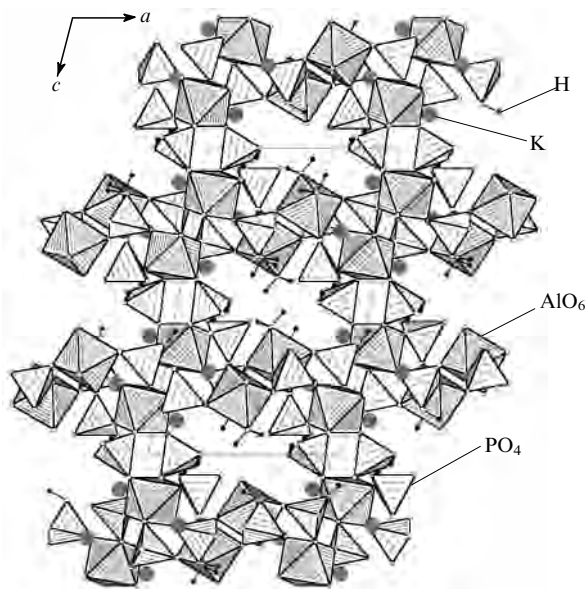


Figure 6. Structure of $\text{KAl}(\text{HPO}_4)_2 \cdot \text{H}_2\text{O}$ projected onto the ac plane.

The difference in the size of the M^{I} and M^{III} cations has a substantial effect on the structural features of hydrogen phosphates $\text{M}^{\text{I}}\text{M}^{\text{III}}(\text{HPO}_4)_2$ ($\text{M}^{\text{I}} = \text{K, Rb, Cs, H}_3\text{O, NH}_4$; $\text{M}^{\text{III}} = \text{Fe, V, In}$), which crystallise in the monoclinic system. This is particularly clearly seen in the case of indium compounds. For example, the unit cell volume in the family of indium hydrogen phosphates $\text{M}^{\text{I}}\text{In}(\text{HPO}_4)_2$ ($\text{M}^{\text{I}} = \text{K, Rb, NH}_4$, space group $P2_1/c$) increases gradually in the series $\text{K} - \text{NH}_4 - \text{Rb}$. However, the unit cell parameters are sharply changed on going to caesium, which has the largest ionic radius of all the alkali metals under consideration, while the space group ($P2_1/c$) is retained. The $\text{CsIn}(\text{HPO}_4)_2$ compound is more similar in crystallographic characteristics to hydrogen phosphates $(\text{H}_3\text{O})\text{Fe}(\text{HPO}_4)_2$, $\beta\text{-(NH}_4\text{)}\text{V}(\text{HPO}_4)_2$ and $\beta\text{-RbV}(\text{HPO}_4)_2$ than to $\text{M}^{\text{I}}\text{In}(\text{HPO}_4)_2$ ($\text{M}^{\text{I}} = \text{K, Rb, NH}_4$).

In the structure of $(\text{H}_3\text{O})\text{Fe}(\text{HPO}_4)_2$,⁶⁷ the FeO_6 octahedra are linked to each other through four PO_4 tetrahedra. The block of the octahedra and tetrahedra forms a framework consisting of columns along the a axis. The cavities in the framework are

occupied by the oxonium cations.[§] The oxygen atom of the H_3O^+ cation is at distances of 2.90–3.14 Å from the seven nearest oxygen atoms of the HPO_4 groups. The structures of hydrogen phosphates $\beta\text{-M}^{\text{I}}\text{V}(\text{HPO}_4)_2$ ($\text{M}^{\text{I}} = \text{NH}_4, \text{Rb}$)⁶¹ and $\text{CsIn}(\text{HPO}_4)_2$ (see Ref. 56) differ from that of $(\text{H}_3\text{O})\text{Fe}(\text{HPO}_4)_2$ (see Ref. 67) in that the VO_6 (as well as the InO_6) octahedra within the channels in these structures are linked to each other only by two PO_4 tetrahedra. On going from $\beta\text{-RbV}(\text{HPO}_4)_2$ to $\text{CsIn}(\text{HPO}_4)_2$, the oxygen polyhedron about the M^{III} atom is enlarged. Thus, the coordination numbers of rubidium and caesium are 7 and 12, respectively.

The triclinic modification of $\text{M}^{\text{I}}\text{M}^{\text{III}}(\text{HPO}_4)_2$ ($\text{M}^{\text{I}} = \text{Rb, NH}_4$; $\text{M}^{\text{III}} = \text{Fe, V}$)^{61,66} and $(\text{NH}_4)(\text{Al}_{1-x}\text{Ga}_x)(\text{HPO}_4)_2$ ($x = 0.36$)⁵⁹ have mixed $\{\text{M}^{\text{III}}[\text{HPO}_4]_2\}_{3\infty}$ frameworks of the $\text{M}^{\text{III}}\text{O}_6$ octahedra and PO_4 tetrahedra. These skeleton frameworks contain large cavities occupied by monovalent cations. The sizes and shapes of the cavities allow mobile ions to migrate in different directions, which indicates that these compounds can exhibit ion-exchange properties.⁶⁸ The $\text{M}^{\text{III}}\text{O}_6$ octahedra share all vertices with six nearest PO_4 tetrahedra. Each tetrahedron shares three vertices with three adjacent octahedra, whereas the fourth proton-bearing vertex of each tetrahedron is not involved in the first coordination sphere of the M^{3+} cations. The functional role of the fourth vertex consists in linking the tetrahedra through hydrogen bonding to form groups of three polyhedra each. The fact that the V^{3+} , Fe^{3+} , Co^{3+} and Ni^{3+} cations have similar radii [$r_{\text{VI}}(\text{M}^{\text{III}}) = 0.64, 0.645, 0.61$ and 0.60 Å, respectively] suggests the existence of the triclinic modification of the $\text{M}^{\text{I}}\text{M}^{\text{III}}(\text{HPO}_4)_2$ compounds with $\text{M}^{\text{I}} = \text{Rb, NH}_4$ and $\text{M}^{\text{III}} = \text{Co, Ni}$.

The $(\text{NH}_4)\text{Fe}(\text{HPO}_4)_2$ compound⁶⁸ exhibits antiferromagnetic properties and has two different magnetic subunits analogous to those found in $\text{Li}_3\text{Fe}_2(\text{PO}_4)_3$.⁷⁰ It should be noted that an increase in the ionic radius of the M^{III} cation in the series $\text{Al} - \text{Ga} - \text{V} - \text{Fe}$ in hydrogen phosphates with composition $(\text{NH}_4)\text{M}^{\text{III}}(\text{HPO}_4)_2$ is accompanied by a substantial deformation of the FeO_6 octahedra resulting in rotation of the PO_4 tetrahedra about FeO_6 . This leads to doubling of the unit cell volume of the Fe-containing analogue (triclinic modification). The triclinic modification of the In-containing analogue was not found, which may be indicative of instability of this modification of hydrogen phosphates containing large M^{III} cations.

The monoclinic modification of $\text{M}^{\text{I}}\text{M}^{\text{III}}(\text{HPO}_4)_2$ differs from their triclinic modification primarily in the mode of linking of the octahedra and tetrahedra in infinite columns along the a axis. For example, the columns in the structure of monoclinic $\beta\text{-(NH}_4\text{)}\text{V}(\text{HPO}_4)_2$ (Fig. 7a) are linked in a framework through the PO_4 tetrahedra, whereas these columns in the more complex structure of triclinic $\alpha\text{-(NH}_4\text{)}\text{V}(\text{HPO}_4)_2$ (Fig. 7b) are linked along the $[100]$ direction due to the presence of an additional VO_6 octahedron. As a result, the structure $\beta\text{-(NH}_4\text{)}\text{V}(\text{HPO}_4)_2$ contains channels of one type occupied by the ordered NH_4^+ cations, whereas two types of channels occupied by the NH_4^+ ions are present in the structure of $\alpha\text{-(NH}_4\text{)}\text{V}(\text{HPO}_4)_2$ (see Fig. 7a, b).

The structure of $\text{RbFe}(\text{HPO}_4)_2$ belonging to the trigonal system⁶⁰ (Fig. 7c) has a fragment typical of the triclinic modification of the $\text{M}^{\text{I}}\text{M}^{\text{III}}(\text{HPO}_4)_2$ compounds. However, in the low-symmetry structure, the tetrahedra through which the octahedra are linked in columns, are 'sunk' into the cavities between the octahedra, whereas the arrangement of the tetrahedra around the FeO_6 octahedra in the trigonal structure corresponds to the symmetry $\bar{3}$.

The structure of $\text{RbFe}(\text{HPO}_4)_2$ contains the $\text{Fe}(1)_2\text{Fe}(2)(\text{HPO}_4)_{12}$ trimers involving two types of the octahedra, viz., $\text{Fe}(1)\text{O}_6$ and $\text{Fe}(2)\text{O}_6$. The trimers form helical columns along the c axis. Each HPO_4 group is linked to one

§ The presence of the H_3O^+ cation was confirmed by IR spectroscopy (a narrow absorption band at 3392 cm^{-1}).

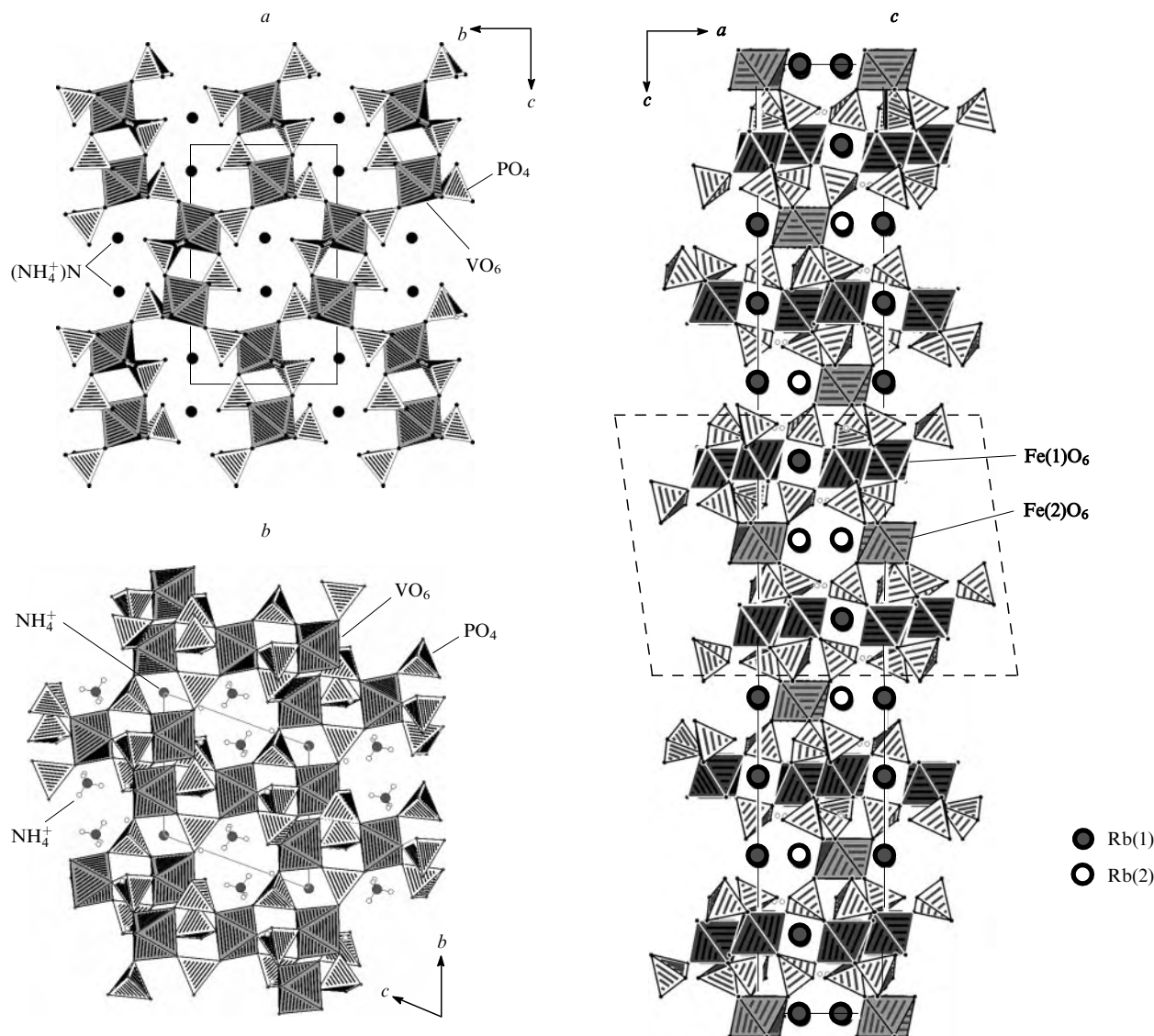


Figure 7. Structures of monoclinic β -(NH_4) $\text{V}(\text{HPO}_4)_2$ (a) and triclinic α -(NH_4) $\text{V}(\text{HPO}_4)_2$ (b) projected onto the bc plane and the structure of trigonal $\text{RbFe}(\text{HPO}_4)_2$ (c) projected onto the ac plane.

$\text{Fe}(1)\text{O}_6$ octahedron and one $\text{Fe}(2)\text{O}_6$ octahedron within the trimer and to one $\text{Fe}(1)\text{O}_6$ octahedron from the adjacent trimer so that the three-dimensional $[\text{Fe}(1)_2\text{Fe}(2)(\text{HPO}_4)_6]_{3\infty}$ framework is formed. The tunnels extended along the $[100]$ and $[110]$ directions are occupied by two types of rubidium cations with the coordination numbers of 12 and 9. As can be seen from the projection of the structure of $\text{RbFe}(\text{HPO}_4)_2$ onto the ab plane, the layers of the $\text{Fe}(1)$ and $\text{Rb}(1)$ atoms alternate with the layers of the $\text{Fe}(2)$ and $\text{Rb}(2)$ atoms and interleaved with the HPO_4 groups. All iron and rubidium atoms are located on threefold axes to form columns along the c axis with the $-\text{Fe}(1)\text{Fe}(2)\text{Fe}(1)\text{Rb}(2)\text{Rb}(1)\text{Rb}(2)\text{Fe}(1)-$ alternation. In $\text{RbFe}(\text{HPO}_4)_2$, the difference between the radii of the rubidium $[r_{\text{XII}}(\text{Rb}^+) = 1.73 \text{ \AA}]$ and iron $[r_{\text{VI}}(\text{Fe}^{3+}) = 0.645 \text{ \AA}]$ cations is $\sim 1.09 \text{ \AA}$. The pair of the caesium $[r_{\text{XII}}(\text{Cs}^+) = 1.88 \text{ \AA}]$ and indium $[r_{\text{VI}}(\text{In}^{3+}) = 0.76 \text{ \AA}]$ cations as well as the pair of rubidium and vanadium $[r_{\text{VI}}(\text{V}^{3+}) = 0.64 \text{ \AA}]$ are characterised by similar values of Δr and, hence, the trigonal modifications of $\text{CsIn}(\text{HPO}_4)_2$ and $\text{RbV}(\text{HPO}_4)_2$ would be expected to occur.

A decrease in $\Delta r_{(\text{M}^+ - \text{M}^{3+})}$ in the series $\text{Cs} - \text{Rb} - \text{K} - \text{Na}$ (for one type of the M^{3+} atoms) leads to a decrease in the coordination number of the alkali-metal cation. As a consequence, a new structural type can be formed. This assumption was confirmed by the structures of indium hydrogen phosphates $\text{M}^{\text{I}}\text{In}(\text{HPO}_4)_2$,

where $\text{M}^{\text{I}} = \text{K}, \text{Rb}$ or NH_4 , which we have established recently. In the framework structures of these compounds, the octahedra and tetrahedra are linked in infinite columns along the $[100]$ and $[001]$ directions. These structures differ from that of $\text{CsIn}(\text{HPO}_4)_2$ in the mode of linking of the columns to form a framework. In addition, the alkali-metal atoms in these structures adopt a smaller coordination number. Thus the coordination number of caesium in $\text{CsIn}(\text{HPO}_4)_2$ is 12, whereas the coordination number of potassium and rubidium in $\text{M}^{\text{I}}\text{In}(\text{HPO}_4)_2$ ($\text{M} = \text{K}$ or Rb) is 9. In $\text{CsIn}(\text{HPO}_4)_2$, each column is linked to four analogous adjacent columns through four PO_4 tetrahedra, whereas there are eight such interactions in the structures of $\text{M}^{\text{I}}\text{In}(\text{HPO}_4)_2$ ($\text{M} = \text{K}, \text{Rb}$) and all tetrahedra are shared by columns (Fig. 8).

The PO_4 tetrahedra in $\text{M}^{\text{I}}\text{In}(\text{HPO}_4)_2$ ($\text{M} = \text{K}$ or Rb) share two vertices with the InO_6 octahedra from one column and one vertex with the octahedron from the adjacent column. The fourth (protonated) oxygen vertex of each tetrahedron is directed inside the channel formed with the participation of three columns linked through the tetrahedra. These channels are occupied by the M^{I} cations. The InO_6 octahedra in the structure of $\text{KIn}(\text{HPO}_4)_2$, unlike those in $\text{RbIn}(\text{HPO}_4)_2$, are strongly distorted. These structural features of $\text{KIn}(\text{HPO}_4)_2$ suggest that the formation of this structural type is highly improbable for the sodium analogue.

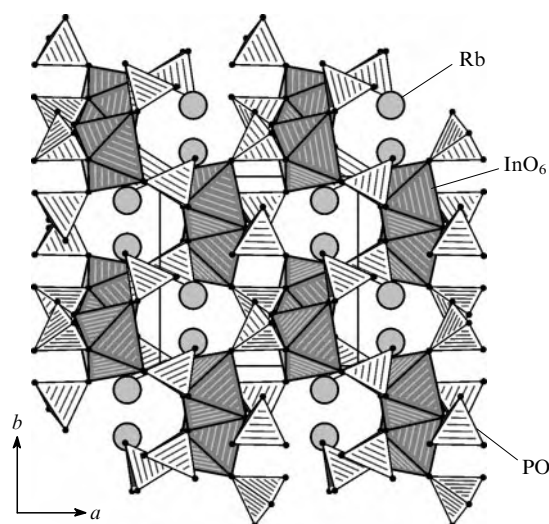


Figure 8. Structure of $\text{RbIn}(\text{HPO}_4)_2$ projected onto the ab plane.

Sodium for which $\Delta r_{(\text{M}^+ - \text{M}^{3+})}$ reaches the maximum value ($\sim 0.23 \text{ \AA}$) forms the $\text{Na}_2\text{In}_2(\text{HPO}_4)_4 \cdot \text{H}_2\text{O}$ ⁵⁷ and $\text{Na}_4\text{In}_8(\text{HPO}_4)_{14}(\text{H}_2\text{O})_6 \cdot 12 \text{H}_2\text{O}$ ⁶⁹ compounds with radically different structures.

The $\text{Na}_2\text{In}_2(\text{HPO}_4)_4 \cdot \text{H}_2\text{O}$ compound has the $[\text{In}_2(\text{HPO}_4)_4]_{3\infty}$ framework built from two types of the InO_6 octahedra and PO_4 tetrahedra. This framework can be described as consisting of the characteristic $[\text{In}(1)\text{In}(2)(\text{HPO}_4)_4]$ structural blocks. The InO_6 octahedra of both types each share vertices with six PO_4 tetrahedra, which, in turn, each have three oxygen atoms in common with three adjacent octahedra. The remaining vertices of the HPO_4 polyhedra occupied by the protonated oxygen atoms are involved in formation of five hydrogen bonds. The octahedra and tetrahedra are packed in layers parallel to the a axis. The framework of $\text{Na}_2\text{In}_2(\text{HPO}_4)_4 \cdot \text{H}_2\text{O}$ contains two types of channels. The channels of one type are extended along the $[100]$ direction and occupied by sodium cations and H_2O molecules (Fig. 9a). The channels of another type are extended along the $[010]$ direction and are empty. It should be noted that the mode of binding of the In, P and O atoms in $\text{Na}_2\text{In}_2(\text{HPO}_4)_4 \cdot \text{H}_2\text{O}$ ⁵⁷ is analogous to that observed in the structures of Al_2O_3 (corundum) and $\text{Ti}^{\text{IV}}\text{Ti}^{\text{IV}}(\text{HPO}_4)_4$.⁷¹

The structure of $\text{Na}_4\text{In}_8(\text{HPO}_4)_{14}(\text{H}_2\text{O})_6 \cdot 12 \text{H}_2\text{O}$ consists of the $[\text{In}_8(\text{HPO}_4)_{14}(\text{H}_2\text{O})_6]$ layers formed by the PO_4 tetrahedra and the $\text{In}(1)\text{O}_6$ and $\text{In}(2)\text{O}_5\text{O}_w$ octahedra. The $[\text{In}_8(\text{HPO}_4)_{14}(\text{H}_2\text{O})_6]$ layers are packed in the $ABAB$ order according to the trigonal symmetry $P3c1$, the channels along the $[001]$ direction being lacking. The layers are linked to each other through the $\text{In}(1)\text{O}_6$ octahedra to form a framework with channels along the crystallographic a and b axis (Fig. 9b). These channels have a 12-membered-ring shape in cross-section and include the Na^+ cations and water molecules. The water molecules fulfil two functions. Some water molecules are involved in the first coordination sphere about the $\text{In}(2)$ cation and the remaining water molecules occupy the channels of the structure (zeolite-type water). The partial occupancies of the sodium positions and the nearest oxygen positions are directly associated with the presence of abnormally short bonds ($2.06\text{--}2.19 \text{ \AA}$) between these atoms. The $\text{Na}\text{--}\text{O}$ interatomic distances in the NaO_x polyhedron are close to the interatomic distances outside these polyhedra. This characteristic feature of the $\text{Na}_4\text{In}_8(\text{HPO}_4)_{14}(\text{H}_2\text{O})_6 \cdot 12 \text{H}_2\text{O}$ compound is also common to some hydrated sodium zeolites.⁷²

The second group of complex hydrogen phosphates of the general formula $\text{M}_x^{\text{I}}\text{M}_y^{\text{III}}(\text{HPO}_4)_z(\text{PO}_4)_u \cdot n \text{H}_2\text{O}$ ($\text{M}^{\text{I}} = \text{Rb}, \text{Cs}$; $\text{M}^{\text{III}} = \text{V}, \text{Ga}, \text{In}$; $n = 0.5\text{--}2$) includes three compounds, viz., $\text{Rb}_2\text{Ga}_4(\text{HPO}_4)(\text{PO}_4)_4 \cdot 0.5 \text{H}_2\text{O}$, $\text{CsIn}_2(\text{HPO}_4)_2(\text{PO}_4)(\text{H}_2\text{O})_2$ and

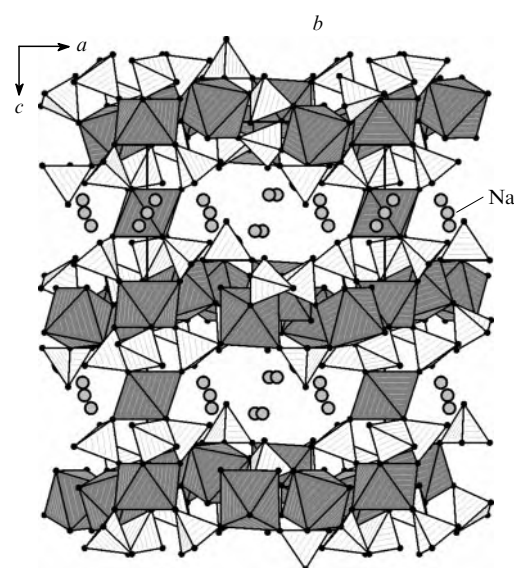
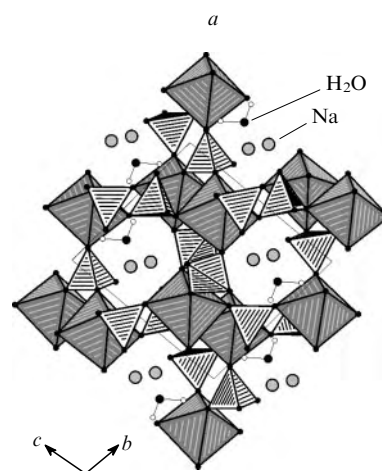


Figure 9. Structure of $\text{Na}_2\text{In}_2(\text{HPO}_4)_4 \cdot \text{H}_2\text{O}$ projected onto the bc plane (a) and structure of $\text{Na}_4\text{In}_8(\text{HPO}_4)_{14}(\text{H}_2\text{O})_6 \cdot 12 \text{H}_2\text{O}$ projected onto the ac plane (b).

$\text{CsV}_2(\text{HPO}_4)_2(\text{PO}_4)(\text{H}_2\text{O})_2$. These compounds crystallise in two structural types (Table 6).

In monoclinic $\text{Rb}_2\text{Ga}_4(\text{HPO}_4)(\text{PO}_4)_4 \cdot 0.5 \text{H}_2\text{O}$,⁵⁸ the GaO_x , HPO_4 and PO_4 polyhedra form an open-type structure with channels containing the rubidium cations and water molecules (Fig. 10a). The presence of the HPO_4 groups and water of crystallisation in the structure was confirmed by IR spectroscopy. The $\text{Rb}(1)$ and $\text{Rb}(2)$ cations are located in the $\text{M}^{\text{I}}\text{O}_9$ and $\text{M}^{\text{I}}\text{O}_{10}$ polyhedra, respectively. Four crystallographically non-equivalent gallium atoms have different coordination environments (an octahedron, two tetrahedra and a trigonal bipyramid). All GaO_x polyhedra share vertices with the phosphate tetrahedra, which, in turn, are coordinated (except for the OH vertices) by the gallium atoms. Two types of channels are formed along the $[100]$ direction. The protonated oxygen vertices of the PO_4 tetrahedra are directed inside the channels of the first type occupied by the $\text{Rb}(1)$ cations. The channels of the second type contain the $\text{Rb}(2)$ cations and H_2O molecules. The minimum $\text{O}\cdots\text{O}$ distances determining the sizes of the channels of the first and second types are 5.34 and $5.43 \text{ \AA}$, respectively. The formation of an analogous structure is also highly probable for the RbAl analogue because the coordination numbers of 6, 5 and 4 are typical of aluminium.

The $\text{CsIn}_2(\text{HPO}_4)_2(\text{PO}_4)(\text{H}_2\text{O})_2$ compound (centrosymmetrical structure)⁶³ has a rather complex structure. The octahedral environment about the In atoms is formed by five oxygen atoms of

Table 6. Crystallographic characteristics of the $M^I_x M^{III}_y (HPO_4)_z (PO_4)_u \cdot nH_2O$ and $M^I_x M^{III}_y (H_2PO_4)_z (HPO_4)_u \cdot nH_2O$ compounds.

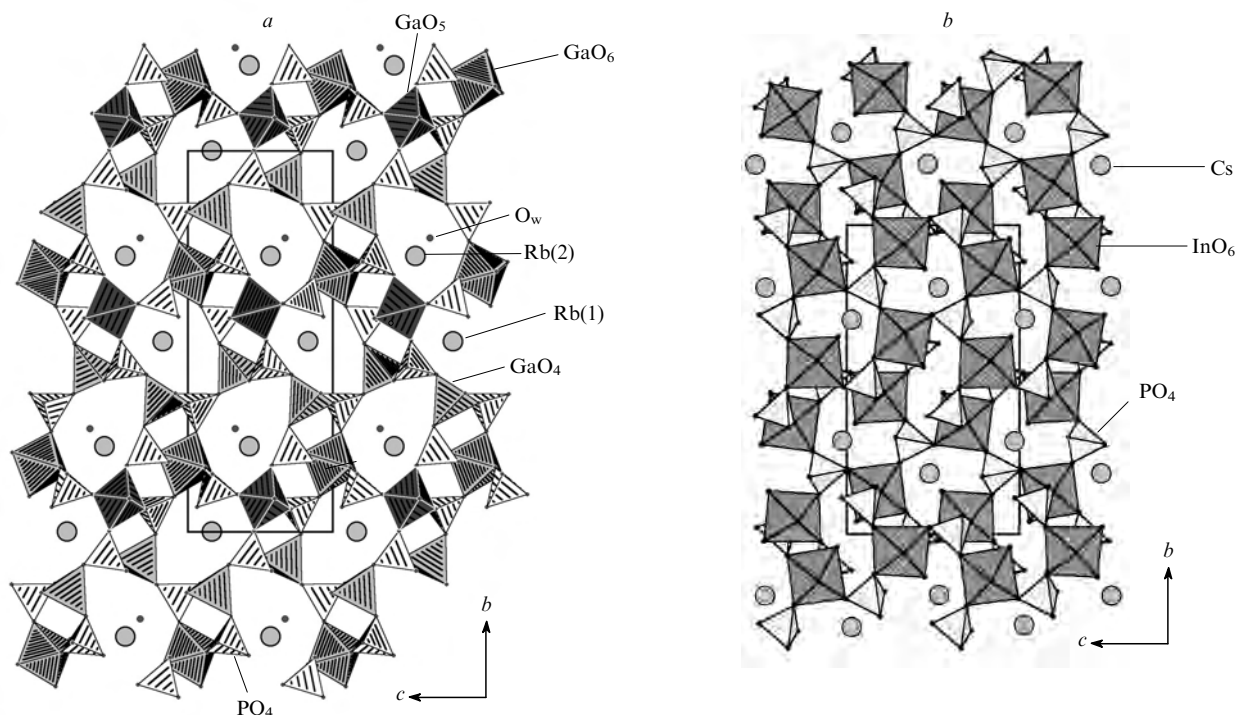
Compound	Crystal system	Space group	Z	Unit cell parameters				Ref.
				$a/\text{\AA}$	$b/\text{\AA}$	$c/\text{\AA}$	β/deg	
$Rb_2Ga_4(HPO_4)(PO_4)_4 \cdot 0.5 H_2O$	monoclinic	$P2_1$	2	5.061	21.643	8.207	91.8	58
$CsV_2(HPO_4)_2(PO_4)(H_2O)_2$	"	$P2_1/a$	4	10.004	17.812	6.370	97.0	62
$CsIn_2(HPO_4)_2(PO_4)(H_2O)_2$	"	$P2_1/c$	4	6.580	18.092	10.180	97.9	63
$(H_3O)Al_3(H_2PO_4)_6(HPO_4)_2 \cdot 4 H_2O$	"	$C2/c$	4	16.722	9.437	17.126	90.9	73
$(H_3O)Fe_3(H_2PO_4)_6(HPO_4)_2 \cdot 4 H_2O$	"	$C2/c$	4	16.797	9.528	17.609	90.6	74
$KFe_3(H_2PO_4)_6(HPO_4)_2 \cdot 4 H_2O$	"	$C2/c$	4	17.01	9.604	17.50	90.9	75
$(NH_4)Fe_3(H_2PO_4)_6(HPO_4)_2 \cdot 4 H_2O$	"	$C2/c$	4	16.845	9.611	17.647	90.9	76
$(NH_4)_{0.33}Al_{0.89}(H_2PO_4)(HPO_4) \cdot 2 H_2O$	trigonal	$P31c$	6	8.905	—	16.488	—	77
$(NH_4)Fe_3(H_2PO_4)_3[PO_3(OH)]_{0.67}O_{0.33} \cdot 6 H_2O$	"	$P31c$	2	9.151	—	16.862	—	78

the PO_4 tetrahedra and one oxygen atom of the water molecule. The HPO_4 polyhedra share three vertices with the adjacent octahedra and their fourth protonated vertex is not involved in the first coordination sphere of the In^{3+} cation. The PO_4 tetrahedron shares all vertices with the nearest InO_6 octahedra. The InO_6 , PO_4 and HPO_4 polyhedra are linked to each other to form one-dimensional ribbons along the c axis (Fig. 10 *b*). These ribbons are linked in a framework through the HPO_4 groups. The large cavities in the framework are occupied by caesium cations (the coordination number of caesium is 11).

Hydrogen phosphate $CsV_2(HPO_4)_2(PO_4)(H_2O)_2$ has an analogous structure.⁶² However, the coordination polyhedron of caesium is enlarged (the coordination number of caesium is 13) due to the smaller ionic radius of vanadium. In this structure, the interactions between the ribbons somewhat resemble the interactions in the well-known structural type $M^V OPO_4$ with the difference that the $M^V O$ component is replaced by $M^{III}OH_2$ and additional phosphate groups are present between the ribbons. Taking into account the difference in the size of the vanadium and indium cations, it is reasonable to suggest that the structures characterised by an analogous topology of the framework must exist for the $CsFe$ - and $CsSc$ -containing compounds because the ionic radii of Fe and Sc are in the range between $r_{VI}(V^{3+})$ and $r_{VI}(In^{3+})$.

The third type of complex hydrogen phosphates includes compounds of the general formula $M^I_x M^{III}_y (H_2PO_4)_z (HPO_4)_u \cdot nH_2O$ ($M^I = K, H_3O, NH_4$; $M^{III} = Al, Fe$; $n = 2-6$) containing two types of hydrogen phosphate anions, *viz.*, HPO_4^{2-} and $H_2PO_4^-$. The crystallographic characteristics of the monoclinic and trigonal structural types of these compounds are given in Table 6. These compounds are characterised by the ratio $M^I : M^{III} = 1 : 3$. Apparently, their stability is associated with the substantial difference in the radii of the M^I and M^{III} cations.

Hydrogen phosphates with composition $M^I M^{III}_3 (H_2PO_4)_6 \cdot (HPO_4)_2 \cdot 4H_2O$ ($M^I = K, H_3O, NH_4$)⁷³⁻⁷⁷ and the ratio $H_2PO_4 : HPO_4 = 3 : 1$ were obtained for aluminium and iron. In the structures of these compounds, water of crystallisation is not involved in the coordination sphere about the M^{III} cations. The structure of monoclinic phosphate with composition $KFe_3(H_2PO_4)_6(HPO_4)_2 \cdot 4H_2O$ (Fig. 11 *a*)⁷⁵ is characterised by a pronounced layered motif. The layers are composed of characteristic structural blocks, which are built from two different FeO_6 octahedra linked through the phosphate groups of two types, *viz.*, $[HPO_4]^{2-}$ and $[H_2PO_4]^-$ (Fig. 11 *b*). The interlayer space is occupied by water molecules. The layers are related by the symmetry elements of the crystal lattice (space group $C2/c$) so that the channels are not formed along the $[001]$ direction. The layers contain cavities occupied by potassium atoms to form the

**Figure 10.** Structures of $Rb_2Ga_4(HPO_4)(PO_4)_4 \cdot 0.5 H_2O$ (*a*) and $CsIn_2(HPO_4)_2(PO_4)(H_2O)_2$ (*b*) projected onto the bc plane.

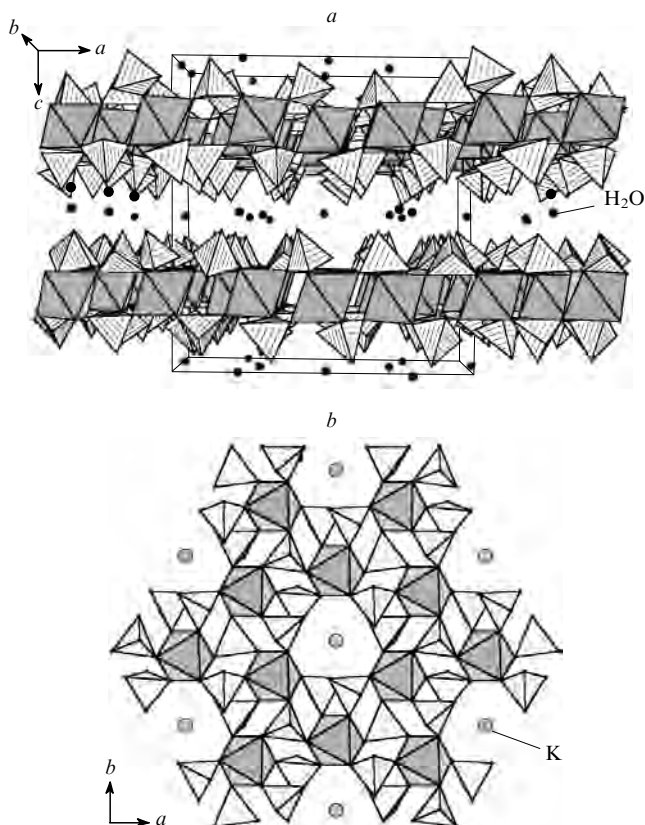


Figure 11. Structure of $\text{KFe}_3(\text{H}_2\text{PO}_4)_6(\text{HPO}_4)_2 \cdot 4\text{H}_2\text{O}$ projected along the $[010]$ direction (a) and projected onto the ab plane (b).

KO_{12} polyhedra. The layers are linked through hydrogen bonds between the oxygen atoms of the phosphate groups and water molecules, which impart additional stability to the structure. Taking into account the data on the structures of the $\text{M}^{\text{I}}\text{Fe}_3(\text{H}_2\text{PO}_4)_6(\text{HPO}_4)_2 \cdot 4\text{H}_2\text{O}$ compounds, where $\text{M}^{\text{I}} = \text{K}, \text{H}_3\text{O}$ or NH_4 , and of their $(\text{H}_3\text{O})\text{Al}$ analogue, compounds with such a composition would be expected to exist also for $\text{M}^{\text{III}} = \text{Ga}$ or V .

The $(\text{NH}_4)_{0.33}\text{Al}_{0.89}(\text{H}_2\text{PO}_4)(\text{HPO}_4) \cdot 2\text{H}_2\text{O}$ (see Ref. 77) and $(\text{NH}_4)\text{Fe}_3(\text{H}_2\text{PO}_4)_3[\text{PO}_3(\text{OH})_{0.67}\text{O}_{0.33}]_3 \cdot 6\text{H}_2\text{O}$ (see Ref. 78) compounds are characterised by the presence of water molecules fulfilling different functions. The structures of these trigonal hydrogen phosphates differ in the number of formula units per unit cell (6 and 2, respectively).^{77, 78} Three crystallographically independent M^{III} cations occupy the virtually non-distorted MO_6 octahedra in which the $\text{M}^{\text{III}}-\text{O}$ distance increases in parallel with the ionic radius of M^{III} . The structural formula $(\text{NH}_4)_{0.33}\text{Al}_{0.89} \cdot (\text{H}_2\text{PO}_4)(\text{HPO}_4)(\text{H}_2\text{O}) \cdot \text{H}_2\text{O}$ reflects the different role of the water molecules in the crystal motif of this compound. Three independent OH groups belonging to the HPO_4 [P(1) O_4 tetrahedron] and H_2PO_4 [P(2) O_4 tetrahedron] groups and two water molecules (coordinated to the Al atom and the NH_4 group) participate in hydrogen bonding. The NH_4^+ ions are surrounded by nine oxygen atoms most of which belong to the OH groups or H_2O molecules.

Trigonal NH_4Al and NH_4Fe phosphates have framework structures. In the crystal structures, the $\text{M}^{\text{III}}(2)\text{O}_6$ and $\text{M}^{\text{III}}(3)\text{O}_6$ octahedra are located on threefold axes and share all their vertices with the phosphate tetrahedra. The $\text{M}^{\text{III}}(1)\text{O}_6$ octahedron has three vertices in common with the PO_4 tetrahedra and the remaining three vertices are occupied by the oxygen atoms of water molecules. In the structure of NH_4Fe phosphate (Fig. 12 a, b),⁷⁸ the position of the protonated oxygen atom in the P(1) tetrahedron is statistically occupied by the hydrogen atom $(\text{OH})_{2/3}\text{O}_{1/3}$.

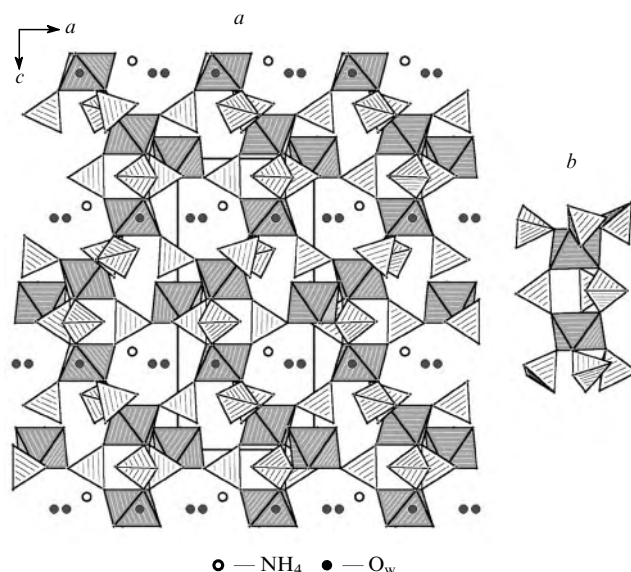


Figure 12. Structure of $(\text{NH}_4)\text{Fe}_3(\text{H}_2\text{PO}_4)[\text{PO}_3(\text{OH})_{0.67}\text{O}_{0.33}]_3 \cdot 6\text{H}_2\text{O}$ projected onto the ac plane (a) and the structural block of two octahedra (b).

The structural block consisting of two octahedra, which are linked to nine tetrahedra through vertices (Fig. 12 b), is present in the crystal structures of many polytypic minerals, for example, of coquimbite, paracoquimbite and ferrinatrite $\text{Na}_3\text{Fe}(\text{SO}_4)_3(\text{H}_2\text{O})_3$. In the latter compound, such fragments formed by the Fe octahedra and SO_4 tetrahedra are linked in chains parallel to the c axis. These chains are 'threaded' on threefold axes of the trigonal unit cell (space group $P\bar{3}$). Hence, the same repeated fragment is present in the crystal motifs of different classes of compounds. The degree of polymerisation of this fragment determines the structural diversity of compounds. It should be noted that if the octahedra with the coordinates $(1/3; 2/3; z)$ located on a threefold axis are linked through tetrahedra to analogous octahedra with the coordinates $(2/3; 1/3; z)$ located on another threefold axis, a large number of structures analogous to NH_4Al and NH_4Fe phosphates are generated. These structures can be assigned to zeolite-type compounds. Compounds in which the M^{I} -cation positions are vacant can also have analogous structures. In this case, the crystal-chemical formula can be written as $\square\text{M}^{\text{III}}(\text{H}_2\text{PO}_4)(\text{HPO}_4)(\text{H}_2\text{O}) \cdot \text{H}_2\text{O}$.⁷⁷

The fourth type of hydrogen phosphates, viz., $\text{M}_2^{\text{I}}\text{M}^{\text{III}}(\text{H}_2\text{PO}_4)(\text{HPO}_4)_2 \cdot \text{H}_3\text{PO}_4 \cdot 0.5\text{H}_2\text{O}$, is known only for gallium.⁶⁴ This compound has a unique composition because it contains protonated phosphate groups of all three types, viz., HPO_4^{2-} , H_2PO_4^- and H_3PO_4 . The $\text{Cs}_2\text{Ga}(\text{H}_2\text{PO}_4)(\text{HPO}_4)_2 \cdot \text{H}_3\text{PO}_4 \cdot 0.5\text{H}_2\text{O}$ compound crystallises in the tetragonal system with a rare non-centrosymmetrical unit cell (space group $I4_1cd$, $a = 20.168$, $c = 18.287$ Å, $Z = 16$). In this compound, the gallium atom is in a slightly distorted octahedral environment formed by four oxygen atoms of the HPO_4 groups and two oxygen atoms of the H_2PO_4 groups (Fig. 13 a). One H_2PO_4 group, two HPO_4 groups and the GaO_6 octahedron are involved in the typical $[\text{Ga}(\text{H}_2\text{PO}_4)(\text{HPO}_4)_2]_{\infty}^{2-}$ structural block. These blocks are linked in infinite columns along the $[001]$ direction with the identity period involving four GaO_6 octahedra (due to the presence of a screw axis 4_1 , Fig. 13 b). Each column is linked to four adjacent columns through hydrogen bonds involving the H_3PO_4 molecules.

The crystal lattice contains large cavities occupied by water molecules and caesium cations. The structure contains two types of Cs atoms. The strongly distorted $\text{Cs}(2)\text{O}_{11}$ polyhedron is formed by the oxygen atoms of the phosphate groups of all three types and by the H_2O molecule, which is involved in formation of

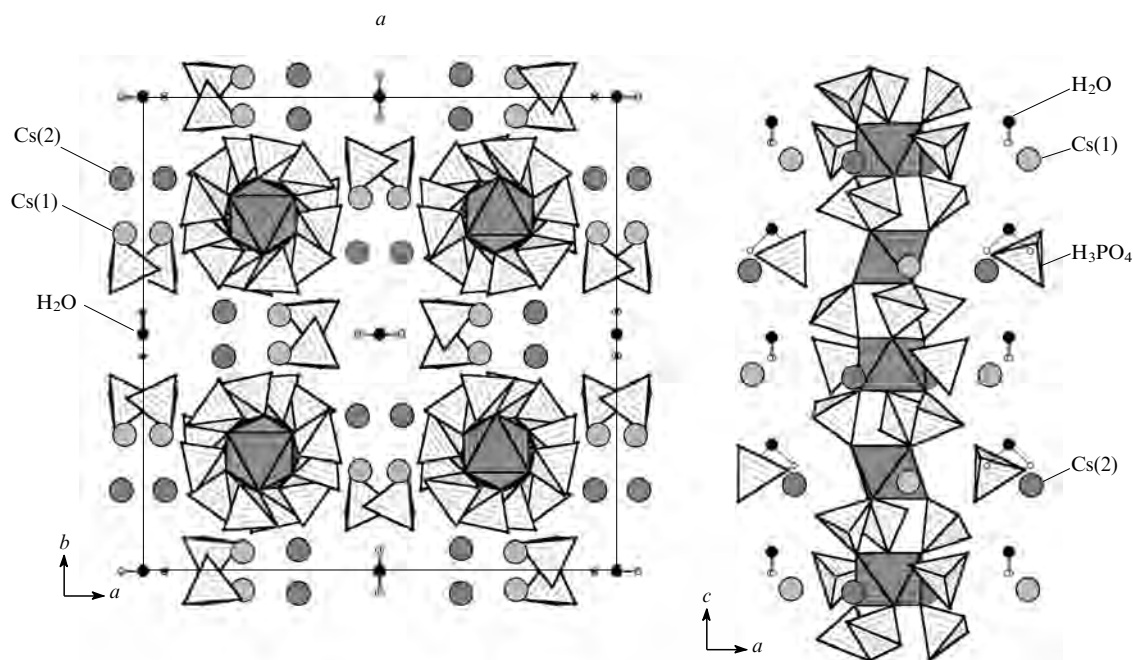


Figure 13. Structure of $\text{Cs}_2\text{Ga}(\text{H}_2\text{PO}_4)(\text{HPO}_4)_2 \cdot \text{H}_3\text{PO}_4 \cdot 0.5 \text{H}_2\text{O}$ projected onto the ab plane (a) and the fragment of the $[\text{Ga}(\text{H}_2\text{PO}_4)(\text{HPO}_4)_2]_\infty$ column in combination with the H_3PO_4 and H_2O molecules and Cs^+ cations (b).

the $\text{Cs}(2)-\text{O}_w-\text{Cs}(2)$ chains. The $\text{Cs}(1)\text{O}_9$ polyhedra are less distorted and are not linked to the water molecules.

Analysis of the interatomic distances in the polyhedra of the $\text{Cs}_2\text{Ga}(\text{H}_2\text{PO}_4)(\text{HPO}_4)_2 \cdot \text{H}_3\text{PO}_4 \cdot 0.5 \text{H}_2\text{O}$ structure showed that the gallium position can, in principle, be occupied by the Al, Fe and V atoms whose ionic radii are not much different from that of gallium. These replacements can lead to distortion of the unit-cell symmetry but the main $[\text{M}^{\text{III}}(\text{H}_2\text{PO}_4)(\text{HPO}_4)_2]_\infty$ structural block must persist. By contrast, the replacement of caesium with rubidium or potassium must lead to degradation of the structure due to the tendency of smaller cations to have smaller coordination polyhedra.

The above-considered structural features of hydrogen phosphates containing mono- and trivalent cations, *viz.*, the presence of the HPO_4 and H_2PO_4 groups and water molecules and the mode of their binding, are responsible both for the temperature range of stability of hydrogen phosphates and the possibility of their use in the synthesis of other classes of compounds.

Thermal decomposition of hydrogen phosphates $\text{M}^{\text{I}}\text{M}^{\text{III}}(\text{HPO}_4)_2 \cdot n\text{H}_2\text{O}$ ($\text{M}^{\text{I}} = \text{Na}, \text{K}, \text{Rb}, \text{Cs}$) is accompanied by the formation of pyrophosphates $\text{M}^{\text{I}}\text{M}^{\text{III}}\text{P}_2\text{O}_7$. Decomposition of

$\text{RbFe}(\text{HPO}_4)_2$ is accompanied by the removal of the water molecule in the temperature range of 350–550 °C to give crystalline RbFeP_2O_7 . Thermal decomposition of $\text{M}^{\text{I}}\text{In}(\text{HPO}_4)_2$ ($\text{M}^{\text{I}} = \text{K}, \text{Rb}, \text{Cs}$) starts at about 280 °C and completes at 550–650 °C to form $\text{M}^{\text{I}}\text{InP}_2\text{O}_7$. Decomposition of $(\text{NH}_4)\text{In}(\text{HPO}_4)_2$ at 800 °C affords a mixture of $\text{In}_4(\text{P}_2\text{O}_7)_3$ and $\text{In}(\text{PO}_3)_3$. Thermal decomposition of $(\text{H}_3\text{O})\text{Fe}(\text{HPO}_4)_2$ proceeds in two steps. In the first step (at 670 °C), H_2O is removed and hydrogen pyrophosphate is formed. The latter decomposes at 870 °C to give $\text{Fe}_2\text{P}_2\text{O}_7$ and $\text{Fe}(\text{PO}_3)_2$. Heating of $\text{Na}_2\text{In}_2(\text{HPO}_4)_4 \cdot \text{H}_2\text{O}$ results in the loss of a water molecule (~ 365 °C) followed by crystallisation of a non-identified phase, which melts at 1208 °C.

Thermal decomposition of hydrogen phosphates of the second and third types is a complex process and does not afford single-phase products. In the case of $\text{Rb}_2\text{Ga}_4(\text{HPO}_4)(\text{PO}_4)_4 \cdot 0.5 \text{H}_2\text{O}$, the removal of water of crystallisation followed by dehydration was observed at 250–600 °C. Dehydration of $(\text{NH}_4)_{0.33}\text{Al}_{0.89}(\text{H}_2\text{PO}_4)(\text{HPO}_4) \cdot 2 \text{H}_2\text{O}$ proceeded successively. First, the water molecules and ammonium ions were eliminated at 320 °C and then the hydro- and dihydrogen phosphate anions

Table 7. Characterisation of different structural types of hydrogen phosphates containing M^{I} and M^{III} cations.

Type of compound	Ratio $\text{M}^{\text{I}} : \text{M}^{\text{III}}$	Type and ratio of phosphate groups	Crystal system	Space group	Structural blocks	Structural type
$\text{M}_x^{\text{I}}\text{M}_y^{\text{III}}(\text{H}_2\text{PO}_4)_z(\text{HPO}_4)_u \cdot n\text{H}_2\text{O}$ $\text{M}^{\text{I}} = \text{K}, \text{NH}_4, \text{H}_3\text{O}; \text{M}^{\text{III}} = \text{Al}, \text{Fe}$	1 : 3	$\text{H}_2\text{PO}_4 : \text{HPO}_4 = 3 : 1$ $\text{H}_2\text{PO}_4 : \text{HPO}_4 = 1 : 1$	monoclinic trigonal	$C2/c$ $P\bar{3}1c$	$[\text{M}^{\text{III}}\text{O}_6] + [\text{HPO}_4]$ and $[\text{H}_2\text{PO}_4]$ $[\text{M}^{\text{III}}\text{O}_{5w}] + [\text{HPO}_4]$ and $[\text{H}_2\text{PO}_4]$	layered framework
$\text{M}_x^{\text{I}}\text{M}_y^{\text{III}}(\text{HPO}_4)_z(\text{PO}_4)_u \cdot n\text{H}_2\text{O}$ $\text{M}^{\text{I}} = \text{Rb}, \text{Cs}; \text{M}^{\text{III}} = \text{Ga}, \text{In}, \text{V}$	1 : 2	$\text{HPO}_4 : \text{PO}_4 = 2 : 1$ $\text{HPO}_4 : \text{PO}_4 = 1 : 4$	monoclinic "	$P2_1/c$ $P2_1/c$	$[\text{M}^{\text{III}}\text{O}_{5w}] + [\text{HPO}_4]$ and $[\text{PO}_4]^a$ $[\text{M}^{\text{III}}\text{O}_{4,5,6}] + [\text{HPO}_4]$ and $[\text{PO}_4]$	" "
$\text{M}_x^{\text{I}}\text{M}_y^{\text{III}}(\text{HPO}_4)_z \cdot n\text{H}_2\text{O}$ $\text{M}^{\text{I}} = \text{Na}; \text{M}^{\text{III}} = \text{In}$	1 : 2	HPO_4	trigonal	$P\bar{3}c1$	$[\text{InO}_6]$ and $[\text{InO}_5\text{O}_w] + [\text{HPO}_4]$	"
$\text{M}_x^{\text{I}}\text{M}_y^{\text{III}}(\text{HPO}_4)_z \cdot n\text{H}_2\text{O}$ $\text{M}^{\text{I}} = \text{Na}, \text{K}, \text{Rb}, \text{Cs}, \text{NH}_4, \text{H}_3\text{O};$ $\text{M}^{\text{III}} = \text{Al}, \text{Ga}, \text{In}, \text{V}, \text{Fe}$	1 : 1	HPO_4	triclinic monoclinic trigonal	$P\bar{1}$ $P2_1/c$ $R\bar{3}c$	$[\text{M}^{\text{III}}\text{O}_6] + [\text{HPO}_4]^b$ $[\text{M}^{\text{III}}\text{O}_6] + [\text{HPO}_4]^c$	" " "
$\text{M}_x^{\text{I}}\text{M}_y^{\text{III}}(\text{H}_2\text{PO}_4)_z(\text{HPO}_4)_u(\text{H}_3\text{PO}_4)_m \cdot n\text{H}_2\text{O}$ ($\text{M}^{\text{I}} = \text{Cs}; \text{M}^{\text{III}} = \text{Ga}$)	2 : 1	$\text{H}_2\text{PO}_4 : \text{HPO}_4 :$ $\text{H}_3\text{PO}_4 = 1 : 2 : 1$	tetragonal	$I4_1cd$	$[\text{M}^{\text{III}}\text{O}_6] + [\text{HPO}_4], [\text{H}_2\text{PO}_4]$ and $[\text{H}_3\text{PO}_4]$	chain

^a Ribbons, ^b columns, ^c helical columns.

decomposed. In the final step, AlPO_4 crystallised (tridymite modification).

A comparison of different procedures for the synthesis and a knowledge of the structural features of hydrogen phosphates containing mono- and trivalent cations lead to the conclusion that the steric factors play the major role in the formation of different types of complex hydrogen phosphates (Table 7). The presence of various organic additives and the use (in some cases) of fluoride ions as a mineraliser have less substantial effects on the compositions of the resulting compounds as compared to the influence of the $\text{M}^{\text{I}}:\text{M}^{\text{III}}$ ratio and the difference in the sizes of these cations. The effect of the M^{I} and M^{III} cations on stability of complex hydrogen phosphates in combination with the use of particular conditions for the formation of various protonated forms of phosphate groups in aqueous solutions provide the basis for the directed synthesis of new compounds.

IV. Fluoride phosphates containing mono- and trivalent cations

Depending on the ratios of the cations (M^{I} and M^{III}) and anions (F^- and PO_4^{3-}), fluoride phosphates containing mono- and trivalent cations form several groups of compounds with compositions $\text{M}^{\text{I}}\text{M}^{\text{III}}\text{FPO}_4$, $\text{M}_2^{\text{I}}\text{M}_2^{\text{III}}\text{F}_3(\text{PO}_4)_2$, $\text{M}_2^{\text{I}}\text{M}^{\text{III}}\text{F}_2(\text{PO}_4)_2$ and $(\text{M}^{\text{I}},\text{M}^{\text{II}},\text{M}^{\text{III}})_5\text{F}(\text{PO}_4)_3$ ($\text{M}^{\text{I}} = \text{Li, Na, K, NH}_4$; M^{II} are alkali-earth elements; M^{III} are *p*-, *d*- or *f*-elements). Four types of REE sodium fluoride phosphates with different compositions were found in studies of the phase formation in the ternary systems $\text{Na}^+,\text{M}^{\text{III}}/\text{F}^-,\text{PO}_4^{3-}$ ($\text{M}^{\text{III}} = \text{La, Nd, Gd, Er}$) by powder X-ray diffraction analysis.^{79,80} Minerals belonging to fluoride phosphates are known, in particular, amblygonite LiAlFPO_4 ,^{81,82} tavorite $\text{LiFe}(\text{OH},\text{F})\text{PO}_4$ (see Ref. 83) and lacroixite NaAlFPO_4 (see Ref. 84) as well as apatite-like deloneite $\text{NaCa}_3\text{CeF}(\text{PO}_4)_3$ and belovite $\text{NaSr}_3\text{CeF}(\text{PO}_4)_3$. In some fluoride phosphates, the fluoride ions are partially replaced with the hydroxide ions of a similar size. The $\text{OH}:\text{F}$ ratio may vary; *cf.*, $\text{Na}_3\text{Fe}_2[(\text{OH})_2\text{F}](\text{PO}_4)_2$ (see Ref. 85) and $\text{M}^{\text{I}}\text{M}^{\text{III}}\text{F}_{1-\delta}(\text{OH})_\delta\text{PO}_4$ ($\text{M}^{\text{I}} = \text{K, Rb, NH}_4$; $\text{M}^{\text{III}} = \text{Al, Ga, In}$; $\delta \approx 0.3, 0.5$).⁸⁶

1. Synthesis

Fluoride phosphates of different types, *viz.*, $\text{M}^{\text{I}}\text{M}^{\text{III}}\text{FPO}_4$ ($\text{M}^{\text{I}} = \text{Na, K, NH}_4$; $\text{M}^{\text{III}} = \text{Al, Cr, Fe, Ga, In, Y, Gd-Ho}$), $\text{Na}_3\text{Fe}_2[(\text{OH})_2\text{F}](\text{PO}_4)_2$, $\text{Na}_3\text{M}_2^{\text{III}}\text{F}_3(\text{PO}_4)_2$ ($\text{M}^{\text{III}} = \text{Al, V, Cr, Fe, Ga}$), $\text{Na}_5\text{M}^{\text{III}}\text{F}_2(\text{PO}_4)_2$ ($\text{M}^{\text{III}} = \text{Al, Cr, Ga}$), and $(\text{Na},\text{M}^{\text{II}},\text{M}^{\text{III}})_5.\text{F}(\text{PO}_4)_3$ (M^{II} are alkali-earth metals; M^{III} are REE), were synthesised in the solid state by crystallisation from flux or by the hydrothermal method.

The $\text{NaM}^{\text{III}}\text{FPO}_4$ compounds ($\text{M}^{\text{III}} = \text{Gd, Tb, Dy}$) were prepared by heating stoichiometric amounts of $\text{M}^{\text{III}}\text{PO}_4$ ($\text{M}^{\text{III}} = \text{Gd, Tb, Dy}$) and NaF in air at 550 °C ($\text{M}^{\text{III}} = \text{Gd, Tb}$) or 500 °C ($\text{M}^{\text{III}} = \text{Dy}$). Potassium fluoride phosphates $\text{KM}^{\text{III}}\text{FPO}_4$ ($\text{M}^{\text{III}} = \text{Cr, Fe}$) were prepared by the reactions of chromium (or iron) oxide with $\text{K}_2\text{O}-\text{P}_2\text{O}_5$ melts in the presence of KF at 600–800 °C. In pure form, these compounds are formed in the $\text{K}_2\text{O}:\text{P}_2\text{O}_5$ range from 1:1 to 1:1.7 ($\text{M}^{\text{III}} = \text{Cr}$) or from 1:1.5 to 1:2 ($\text{M}^{\text{III}} = \text{Fe}$); otherwise the reactions afford the corresponding pyrophosphate $\text{KM}^{\text{III}}\text{P}_2\text{O}_7$.

The solid-phase synthesis of fluoride phosphates $\text{Na}_3\text{M}_2^{\text{III}}\text{F}_3(\text{PO}_4)_2$ containing aluminium, chromium or iron was carried out with the use of two-, three- or four-component mixtures ($\text{NaF}-\text{M}^{\text{III}}\text{PO}_4$, $\text{M}^{\text{III}}\text{F}_3-\text{M}^{\text{III}}\text{PO}_4-\text{Na}_3\text{PO}_4$, $\text{NaF}-\text{M}^{\text{III}}\text{PO}_4-\text{NaCl}-\text{ZnCl}_2$, $\text{Na}_2\text{O}-\text{M}_2^{\text{III}}\text{O}_3-\text{P}_2\text{O}_5-\text{NaF}$).^{85,87–90} The reactions were carried out under an atmosphere of argon at $T = 600-880$ °C. Aluminium (iron) sodium fluoride phosphates were prepared by recrystallisation of fluoride phosphate glasses formed upon heating of the $\text{NaPO}_3-\text{M}^{\text{III}}\text{F}_3$ or $\text{NaF}-\text{M}^{\text{III}}\text{PO}_4-\text{M}^{\text{III}}\text{F}_3$ mixtures ($\text{M}^{\text{III}} = \text{Al, Fe}$) above the melting point followed by cooling in air to the crystallisation temperature. Aluminium-containing glass characterised by a large difference between the

crystallisation and glass-transition temperatures is more stable than iron-containing glass.

Of fluoride phosphates of the $\text{M}_5^{\text{I}}\text{M}^{\text{III}}\text{F}_2(\text{PO}_4)_2$ family ($\text{M}^{\text{III}} = \text{Al, Cr, Fe, Ga}$), only sodium-containing derivatives were prepared. The solid-phase synthesis of most of compounds with this composition was performed in the $\text{M}_2^{\text{III}}\text{O}_3-\text{Na}_2\text{O}-\text{P}_2\text{O}_5-\text{NaF}$ (or NaCl) system ($\text{M}^{\text{III}} = \text{Cr, Fe, Ga}$) at $T \approx 750-1300$ °C by crystallisation from flux.^{91–95} The aluminium derivative was prepared according to two procedures, *viz.*, by the solid-phase reaction in the $\text{AlF}_3-\text{Al}(\text{OH})_3-\text{NaH}_2\text{PO}_4-\text{Na}_3\text{PO}_4$ system at $T = 1000$ °C and precipitation from a solution.⁹⁶ In the latter case, $\text{AlF}_3 \cdot 3\text{H}_2\text{O}$ was added to an aqueous solution of NaH_2PO_4 at 80 °C. The suspension was kept at $T = 60$ °C for several days after which crystallisation started.

Mixed sodium- and REE-containing fluoride phosphates were prepared with the use of two-, three- or four-component $\text{Na}^+,\text{M}^{\text{III}}/\text{F}^-,\text{PO}_4^{3-}$ mixtures ($\text{M}^{\text{III}} = \text{La, Nd, Gd, Er}$). The mixtures were annealed under an inert or reductive atmosphere and also *in vacuo* at a temperature from 750 to 1150 °C.^{79,80} When synthesising REE fluoride phosphates in air, the duration of annealing of the samples must be rigidly controlled because the time of annealing has a substantial effect on the composition of the final product. Thus, annealing of samples for 12–18 h (750 °C) gave rise to fluoride phosphate with specified composition. More prolonged heating (72 h) afforded REE oxofluorides and double phosphates $\text{Na}_3\text{M}^{\text{III}}(\text{PO}_4)_2$ ($\text{M}^{\text{III}} = \text{REE}$).

Apatite-like REE fluoride phosphates were synthesised by the solid-phase method from $\text{M}^{\text{II}}\text{CO}_3$ ($\text{M}^{\text{II}} = \text{Ca, Sr, Ba}$), ammonium hydrogen phosphate, REE oxide and an excess of NaF at ~ 1200 °C.^{97–99} Phases with variable composition $\text{Li}_x\text{M}_x^{\text{III}}\text{Y}_{1-x}\text{F}_{4x}(\text{PO}_4)_{1-x}$ ($\text{M}^{\text{III}} = \text{Gd-Lu}$; Y ; $0 \leq x \leq 0.45$) were prepared by heating stoichiometric amounts of double fluoride $\text{LiM}^{\text{III}}\text{F}_4$ and yttrium orthophosphate at 800 °C.¹⁰⁰

Fluoride phosphates with different compositions can be obtained in the multicomponent $\text{M}^{\text{I}}\text{F}-\text{M}_2^{\text{III}}\text{O}_3-\text{H}_3\text{PO}_4-\text{H}_2\text{O}$ systems ($\text{M}^{\text{I}} = \text{Li, Na, K, NH}_4$; $\text{M}^{\text{III}} = \text{Al, Fe, Ga, In, Y, Ho, Er}$) under the hydrothermal conditions.^{83,85,86,101,102} For example, $\text{LiFe}(\text{OH},\text{F})\text{PO}_4$ (synthetic mineral tavorite)⁸³ and analogues of natural iron phosphates, such as triphylite LiFePO_4 , sarcopside $\text{Fe}_3(\text{PO}_4)_2$ and zieselite Fe_2FPO_4 ,¹⁰² were obtained from the $\text{LiF}-\text{Fe}_2\text{O}_3-\text{H}_3\text{PO}_4-\text{H}_2\text{O}$ system at $\approx 300-500$ °C and $p \approx 1.5$ kbar. Attempts to prepare gallium potassium fluoride phosphate KGaFPO_4 , unlike analogous aluminium and iron compounds, failed although different modes of the solid-phase synthesis ($\text{Ga}_2\text{O}_3-\text{NH}_4\text{H}_2\text{PO}_4-\text{KF}$ mixture) and crystallisation from flux (anhydrous $\text{Ga}_2\text{O}_3-\text{KPO}_3-\text{KF}$ system) were used. Compounds in which the fluoride ions are partially replaced by the hydroxide groups, *viz.*, $\text{M}^{\text{I}}\text{M}^{\text{III}}\text{F}_{1-\delta}(\text{OH})_\delta\text{PO}_4$ ($\text{M}^{\text{I}} = \text{K, Rb, NH}_4$; $\text{M}^{\text{III}} = \text{Al, Ga, In}$; $\delta \approx 0.3; 0.5$)^{86,103,104} and $\text{Na}_3\text{Fe}_2[(\text{OH})_2\text{F}](\text{PO}_4)_2$,⁸⁵ were prepared only under the hydrothermal conditions.

After the successful synthesis of a series of porous crystalline aluminosilicates (zeolites) and aluminophosphates, attempts were made to prepare porous fluoride phosphates of the general formula $\text{A}_n\text{M}_x^{\text{III}}\text{F}_y(\text{PO}_4)_z$ ($\text{M}^{\text{III}} = \text{Ga, Fe, In}$; A is organic amine). It was expected that these compounds would find use as catalysts, molecular sieves or ion exchangers. In studies of the phase formation in the $\text{NH}_4\text{F}-\text{M}_2^{\text{III}}\text{O}_3-\text{H}_3\text{PO}_4$ -amine- H_2O ($\text{M}^{\text{III}} = \text{Ga, Fe}$) and $\text{NH}_4\text{F}-\text{Ce}^{\text{IV}}(\text{SO}_4)_2-\text{H}_3\text{PO}_4$ -amine- H_2O systems at $T = 180$ °C and $p = 18$ bar, ammonium-containing fluoride phosphates $\text{NH}_4\text{M}^{\text{III}}\text{FPO}_4$ ($\text{M}^{\text{III}} = \text{Ga, Fe}$)^{105,106} and $\text{NH}_4\text{Ce}^{\text{IV}}\text{F}_2\text{PO}_4$ (see Ref. 107) were obtained. When Ga_2O_3 was used, ammonium-containing fluoride phosphate with unusual composition $(\text{NH}_4)_2\text{Ga}_2\text{F}_3(\text{PO}_4)(\text{HPO}_4)$ was obtained along with $\text{NH}_4\text{GaFPO}_4$.¹⁰⁶

Polycrystalline samples of the $\text{Na}_3\text{M}_2^{\text{III}}\text{F}_3(\text{PO}_4)_2$ compounds ($\text{M}^{\text{III}} = \text{V, Ga}$) were prepared under low-temperature hydrothermal conditions ($T = 180$ °C, $p = 18$ bar). However, the final products were contaminated by intermediates produced in the synthesis. The procedure used for the synthesis of sodium vana-

dium fluoride phosphate $\text{Na}_3\text{V}_2\text{F}_3(\text{PO}_4)_2$ (see Ref. 87) differs from a conventional method. Vanadium oxide V_2O_5 was dissolved in phosphoric acid and reduced with an aqueous solution of N_2H_4 until the solution turned green (V^{3+} ions) and then NaF was added (the molar ratio $\text{Na}:\text{V} = 4.3:2$). The resulting solution was heated first at 180°C and 18 bar and then at 700°C and 2 kbar after which it was slowly cooled to room temperature with a rate of 10°C per hour to obtain finally fluoride phosphate $\text{Na}_3\text{V}_2\text{F}_3(\text{PO}_4)_2$. The $\text{Na}_3\text{Ga}_2\text{F}_3(\text{PO}_4)_2$ compound⁸⁷ was not isolated in pure form (it contained impurities of GaPO_4 and GaF_3).

Aluminium fluoride phosphates $\text{K}_3\text{Al}_4\text{F}_9(\text{PO}_4)_2$ (see Ref. 108) and $(\text{NH}_4)\text{Al}_2\text{F}(\text{PO}_4)_2$ (see Ref. 109) were obtained by the hydrothermal method as by-products in the studies of the $\text{M}^{\text{III}}\text{F}-\text{M}_2^{\text{III}}\text{O}_3-\text{H}_3\text{PO}_4-\text{H}_2\text{O}$ systems.

2. Structure and properties

Sodium-containing fluoride phosphates with composition $\text{NaM}^{\text{III}}\text{FPO}_4$ are known only for $\text{M}^{\text{III}} = \text{Al}$, REE. In the structures of the $\text{NaM}^{\text{III}}\text{FPO}_4$ compounds ($\text{M}^{\text{III}} = \text{Y}$, Gd–Er),^{110, 111} the M^{III} atoms are located in the $[\text{M}^{\text{III}}\text{O}_6\text{F}_2]$ eight-vertex polyhedra (dodecahedra), the F atoms being in *cis* positions. The $\text{M}^{\text{III}}\text{O}_6\text{F}_2$ polyhedra are linked in infinite chains through common edges composed of two oxygen atoms. Every second polyhedron of one chain shares the edge composed of two fluorine atoms with the polyhedron from the adjacent chain giving rise to layers. These parallel layers are linked to each other through the PO_4 tetrahedra to form a framework (Fig. 14). The channels between the layers are occupied by sodium cations. The NaO_8F_2 coordination polyhedron is most preferable for sodium. The structural motif in the $\text{NaM}^{\text{III}}\text{FPO}_4$ compounds remains unchanged on going from Gd to Er and only the PO_4 tetrahedra are slightly rotated.

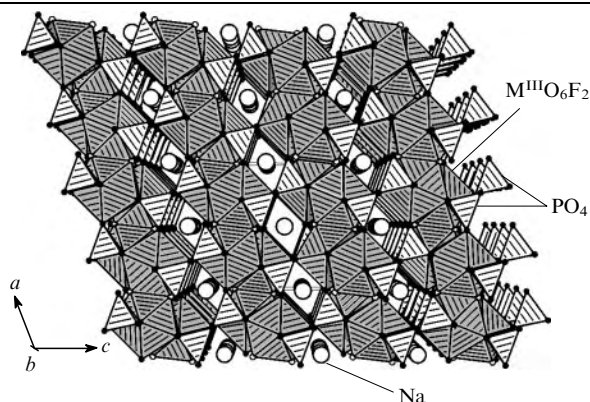


Figure 14. Fragment of the structure of $\text{NaM}^{\text{III}}\text{FPO}_4$ ($\text{M}^{\text{III}} = \text{Y}$, Gd–Er).

Considering the crystal structures of this type of compounds and taking into account that REE of the second half of the series (Gd–Er) tend to adopt high coordination numbers (>7), the formation of analogous sodium-containing fluoride phosphates would be highly improbable in the case of small trivalent REE cations (Yb, Lu) as well as in the case of In and Sc cations for which the coordination number of 6 is most typical. The exception is the mineral lacroixite NaAlFPO_4 .⁸⁴ There is evidence for the formation of REE sodium fluoride phosphates with composition $\text{Na}_3\text{M}_2^{\text{III}}\text{F}_3(\text{PO}_4)_2$ ($\text{M}^{\text{III}} = \text{Tm}$, Yb, Lu)[¶] but the structures of these compounds remain to be established.

The $\text{NaM}^{\text{III}}\text{FPO}_4$ compounds ($\text{M}^{\text{III}} = \text{Gd}-\text{Er}$) melt incongruently. According to the DTA data, their melting points decrease in the series Gd–Er from 903 to 837°C . In the case of stepwise annealing in air in the temperature range of $500-850^\circ\text{C}$, decomposition started already at 600°C , proceeded through the intermediate formation of $\text{M}^{\text{III}}\text{OF}$, Na_3PO_4 and $\text{M}^{\text{III}}\text{PO}_4$ and

afforded finally a mixture of double phosphate $\text{Na}_3\text{M}^{\text{III}}(\text{PO}_4)_2$ and oxide $\text{M}_2^{\text{III}}\text{O}_3$.

Potassium-containing fluoride phosphates $\text{KM}^{\text{III}}\text{FPO}_4$ are known for $\text{M}^{\text{III}} = \text{Al}$, Cr, Fe, In. In the crystal structure of KAlFPO_4 ,^{101, 112} the aluminium atoms are located in the $[\text{AlO}_4\text{F}_2]$ octahedra of two types, which differ in the positions of the F atoms (*trans* and *cis*). The structure of KInFPO_4 , unlike KAlFPO_4 , contains octahedra of only one type with a *cis* arrangement of the F atoms. In both $\text{KM}^{\text{III}}\text{FPO}_4$ compounds ($\text{M}^{\text{III}} = \text{Al}$, In), the $\text{M}^{\text{III}}\text{O}_4\text{F}_2$ octahedra are linked in parallel helical chains through fluoride bridges and these chains are linked to each other to form a framework.

Fluoride phosphates $\text{M}^{\text{I}}\text{M}^{\text{III}}\text{FPO}_4$ ($\text{M}^{\text{III}} = \text{Fe}$, Cr, Ga)^{113–116} containing the large monovalent K^+ or NH_4^+ cations are isostructural to potassium titanyl phosphate KTiOPO_4 (KTP).¹¹⁶ In the structures of $\text{M}^{\text{I}}\text{M}^{\text{III}}\text{FPO}_4$ with $\text{M}^{\text{I}} = \text{K}^+$ or NH_4^+ , the PO_4 tetrahedra and $\text{M}^{\text{III}}\text{O}_4\text{F}_2$ octahedra are less distorted than the TiO_6 octahedra in KTiOPO_4 . The $\text{M}^{\text{III}}\text{O}_4\text{F}_2$ octahedra are linked in chains extended in two mutually perpendicular directions (Fig. 15). These chains are linked to each other through the PO_4 tetrahedra to form a framework. The chains differ in that the PO_4 tetrahedra in these chains are oriented in opposite directions. The cavities in the framework are occupied by the potassium or ammonium cations.

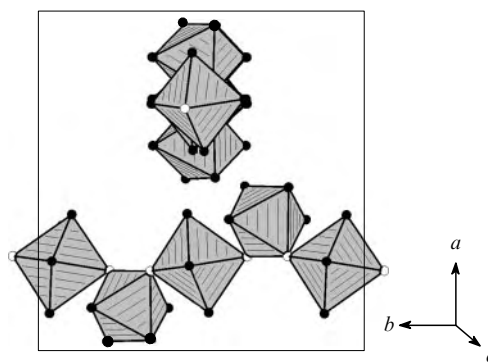


Figure 15. Chains of the $\text{M}^{\text{III}}\text{O}_4\text{F}_2$ octahedra in the structure of $\text{M}^{\text{I}}\text{M}^{\text{III}}\text{FPO}_4$ ($\text{M}^{\text{I}} = \text{K}$, NH_4 , $\text{M}^{\text{III}} = \text{Cr}$, Fe, Ga).

Two types of potassium atoms in the structures of $\text{KM}^{\text{III}}\text{FPO}_4$ are in a complicated coordination environment formed by fluorine and oxygen atoms. The coordination numbers of the K(1) and K(2) atoms are 8 and 9, respectively. The structure of KTiOPO_4 contains K atoms of one type with the coordination number of 9. The coordination polyhedra about the potassium atoms have one edge (F–O) in common. The cavities occupied by the potassium atoms are linked in pairs and form two types of helical channels perpendicular to each other. The crystallographic characteristics of the $\text{M}^{\text{I}}\text{M}^{\text{III}}\text{FPO}_4$ compounds are given in Table 8.

In recent years, the structural features and physical properties of KTP-type compounds have attracted considerable attention, which is associated with a search for new promising nonlinear optical materials. Taking into account the results of dielectric measurements and studies of conductivity, it was suggested that the structures of KTP-type compounds are changed at 0°C due to disordering in the potassium sublattice. An analogous phenomenon was found for fluoride phosphates $\text{KM}^{\text{III}}\text{FPO}_4$ ($\text{M}^{\text{III}} = \text{Al}$, Fe). Like in the structure of KTiOPO_4 , disordering in the potassium sublattice was observed in the structure of KFeFPO_4 . As a result, two additional positions are present along with two statistically occupied potassium positions. The occupancies of these four positions are 0.9, 0.92, 0.1 and 0.08. At a temperature of about -100°C , the K atoms are partially ordered, two main and one additional positions with the occupancies of 1.0, 0.94 and 0.06, respectively, being retained. Disorder in the potassium sublattice disappeared as the temperature was lowered to

¶ Our data.

Table 8. Crystallographic characteristics of the $M^I M^{III} FPO_4$ and $M^I M^{III} F_{1-\delta}(OH)_\delta PO_4$ compounds.

Compound (mineral name)	Crystal system	Space group	Z	Unit cell parameters				Ref.
				$a/\text{\AA}$	$b/\text{\AA}$	$c/\text{\AA}$	β (or α, β, γ) /deg	
LiAlFPO ₄ (amblygonite)	triclinic	$P\bar{1}$	2	5.060	5.160	7.080	$\alpha = 109.9, \beta = 107.5, \gamma = 97.9$	82
LiFe[(OH),F]PO ₄ (tavorite)	"	$C\bar{1}$	4	6.644	7.744	6.910	$\alpha = 90.3, \beta = 117.3, \gamma = 91.0$	81
		$P\bar{1}$	2	5.138	5.307	7.422	$\alpha = 67.5, \beta = 67.7, \gamma = 82.0$	83
NaAlFPO ₄ (lacroixite)	monoclinic	$C2/c$	4	6.414	8.207	6.885	115.47	84
NaYFPO ₄	"	$C2/m$	4	8.944	6.930	6.469	106.11	110
NaM ^{III} FPO ₄ (M ^{III} = Tb–Er)	"	$C2/m$	4	9.000 (Tb)– 8.943 (Er)	6.985 (Tb)– 6.923 (Er)	6.506 (Tb)– 6.468 (Er)	105.98 (Tb)– 106.21 (Er)	111
KAIFPO ₄	orthorhombic	$Pn2_1a$	8	12.522	10.149	6.226	—	101
KCrFPO ₄	"	$Pnna$	8	12.612	10.172	6.205	—	112
		$Pc2_1n$	8	6.346	10.555	12.776	—	115
KFeFPO ₄	"	$P2_1nb$	8	10.656	12.885	6.370	—	113
KInFPO ₄	tetragonal	$Pna2_1$	8	12.847	6.353	10.642	—	114
		$P4_32_12$	8	9.351	—	11.101	—	see ^a
KInF _{0.7} (OH) _{0.3} PO ₄	"	$P4_32_12$	8	9.345	—	11.096	—	see ^a
RbInF _{0.7} (OH) _{0.3} PO ₄	"	$P4_32_12$	8	9.437	—	11.048	—	see ^a
NH ₄ InF _{0.7} (OH) _{0.3} PO ₄	"	$P4_32_12$	8	9.447	—	11.103	—	see ^a
(NH ₄) _{0.88} (H ₃ O) _{0.12} · AlF _{0.67} (OH) _{0.33} PO ₄	orthorhombic	$P2_12_12_1$	8	9.416	9.563	9.933	—	103
KGaF _{0.7} (OH) _{0.3} PO ₄	"	$Pna2_1$	8	12.717	6.302	10.431	—	86
(NH ₄) _{0.93} (H ₃ O) _{0.07} · GaF _{0.5} (OH) _{0.5} PO ₄	"	$P2_12_12_1$	8	9.593	9.742	9.981	—	104
(NH ₄)FeFPO ₄	"	$Pna2_1$	8	12.993	6.468	10.640	—	105
(NH ₄)GaFPO ₄	"	$Pna2_1$	8	12.921	6.440	10.415	—	106

^a Our data.

–173 °C.^{113, 114} Apparently, a more detailed study of this phenomenon will allow one to reveal correlations between the ionic conductivity and nonlinear optical properties of these compounds.

The $KM^{III}FPO_4$ compounds ($M^{III} = Cr, Fe$) exhibit high thermal stability. The chromium compound is more stable and it melts congruently at a temperature above 1600 °C. For fluoride phosphate KFeFPO₄, a phase transition was found at $T = 850$ °C. At $T > 1150$ °C, this compound decomposes with the loss of oxygen to form complex iron(II) phosphates, viz., KFePO₄ and K₂Fe₂P₂O₇F₂ (as black melts).

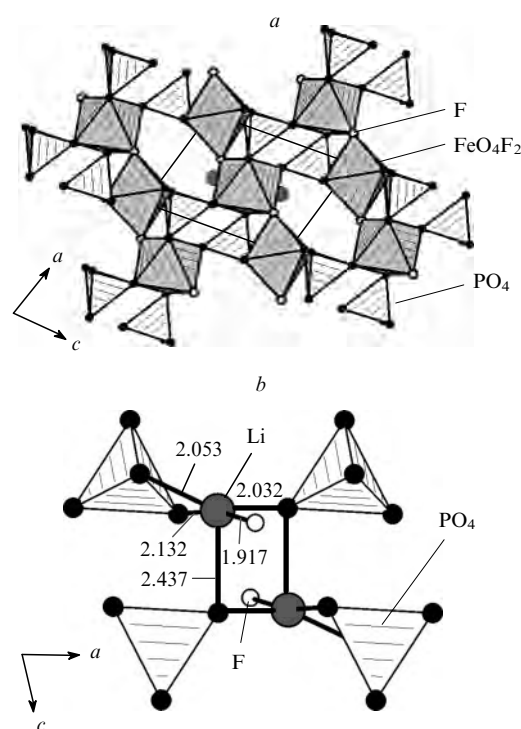
The formation of complex fluoride hydroxide phosphates with composition $M^I M^{III}(OH)_\delta F_{1-\delta} PO_4$ is typical of such trivalent elements as Al, Fe, Ga and In in combination with lithium and large monovalent cations (K^+ , Rb^+ and NH_4^+) (see Table 8). As examples we refer to synthetic tavorite LiFe[(OH),F]PO₄ (see Ref. 83) and the natural mineral amblygonite LiAl[(OH),F]PO₄.^{81, 82} These compounds have framework structures. The PO₄ tetrahedra and $M^{III}O_6$ octahedra are the main structural elements of tavorite and amblygonite. These polyhedra are linked in chains along the [101] direction through the common (OH, F) vertices. These chains are linked in a three-dimensional framework through the PO₄ tetrahedra (Fig. 16a). The framework is penetrated by a series of rather broad channels occupied by lithium atoms.

The environment about the lithium atom in the structures of tavorite and amblygonite deserves attention (Fig. 16b). Thus, the structure of natural amblygonite contains two lithium positions with occupancies of 1/2, which are separated by a distance of 0.5 Å. These half-occupied positions are located in face-sharing five-vertex polyhedra which together form a distorted octahedron.

In the structure of montebrasite (OH-containing analogue of amblygonite), the nearest environment about the lithium atoms[†] is formed by five oxygen atoms. This is attributed to the fact that

[†] The lithium atoms statistically occupy two positions separated by a distance of 0.24 Å.

the oxygen atom belonging to the AlO₆ octahedron of one chain is involved in hydrogen bonding with the hydroxy group of the adjacent chain. In the structure of synthetic tavorite LiFe[(OH),F]PO₄, the coordination polyhedron about the lithium atom is the axially elongated strongly distorted square pyramid

**Figure 16.** Structure of LiFe[(OH),F]PO₄ projected onto the ac plane (a) and the $[LiO_4(O,F)]$ polyhedra (b).

LiO_4F whose base is formed by the O and F atoms located at virtually equal distances from the Li atom (1.92–2.13 Å). The oxygen atom occupying the fifth vertex is at a distance of 2.44 Å from lithium.

The compositions of the known indium fluoride hydroxide phosphates correspond to the formula $\text{M}^{\text{I}}\text{InF}_{0.7}(\text{OH})_{0.3}\text{PO}_4$ ($\text{M}^{\text{I}} = \text{K}, \text{Rb}, \text{NH}_4$) (see Table 8). Apparently, the most stable structures are formed at the $\text{F}^-:\text{OH}^-$ ratio of 0.7:0.3. This conclusion is confirmed by the occurrence of analogous aluminium fluoride hydroxide phosphate $(\text{NH}_4)_{0.88}(\text{H}_3\text{O})_{0.12}\text{AlF}_{0.67}(\text{OH})_{0.33}\text{PO}_4$,¹⁰³ and gallium fluoride hydroxide phosphate $\text{KGaF}_{0.7}(\text{OH})_{0.3}\text{PO}_4$.⁸⁶ The $\text{M}^{\text{I}}\text{InF}_{0.7}(\text{OH})_{0.3}\text{PO}_4$ compounds ($\text{M}^{\text{I}} = \text{K}, \text{Rb}, \text{NH}_4$) are isostructural to KInFPO_4 and $\text{RbIn}(\text{OH})\text{PO}_4$.¹¹⁷ The $\text{KGaF}_{0.7}(\text{OH})_{0.3}\text{PO}_4$ compound belongs to the KTiOPO_4 structural type.

In the structure of $\text{M}^{\text{I}}\text{InF}_{0.7}(\text{OH})_{0.3}\text{PO}_4$, the fluoride and hydroxide ions statistically occupy one position. This replacement is quite reasonable and results from the similar sizes of these anions [$r(\text{F}^-) = 1.15 \text{ Å}$, $r(\text{OH}^-) = 1.18 \text{ Å}$]. The transformation of structurally similar fluorine-containing indium potassium phases $\text{KInF}_{1-\delta}(\text{OH})_{\delta}\text{PO}_4$ ($\delta = 0$ and 0.3) into hydroxide phosphate $\text{KIn}(\text{OH})\text{PO}_4$ is accompanied by lowering of the symmetry of the crystal lattice from tetragonal to orthorhombic. Hence, even the partial replacement of the OH groups by the fluoride ions in the structure of $\text{KIn}(\text{OH})\text{PO}_4$ leads to stabilisation of a more symmetrical structure, which is confirmed by X-ray diffraction analysis, electron diffraction study and the results of IR and Raman spectroscopy. Decomposition of $\text{KInF}_{0.7}(\text{OH})_{0.3}\text{PO}_4$ in air is a complex process giving rise to fluoride InF_3 and indium oxofluoride InOF as intermediates, which are transformed into $\text{K}_3\text{In}(\text{PO}_4)_2$, InPO_4 and cubic In_2O_3 .

The structure of the $(\text{NH}_4)_{0.93}(\text{H}_3\text{O})_{0.07}\text{GaF}_{0.5}(\text{OH})_{0.5}\text{PO}_4$ compound contains the $\text{GaO}_4(\text{OH})$ trigonal bipyramid and the $\text{GaO}_4[\text{F},(\text{OH})]_2$ octahedron as the main building blocks linked to each other by two PO_4 tetrahedra.¹⁰⁶ These blocks are linked in layers. The channels extended along the [001] direction are occupied by the NH_4^+ cations. The replacement of one-half of fluoride ions in the $(\text{NH}_4)\text{GaFPO}_4$ compound by the hydroxide ions leads to a radical rearrangement of the fluoride phosphate structure. In the structure of the $(\text{NH}_4)_{0.93}(\text{H}_3\text{O})_{0.07}\text{GaF}_{0.5}(\text{OH})_{0.5}\text{PO}_4$ compound,¹⁰⁴ the bridging position linking the gallium cations is completely occupied by the hydroxy groups. The ammonium-containing compounds readily decompose to the corresponding orthophosphates $\text{M}^{\text{III}}\text{PO}_4$.

Polymorphism was found in most of representatives of fluoride phosphates with composition $\text{Na}_3\text{M}_2^{\text{III}}\text{F}_3(\text{PO}_4)_2$ ($\text{M}^{\text{III}} = \text{Al}, \text{V}, \text{Cr}, \text{Fe}$) and several (up to three) polymorphic modification (α, β, γ) were revealed.⁸⁷ The relationships between the unit cell parameters of the α, β and γ modifications are shown in Fig. 17. The high-temperature α modifications of Al, V, Cr and Fe fluoride phosphates are isostructural, whereas the β modifications stable at low temperatures are structurally different (β' and β'') (Table 9). The unit cell volumes of the β' modifications are four times

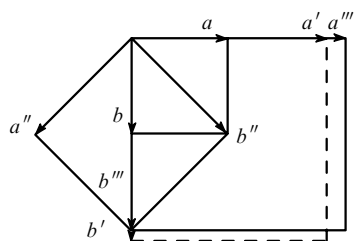


Figure 17. Relationship between the unit cell parameters of the α, β and γ modifications $\text{M}_3^{\text{I}}\text{M}_2^{\text{III}}\text{F}_3(\text{PO}_4)_2$.⁸⁷ The a and b parameters correspond to the α modification, a' and b' correspond to the β' modification, a'' and b'' correspond to the β'' modification and a''' and b''' correspond to the γ modification.

larger than those of the α modifications of the same compounds. The β' polymorphic modification is typical of Al, Cr(III) and Ga fluoride phosphates. The unit cell volumes for the β'' modification of vanadium(III) and iron(III) fluoride phosphates are twice as large as those for the α modifications. The γ modification was found only for an iron compound.

The β and α modifications differ primarily in the arrangement of the sodium atoms. In the high-temperature tetragonal unit cell of the β' modification (space group $I4/mmm$), the alkali-metal atoms are shifted only slightly as compared to the sodium positions in the unit cell of the α modification, whereas substantial shifts (by 0.3–0.5 Å) are observed in the tetragonal structures of the β' and β'' modifications (space group $I4_2/mbc$ and $I4_2/mnm$, respectively). The volume of the orthorhombic unit cell of the γ modification ($T = -190^\circ\text{C}$) of $\text{Na}_3\text{Fe}_2\text{F}_3(\text{PO}_4)_2$ (space group $Pbam$) is twice as large as the unit cell volume of the β'' modification. The γ and β'' modifications of $\text{Na}_3\text{Fe}_2\text{F}_3(\text{PO}_4)_2$ differ primarily in the positions occupied by sodium cations and distortion of the polyhedra in the structures. The transformation $\gamma \rightarrow \beta''$ is accompanied by deformation of the $[\text{Fe}_2\text{F}_3\text{O}_8]^{3-}$ polyhedron and displacement of the Na^+ cation by 0.7 Å.

The tetragonal α modification of the $\text{Na}_3\text{M}_2^{\text{III}}\text{F}_3(\text{PO}_4)_2$ compounds ($\text{M}^{\text{III}} = \text{Al}, \text{Fe}, \text{Cr}$) consists of the $\text{M}^{\text{III}}\text{O}_4\text{F}_2$ octahedra and the isolated PO_4 tetrahedra as the structural blocks (Fig. 18a). The octahedra are linked in pairs through the fluoride bridges. These doubled octahedra $\text{M}_2^{\text{III}}\text{O}_8\text{F}_3$ are linked in a mixed framework through the phosphate tetrahedra. The sodium atoms occupy the channels. The characteristic structural feature of these compounds is the statistical distribution of the alkali-metal atoms in the unit cell. Due to triple disorder, there are three modes of coordination of the sodium ions, all these atoms being located approximately on a circle with a diameter of 1.9–2.2 Å (Fig. 18b).

At room temperature, the β' - $\text{Na}_3\text{Al}_2\text{F}_3(\text{PO}_4)_2$ compound crystallises in the tetragonal system (space group $P4_2/mbc$) but exhibits a superstructure.

The partial replacement of the fluoride ions in the $\text{Na}_3\text{Fe}_2\text{F}_3(\text{PO}_4)_2$ compound by the hydroxy groups leads to the formation of $\text{Na}_3\text{Fe}_2[(\text{OH})_2\text{F}](\text{PO}_4)_2$ (see Ref. 85) isostructural to β' - $\text{Na}_3\text{V}_2\text{F}_3(\text{PO}_4)_2$ (see Table 9). In the structure of $\text{Na}_3\text{Fe}_2[(\text{OH})_2\text{F}](\text{PO}_4)_2$, the $[\text{Fe}_2\text{O}_8\text{F}_3]$ bioctahedra are deformed resulting in a doubling of the unit cell volume as compared to that of $\text{Na}_3\text{Fe}_2\text{F}_3(\text{PO}_4)_2$.

Ammonium-containing gallium fluoride phosphate $(\text{NH}_4)_2\text{Ga}_2\text{F}_3(\text{PO}_4)(\text{HPO}_4)$ ¹⁰⁶ (see Table 9) was assigned to the 'pseudo-KTP' type related to the KTP type (KTiOPO_4) (Fig. 19a). In compounds of the 'pseudo-KTP' type, only three of four oxygen atoms of each PO_4 tetrahedron are involved in the octahedral environment about gallium to form the GaO_4F_2 and

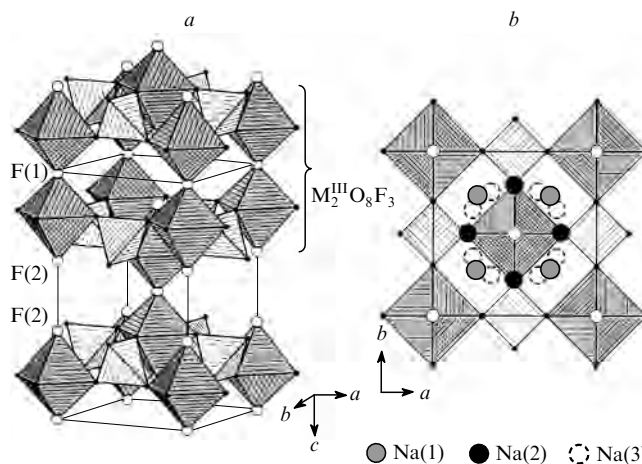


Figure 18. Structure $\text{Na}_3\text{Al}_2\text{F}_3(\text{PO}_4)_2$. Overall view (a); a one-layer fragment projected onto the ab plane (b).

Table 9. Synthesis conditions and crystallographic characteristics of the $\text{Na}_3\text{M}_2^{\text{III}}\text{F}_3(\text{PO}_4)_2$ ($\text{M}^{\text{III}} = \text{Al, V, Cr, Fe}$), $\text{Na}_3\text{Fe}_2(\text{OH})_2\text{F}(\text{PO}_4)_2$ and $(\text{NH}_4)_2\text{Ga}_2\text{F}_3(\text{PO}_4)(\text{HPO}_4)$ compounds.

Compound	Method of synthesis	Synthesis conditions		$T_{\text{m}} (T_{\text{tr}})$ / $^{\circ}\text{C}$	Crystal system	Space group	Z	Unit cell parameters			Ref.
		$T / ^{\circ}\text{C}$	p /bar					$a / \text{\AA}$	$b / \text{\AA}$	$c / \text{\AA}$	
β' - $\text{Na}_3\text{Al}_2\text{F}_3(\text{PO}_4)_2$	hydrothermal	650	2000	43 ($\beta \rightarrow \alpha$)	tetragonal	$P4_2/mbc$	4	12.406	—	10.411	87
α - $\text{Na}_3\text{Al}_2\text{F}_3(\text{PO}_4)_2$	"	300	80	—	"	$I4/mmm$	2	6.211	—	10.407	88
	solid-phase (from NaCl flux)	700	—	726 (sh.)	"	$I4/mmm$	2	6.206	—	10.418	87
β'' - $\text{Na}_3\text{V}_2\text{F}_3(\text{PO}_4)_2$	hydrothermal	650	2000	—	"	$P4_2/mnm$	4	9.047	—	10.705	87
β' - $\text{Na}_3\text{Cr}_2\text{F}_3(\text{PO}_4)_2$	solid-phase (under Ar)	700	—	55 ($\beta \rightarrow \alpha$)	"	$I4/mmm$	4	12.666	—	10.608	87
α - $\text{Na}_3\text{Cr}_2\text{F}_3(\text{PO}_4)_2$	solid-phase (from flux)	950	—	1045 (sh.)	"	$I4/mmm$	2	6.341	—	10.613	89
γ - $\text{Na}_3\text{Fe}_2\text{F}_3(\text{PO}_4)_2$	—	—	—	27 ($\gamma \rightarrow \beta$)	orthorhombic	$Pbam$	8	12.756 ^a	12.803 ^a	10.602 ^a	87
β'' - $\text{Na}_3\text{Fe}_2\text{F}_3(\text{PO}_4)_2$	solid-phase (from NaCl flux)	700	—	—	tetragonal	$I4/mmm$	4	9.037	—	10.668	87
α - $\text{Na}_3\text{Fe}_2\text{F}_3(\text{PO}_4)_2$	hydrothermal	300	80	746 (sh.)	"	$I4/mmm$	2	6.399	—	10.679	90
$\text{Na}_3\text{Fe}_2(\text{OH})_2\text{F}(\text{PO}_4)_2$	"	200	20	—	"	$P4_2/mnm$	4	9.050	—	10.679	85
$\text{Na}_3\text{Ga}_2\text{F}_3(\text{PO}_4)_2$	"	180	18	701 (sh.)	"	$I4/mmm$	2	6.291	—	10.646	87
$(\text{NH}_4)_2\text{Ga}_2\text{F}_3(\text{PO}_4)(\text{HPO}_4)$	hydrothermal (with guanidine)	180	18	—	orthorhombic	$Pna2_1$	4	12.497	7.702	9.846	106

^a Data obtained at $T = -190$ $^{\circ}\text{C}$.**Table 10.** Synthesis conditions and crystallographic characteristics of the $\text{Na}_5\text{M}^{\text{III}}\text{F}_2(\text{PO}_4)_2$ ($\text{M}^{\text{III}} = \text{Al, Ga, Cr, Fe}$) and $\text{Na}_{5-x}\text{Fe}(\text{O}_{\delta}\text{F}_{1-\delta})(\text{PO}_4)_2$ compounds.

Compound	Method of synthesis	$T / ^{\circ}\text{C}$	Crystal system	Space group	Z	Unit cell parameters			Ref.
						$a / \text{\AA}$	$b / \text{\AA}$	$c / \text{\AA}$	
$\text{Na}_5\text{AlF}_2(\text{PO}_4)_2$	solid-phase (from flux)	730	trigonal	$P\bar{3}$	3	10.468	—	6.599	91
	from aqueous solution	60	"	$P\bar{3}$	3	10.483	—	6.607	96
	solid-phase	1000	"	$P\bar{3}$	3				96
$\text{Na}_5\text{GaF}_2(\text{PO}_4)_2$	solid-phase (from flux)	730	"	$P\bar{3}$	3	10.560	—	6.660	91
$\text{Na}_5\text{CrF}_2(\text{PO}_4)_2$	the same	850–700	"	$P\bar{3}$	3	10.576	—	6.669	92
$\text{Na}_5\text{FeF}_2(\text{PO}_4)_2$	"	850–700	orthorhombic	$Pbca$	16	11.643	21.777	13.750	93
$\text{Na}_{4.6}\text{Fe}(\text{O}_{0.6}\text{F}_{0.4})(\text{PO}_4)_2$	"	750	"	$Ibam$	8	15.514	14.809	7.116	94
$\text{Na}_{4.5}\text{Fe}(\text{O, F})(\text{PO}_4)_2$ (see ^a)	"	750	"	$Bmcm$	4	15.520	7.410	7.119	95
$\text{Na}_{4.5}\text{Fe}(\text{O, F})(\text{PO}_4)_2$ (see ^b)	"	750	"	$Bmcm$	4	15.645	7.433	7.144	95

^a Modulated phase I stable at $T = 0$ $^{\circ}\text{C}$. ^b Modulated phase II stable at $T = 350$ $^{\circ}\text{C}$.

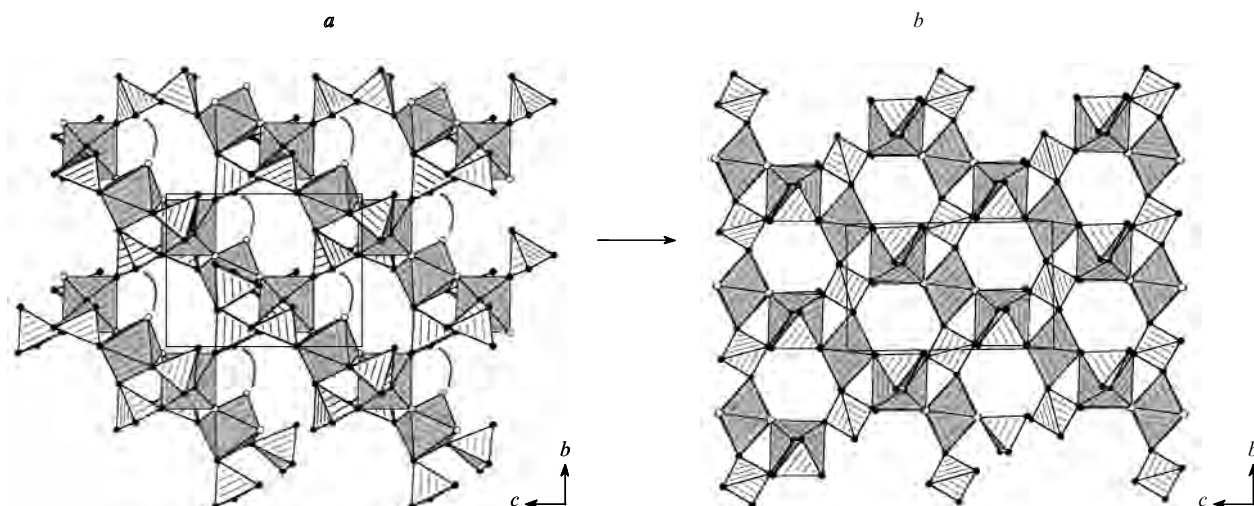


Figure 19. Relationship between the 'pseudo-KTP'-type structure of $(\text{NH}_4)_2\text{Ga}_2\text{F}_3(\text{PO}_4)(\text{HPO}_4)$ (a) and the KTP-type structure of $(\text{NH}_4)\text{GaF}(\text{PO}_4)$ (b). Layered fragments are shown. The ammonium groups are omitted.

GaO_3F_3 octahedra, as distinct from compounds of the KTP type in which all oxygen atoms of the PO_4 tetrahedra are involved in the $\text{M}^{\text{III}}\text{O}_6$ octahedra. The structure of the 'pseudo-KTP' type can be transformed into the structure of the KTP type by rotation of the corresponding PO_4 tetrahedra and GaO_3F_3 octahedra (see Fig. 19). In the KTP-type structures, the channels extended along the [100] direction have regular hexagonal cross-sections, whereas the channels along the [010] direction have distorted hexagonal cross-sections (Fig. 19 b). The framework structure of the $(\text{NH}_4)_2\text{Ga}_2\text{F}_3(\text{PO}_4)(\text{HPO}_4)$ compound is more distorted as compared to the structure of $(\text{NH}_4)\text{GaFPO}_4$.

Fluoride phosphates $\text{Na}_5\text{M}^{\text{III}}\text{F}_2(\text{PO}_4)_2$ with $\text{M}^{\text{III}} = \text{Al}, \text{Cr}, \text{Ga}$ ^{91, 92} crystallise in the trigonal system (Table 10), whereas an analogous iron compound is characterised by lower symmetry (orthorhombic). The $\text{Na}_5\text{M}^{\text{III}}\text{F}_2(\text{PO}_4)_2$ compounds can be assigned to layered structures. These structures contain corrugated layers parallel to the *ab* plane. The layers are built from the $\text{M}^{\text{III}}\text{O}_4\text{F}_2$ octahedra and the PO_4 tetrahedra (Fig. 20 a,b). One-third of all sodium atoms are located in these layers. The sodium atoms occupy from 6 (in the aluminium-containing compound) to 9 (in the chromium- and gallium-containing compounds) and 10 (in the iron-containing compounds) crystallographically independent positions most of which are statistically occupied. In the structures of these compounds, the alkali-metal atoms are located only in the centres of octahedra, which are formed either by oxygen atoms or together by fluorine and oxygen atoms (NaO_6 , NaO_5F , NaO_4F_2 , NaO_3F_3). For iron, not only fluoride phosphate with composition $\text{Na}_5\text{FeF}_2(\text{PO}_4)_2$ but also oxofluoride phosphates with variable composition $\text{Na}_{5-x}\text{Fe}(\text{O},\text{F})(\text{PO}_4)_2$ ($x = 0.4$ and 0.5) are known. Modulations of the atomic positions were revealed in the structures of the latter compounds.^{93–95} The reversible phase transition from one modulated phase to another (I→II) observed at $T = 257^\circ\text{C}$ is associated with slight displacements of the atoms and a change in the direction of the modulation vector. The investigation of polymorphism in $\text{Na}_{4.5}\text{Fe}(\text{O},\text{F})(\text{PO}_4)_2$ (see Ref. 95) depending on the temperature ($T < 1000^\circ\text{C}$) and pressure ($p = 1 \times 10^5 - 1.2 \times 10^{10}$ Pa) revealed the presence of one (at $T \approx 260^\circ\text{C}$, $p = 101.3$ kPa) and two [at $p_1 = 1.39(8)$ GPa and $p_2 = 4.52(32)$ GPa] polymorphic transformations, respectively. The modulation effect in the structure of $\text{Na}_{4.6}\text{Fe}(\text{O}_{0.6}\text{F}_{0.4})(\text{PO}_4)_2$ has no influence on the ionic transport ($\sigma_0 \approx 1.17 \times 10^4 - 1.88 \times 10^4$ S cm⁻¹, $E_a = 0.33$ eV) and dielectric properties.

The difference in occupancies of the same positions by sodium atoms in the isotopic structures of fluoride phosphates $\text{Na}_3\text{M}^{\text{III}}\text{F}_3(\text{PO}_4)_2$ and $\text{Na}_5\text{M}^{\text{III}}\text{F}_2(\text{PO}_4)_2$ ($\text{M}^{\text{III}} = \text{Al}, \text{Fe}, \text{Ga}$) is indicative of the possible ionic conductivity. At $T = 0^\circ\text{C}$, the

measured specific conductivity (σ) of the $\text{Na}_5\text{M}^{\text{III}}\text{F}_2(\text{PO}_4)_2$ compounds ($\text{M}^{\text{III}} = \text{Al}, \text{Ga}$) is approximately equal to 10^{-7} S cm⁻¹ and it increases by only three orders of magnitude (to $\sigma \approx 10^{-4}$ S cm⁻¹) as the temperature is raised to 327°C .⁹¹ As mentioned above, the Na^+ ions can migrate only in some of the

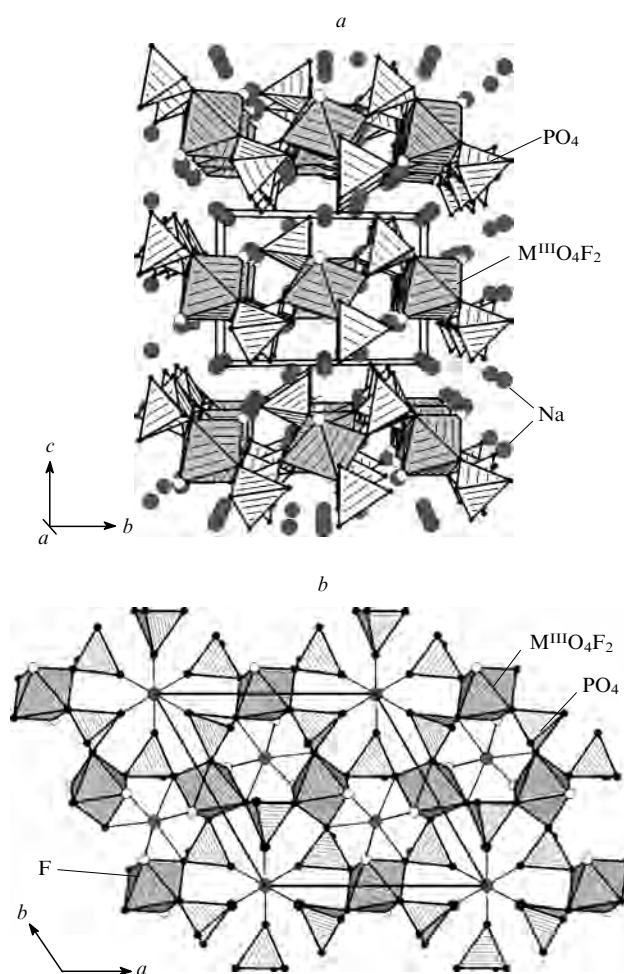


Figure 20. Structure of $\text{Na}_5\text{M}^{\text{III}}\text{F}_2(\text{PO}_4)_2$ ($\text{M}^{\text{III}} = \text{Al}, \text{Cr}, \text{Ga}$) projected along the [001] direction (a) and the one-layer fragment projected onto the *ab* plane (b).

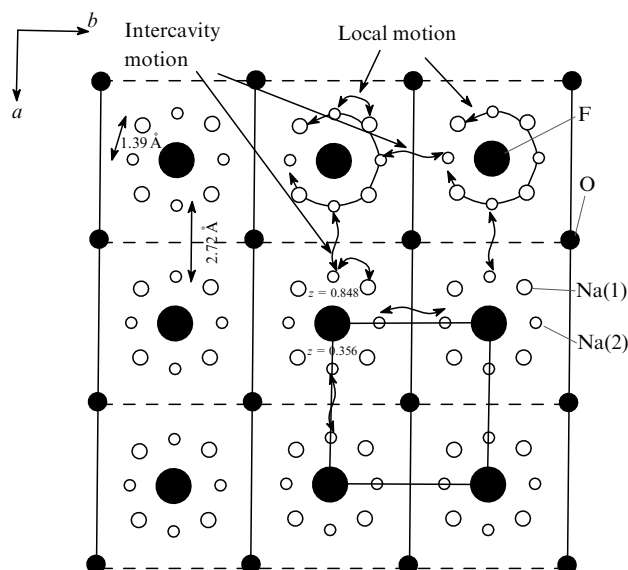


Figure 21. Structure of $\text{Na}_3\text{Al}_2\text{F}_3(\text{PO}_4)_2$ projected onto the ab plane. Different trajectories of motion of the Na^+ ions are shown.

channels in the structures of $\text{Na}_3\text{M}_2^{\text{III}}\text{F}_3(\text{PO}_4)_2$. The $\text{Na}_3\text{Al}_2\text{F}_3(\text{PO}_4)_2$ compound is characterised by a rather high activation energy (0.80 eV at 500 °C), which prevents the wide use of this fluoride phosphate as a ionic conductor. This compound is inferior to the recognised sodium conductors, such as compounds of the NASICON type ($E_a \approx 0.35$ eV) or $\text{Na}-\beta\text{-Al}_2\text{O}_3$ ($E_a \approx 0.14$ eV).

Based on the analysis of the sizes and geometry of the cavities occupied by the sodium atoms, several possible trajectories of motion of alkali cations in the structure were proposed, *viz.*, the migration from one cavity to another through a distance of 2.72 Å and/or the local motion around a circle within each cavity. These trajectories are schematically shown in Fig. 21.[‡]

Fluoride phosphate $\text{K}_3\text{Al}_4\text{F}_9(\text{PO}_4)_2$ (see Ref. 108) crystallises in another structural type characterised by the presence of the $[\text{Al}_4\text{F}_9\text{O}_8]_n$ chains (Fig. 22 *a*). The structural block of the chain is formed by four vertex-sharing AlO_2F_4 octahedra with the *cis* arrangement of the oxygen atoms (Fig. 22 *b*). In the perpendicular direction, the chains are linked to each other through the PO_4 tetrahedra to form a three-dimensional framework whose channels are occupied by the potassium ions (Table 11). A change in

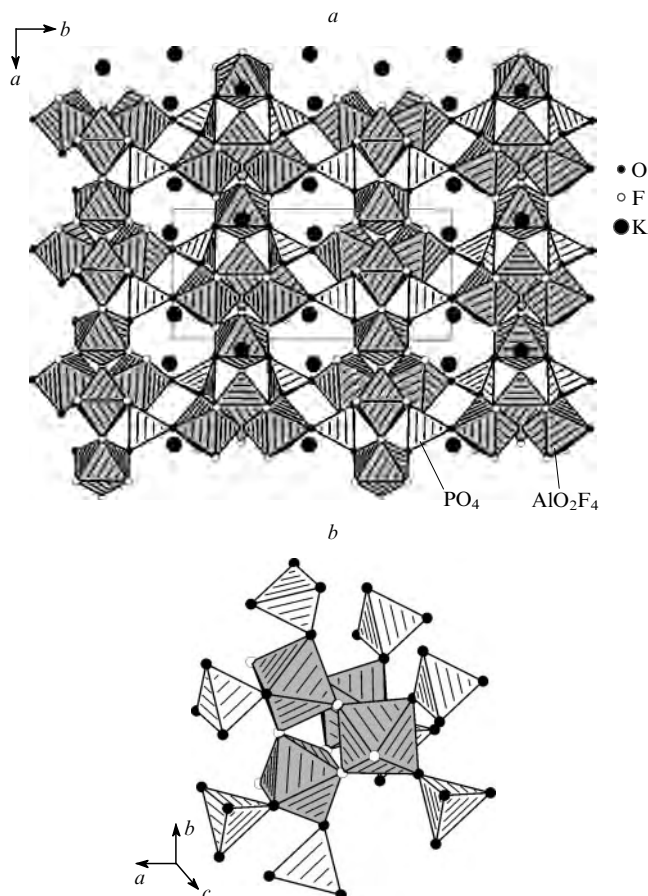


Figure 22. Structure of $\text{K}_3\text{Al}_4\text{F}_9(\text{PO}_4)_2$ projected onto the ab plane (*a*) and the mode of linkage of the AlO_2F_4 octahedra in the chain (*b*).

the Al:F:P ratio from 1:1:1 corresponding to the KAIFPO_4 compound to 2:4.5:1 corresponding to the $\text{K}_3\text{Al}_4\text{F}_9(\text{PO}_4)_2$ compound is associated with a more complex mode of linkage of the octahedra in the chains in the latter compound.

The data on apatite-type compounds containing M^{I} , M^{II} and M^{III} cations instead of (or along with) calcium are concerned primarily with sodium derivatives of particular REE (see Table 11). The parent compound of this family, *viz.*, potassium fluoride phosphate $\text{Ca}_{10}\text{F}_2(\text{PO}_4)_6$ (fluoroapatite), crystallises in the hexagonal system (space group $P6_3/m$) (Fig. 23 *a*).¹¹⁸ In the unit cell of $\text{Ca}_{10}\text{F}_2(\text{PO}_4)_6$, six PO_4 tetrahedra are located on mirror planes ($z = 1/4$ and $3/4$). The calcium cations occupy two crys-

[‡] From J-M Le Meins, O Bohnke, G Courbion *Solid. State Ion.* **111** 67 (1998).

Table 11. Synthesis conditions and crystallographic characteristics of apatite-type fluoride phosphates.

Compound	Method of synthesis	$T/^\circ\text{C}$	Crystal system	Space group	Z	Unit cell parameters				Ref.
						$a/\text{\AA}$	$b/\text{\AA}$	$c/\text{\AA}$	β/deg	
$\text{K}_3\text{Al}_4\text{F}_9(\text{PO}_4)_2$	hydrothermal ^a	180	monoclinic	$P2_1/m$	2	6.721	13.856	7.276	105.9	108
$(\text{NH}_4)\text{Al}_2\text{F}_3(\text{PO}_4)_2$	"	180	orthorhombic	$P2_12_12_1$	4	9.456	9.621	9.965	—	109
$\text{Li}_x\text{M}^{\text{III}}\text{Y}_{1-x}(\text{PO}_4)_{1-x}\text{F}_{4x}$ ($\text{M}^{\text{III}} = \text{Gd}-\text{Lu}, \text{Y};$ $0 \leq x \leq 0.45$) (zircon type)	solid-phase ($\text{LiMF}_4-\text{YPO}_4$)	800	tetragonal	$I4_1/amd$	2	6.958– 6.900	—	6.188– 6.055	—	100
$\text{Na}_2\text{Ba}_6\text{La}_2\text{F}_2(\text{PO}_4)_6$	solid-phase	1000	hexagonal	$P\bar{6}$	2	9.939	—	7.442	—	97
$\text{Na}_3\text{Ba}_4\text{Nd}_3\text{F}_2(\text{PO}_4)_6$	"	1000	trigonal	$P\bar{3}$	1	9.786	—	7.281	—	97
$\text{Na}_2\text{Ca}_6\text{Sm}_2\text{F}_2(\text{PO}_4)_6$	"	1200	hexagonal	$P6_3/m$	1	9.390	—	6.895	—	98
$\text{Na}_2\text{Ca}_6\text{Eu}_2\text{F}_2(\text{PO}_4)_6$	"	1200	"	$P6_3/m$	1	9.385	—	6.893	—	99
$(\text{NH}_4)\text{Ce}^{\text{IV}}\text{F}_2(\text{PO}_4)$	hydrothermal ^a	180	monoclinic	$P2_1/m$	2	6.660	5.875	7.177	114.31	107

^a The pressure was 18 bar.

tallographically independent positions. The Ca(1) cations lie on threefold axes in the positions $(1/3, 2/3, z)$ and form the CaO_9 polyhedra in which six Ca–O distances have close values and are substantially shortened (2.43–2.47 Å) as compared to the remaining three distances (2.83 Å). The Ca(2) cations are located on the planes m in the positions $(x, y, 1/4)$ and form the $\text{Ca(2)O}_8\text{F}$ polyhedra in which six O atoms are at distances of 2.36–2.53 Å, the F atom is located at a distance of 2.26 Å and two substantially remote O atoms are at distances of 3.27 Å. Two F^- ions lie on the 6_3 axis.

In apatite-type structures, impurity cations (in particular, REE) are differently distributed over two crystallographically non-equivalent calcium positions (Fig. 23b).[§] In the structure of Nd-doped fluoroapatite, the positions occupied by neodymium atoms depend on the mechanism of replacement.⁹⁷ When neodymium was introduced as trifluoride NdF_3 , the Ca(1) and Ca(2) positions were equally replaced by Nd. By contrast, the use of Nd_2O_3 as a source of REE led to the structure in which neodymium atoms occupy predominantly the Ca(2) position. In the hexagonal structure of $\text{Na}_2\text{Ba}_6\text{La}_2\text{F}_2(\text{PO}_4)_6$, the La^{3+} and Na^+ ions statistically occupy both positions, viz., Ca(1) and Ca(2). In the trigonal structure of $\text{Na}_3\text{Ba}_4\text{Nd}_3\text{F}_2(\text{PO}_4)_6$, two-third of all Nd^{3+} and Na^+ ions occupy the Ca(1) positions, whereas the remaining atoms are disordered in the Ca(2) positions.

Fluoride phosphates with composition $\text{Na}_2\text{Ca}_6\text{M}_2^{\text{III}}\text{F}_2(\text{PO}_4)_6$ ($\text{M}^{\text{III}} = \text{Sm}, \text{Eu}$),^{98, 99} like non-doped fluoroapatite, crystallise in the hexagonal system. The Eu^{3+} ions occupy the Ca(1) positions by approximately 75% and the alkali-metal ions are located only in the Ca(2) positions, whereas the opposite situation is observed in the structure of the samarium compound. In the latter structure, the sodium atoms are located only in the Ca(1) positions, whereas the REE ions replace the Ca(2) atoms by 78.5%. In fluoroapatite-type structures, the REE atoms have different coordination numbers (7 and 9).

The REE compounds, which crystallise in the apatite structural type, can be used as catalysts, ion-exchange phases and luminescent materials. The $\text{Na}_2\text{Ca}_6\text{Tb}_{1.75}\text{Y}_{0.25-x}\text{Eu}_x\text{F}_2(\text{PO}_4)_6$ compound was found to exhibit luminescence properties.¹¹⁹ The introduction of europium leads to weakening of radiation by the Tb^{3+} cations, which is indicative of the charge transfer from Tb^{3+} to Eu^{3+} .

§ Figure 23b was published by P K Rastsvetaeva, A P Khomyakov *Kristallografiya* **41** 831 (1996); [*Crystallogr. Rep. (Engl. Transl.)* **41** 789 (1996)].

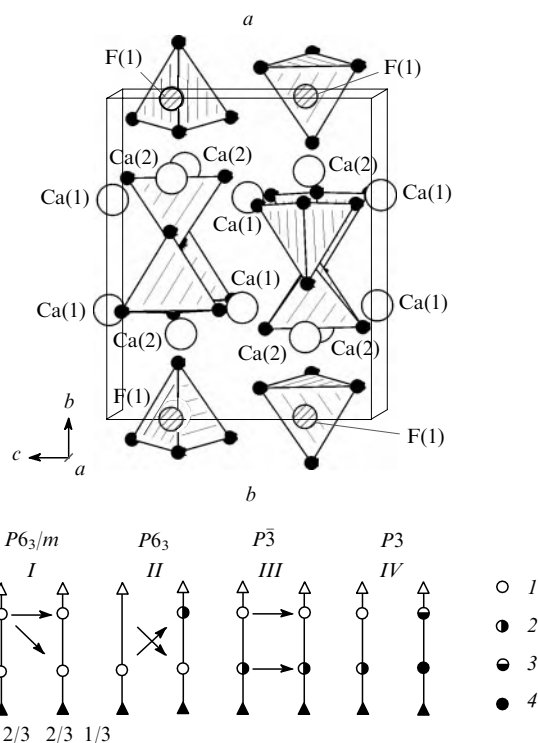


Figure 23. Structure of $\text{Ca}_5\text{F}(\text{PO}_4)_3$ projected along the $[100]$ direction (a) and the schematic representation of the arrangement of the cations (I–IV) in the Ca(1) positions in the hexagonal and trigonal apatite-type structures (I–IV) (b).

(I) $\text{Ca}_5\text{F}(\text{PO}_4)_3$; (II) $\text{Sr}_5\text{F}(\text{PO}_4)_3$; (III) $\text{NaSr}_3\text{CeF}(\text{PO}_4)_3$; (IV) $\text{NaCa}_3.\text{CeF}(\text{PO}_4)_3$.

Hence, there are several types of fluoride phosphates containing mono- and trivalent cations, which differ in composition and structure (Table 12). Compounds belonging to the same type are either isostructural or structurally related. Variations in the type and ratio of the ions in the cation sublattice as well as a change of the anion composition in complex phosphates containing mono- and trivalent cations by partially replacing the PO_4 tetrahedral groups with anions of different nature (F^-) lead not only to the formation of compositionally different compounds with different $\text{M}^{\text{I}}:\text{M}^{\text{III}}:\text{PO}_4^{3-}$ ratios but also to a radical rearrangement of the

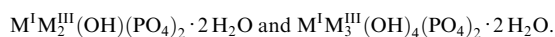
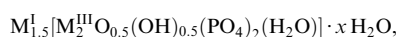
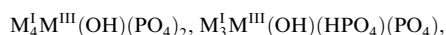
Table 12. Characterisations of the structures of different types of complex fluoride phosphates with M^{I} and M^{III} cations.

Type of compound	Ratio $\text{M}^{\text{I}}:\text{M}^{\text{III}}$	Crystal system	Space group	Building blocks	Structural type
$\text{M}_3^{\text{I}}\text{M}_4^{\text{III}}\text{F}_9(\text{PO}_4)_2$ ($\text{M}^{\text{I}} = \text{K}, \text{M}^{\text{III}} = \text{Al}$)	3 : 4	monoclinic	$P2_1/m$	$[\text{M}_4^{\text{III}}\text{O}_8\text{F}_9]_\infty$ (chains) + $[\text{PO}_4]$	framework
$\text{M}_{2+x}^{\text{I}}\text{M}_{6-2x}^{\text{II}}\text{M}_{2+x}^{\text{III}}\text{F}_2(\text{PO}_4)_6$ ($x = 0, 1$) ($\text{M}^{\text{I}} = \text{Na}; \text{M}^{\text{III}} = \text{Sm}, \text{Nd}, \text{Eu}$)	(2 : 4) – (3 : 3)	trigonal hexagonal	$P\bar{3}$ $P\bar{6}, P6_3/m$	$[\text{M}^{\text{III}}\text{O}_x\text{F}_y]$ (isolated polyhedra) + $[\text{PO}_4]$	"
$\text{M}^{\text{I}}\text{M}^{\text{III}}\text{F}(\text{PO}_4)$ ($\text{M}^{\text{I}} = \text{Na}; \text{M}^{\text{III}} = \text{Y}, \text{Gd} - \text{Er}$)	1 : 1	monoclinic	$C2/m$	$[\text{M}^{\text{III}}\text{O}_6\text{F}_2]_{2\infty}$ (layers) + $[\text{PO}_4]$	"
$\text{M}^{\text{I}}\text{M}^{\text{III}}\text{F}(\text{PO}_4)$ ($\text{M}^{\text{I}} = \text{Li}, \text{Na}, \text{K}, \text{NH}_4, \text{Rb}; \text{M}^{\text{III}} = \text{In}, \text{Ga}, \text{Sc}, \text{Al}, \text{Fe}, \text{Cr}$)	1 : 1	triclinic tetragonal orthorhombic	$P\bar{1}, C\bar{1}$ $P4_32_1$ $P2_12_12_1, P6_32_1, Pnna, Pna2_1$	$[\text{M}^{\text{III}}\text{O}_4\text{F}_2]_\infty$ (chains) + $[\text{PO}_4]$	"
$\text{M}_3^{\text{I}}\text{M}_2^{\text{III}}\text{F}_3(\text{PO}_4)_2$ ($\text{M}^{\text{I}} = \text{Na}; \text{M}^{\text{III}} = \text{Ga}, \text{Al}, \text{Fe}, \text{Cr}, \text{V}$)	3 : 2	tetragonal orthorhombic	$I4/mmm, P4_2/mnm,$ $P4_2/mbc, I4/mmm$ $Pbam$	$[\text{M}_2^{\text{III}}\text{O}_8\text{F}_3]$ (bioctahedra) + $[\text{PO}_4]$	"
$\text{M}_5^{\text{I}}\text{M}^{\text{III}}\text{F}_2(\text{PO}_4)_2$ ($\text{M}^{\text{I}} = \text{Na}; \text{M}^{\text{III}} = \text{Ga}, \text{Al}, \text{Fe}, \text{Cr}$)	5 : 1	trigonal orthorhombic	$P3, P\bar{3}$ $Pbca, Ibam, Bmcm$	$[\text{M}^{\text{III}}_4\text{F}_2]$ (octahedra) + $[\text{PO}_4]$	layered

structure from layered (typical only of fluoride phosphates with a high content of alkali cations, $M^I:M^{III} = 5:1$) to framework consisting of $[M_2^{III}O_8F_3]$ and $[M_4^{III}O_8F_9]$ island fragments, chains or layers built from the $M^{III}O_3F_y$ polyhedra.

V. Hydroxide phosphates containing mono- and trivalent cations

Like fluoride-containing analogues, hydroxide phosphates are characterised by complex compositions combining tri- and mono-valent cations. The similarity between the effective ionic radii of the F^- and OH^- anions and the formation of bonds between these anions and the M^{III} cations of comparable strength are responsible for the occurrence of the $M^IM^{III}(OH)PO_4$ compounds compositionally similar to $M^IM^{III}FPO_4$. However, hydroxide phosphates with compositions untypical of fluoride phosphates are also known:



Some compounds of the $M^IM^{III}(OH)PO_4$ group as well as a series of phases with composition $M^IM_2^{III}(OH)(PO_4)_2 \cdot 2H_2O$ were found as minerals. Complex hydroxide phosphates of all these types are known for M^{III} cations with small ionic radii (Al, Ga, In, V, Fe, Mn).

1. Synthesis

The mineral tavorite $LiFe(OH,F)PO_4$ is the Fe-containing analogue of montebrazite $LiAl(OH)PO_4$ (see Ref. 81) belonging to the group of amblygonite $LiAl(OH,F)PO_4$. The ideal compositions of tavorite and amblygonite are described by the formulas

$LiFe(OH)PO_4$ (see Ref. 120) and $LiAlFPO_4$ (see Ref. 81), respectively. Being a rare mineral from lithium pegmatites, tavorite is unstable under natural conditions. Various paragenetic associations are typical of minerals of the leucophosphate group of the general formula $M^IM_2^{III}(OH)(PO_4)_2 \cdot 2H_2O$, where $M^I = K, NH_4$ and $M^{III} = Al, Fe$. Leucophosphate $KFe_2(OH)(PO_4)_2 \cdot 2H_2O$ ^{121, 122} by itself is a product formed by the action of organic solutions derived from bat guano with iron oxides in serpentine rocks or is generated in late stages of the hydrothermal transformation of triphylite in pegmatites. Tinsleyite¹²³ (Al analogue of leucophosphate) was found together with $KFe_2(OH)(PO_4)_2 \cdot 2H_2O$ in pegmatites. Spheniscidite $(NH_4)Fe_2(OH)(PO_4)_2 \cdot 2H_2O$ ^{124, 125} is formed by the actions of ammonium phosphate solutions of penguin guano with mica and chlorite minerals. Cyrilovite $NaFe_3(OH)_4(PO_4)_2 \cdot 2H_2O$ ¹²⁶ which is the Fe-containing final member of the series of minerals belonging to the group of wardite $Na(Al,Fe)_3(OH)_4(PO_4)_2 \cdot 2H_2O$, is fragmentary present in pegmatites and can occupy cavities of oxidation zones of ferrous precipitates.

Most of the compounds under consideration were synthesised under hydrothermal conditions (Table 13).^{117, 122, 125, 127–135} The simultaneous action of pressure and temperature leads to a substantial increase in solubility of the compounds under study in active aqueous media and is favourable for the preparation of complex M^{III} hydroxide phosphates as highly crystalline powders and well-faceted crystals, which cannot, in principle, be grown by alternative methods. Unlike Al- and Fe-containing phases of the $M^IM^{III}(OH)PO_4$ type, their indium analogues do not form minerals of their own. Single crystals of hydroxide phosphates $KIn(OH)PO_4$ (see Ref. 127) and $RbIn(OH)PO_4$ (see Ref. 117) were obtained under drastic conditions (900 and 550 °C, respectively) followed by stepwise cooling. It should be noted that these phases are stable at pH 7–8. Attempts to prepare polycrystalline

Table 13. Hydrothermal synthesis of complex hydroxide phosphates with M^{III} cations.

Composition	Compound	Starting reagents (molar ratio), pH	Conditions of synthesis			Ref.
			$T/^\circ C$	p/bar	τ/h	
$M^IM^{III}(OH)PO_4$	$LiMn(OD)PO_4$	$MnPO_4 \cdot D_2O$, $LiNO_3$ (Li : Mn = 2 : 1)	200	20	504	134
	$KIn(OH)PO_4$	In_2O_3 , $K_2HPO_4(\text{sol.})$	900 ^a	3000	12	127
	$RbIn(OH)PO_4$	In_2O_3 , 2.5 M Rb_2HPO_4 , 3 M RbH_2PO_4 (Rb : P = 1.5)	550 ^b	2200	8	117
	$NH_4In(OH)PO_4$	In_2O_3 , $NH_4H_2PO_4$, $NH_4OH(\text{sol.})$ ($NH_4 : In : P = 8.1 : 1 : 2.41$)	200	20	168	135
$M^IM_2^{III}(OH)(PO_4)_2 \cdot 2H_2O$	$KFe_2(OH)(PO_4)_2 \cdot 2H_2O$ (leucophosphate)	$FePO_4 \cdot nH_2O$, 2.5 M K_3PO_4 , pH 2	150	—	336	122
	$(NH_4)V_2(OH)(PO_4)_2 \cdot 2H_2O$	VCl_4 , H_3PO_4 , H_2O , 1,3-diamino- propane (1 : 7.4 : 1004 : 8.6)	200	—	87	128
	$(NH_4)Fe_2(OH)(PO_4)_2 \cdot 2H_2O$ (spheniscidite)	$FeO(OH)$, H_3PO_4 , HF , H_2O , 1,3-diaminopropane (2 : 2 : 2 : 3 : 80)	200	—	24	125
	$K_{1.5}[Al_2P_2O_{8.5}(OH)_{0.5}(H_2O)] \cdot xH_2O$	$Al(OH)_3$, KH_2PO_4 (K : Al = 3 : 2; 3 : 4; 1 : 1; 3 : 2)	175–225	—	—	129
	$Rb_{1.5}[Al_2P_2O_{8.5}(OH)_{0.5}(H_2O)] \cdot xH_2O$	$Al(OH)_3$, RbH_2PO_4 (Rb : Al = 3 : 2; 3 : 1)	225	—	—	129
$M^IM^{III}(OH)(PO_4)_2$	$Na_4Al(OH)(PO_4)_2$	$Al(NO_3)_3 \cdot 9H_2O$, H_3PO_3 , $NaOH$, 1,4-diazabicyclo[2.2.2]octane, H_2O , pH 10	200	20	96	132
	$Na_4Ga(OH)(PO_4)_2$	Ga_2O_3 , $NH_4H_2PO_4$, $NaOH$ (Na : Ga : P = 3 : 1 : 2.4), pH 12	400 160	— 18	96 96	see ^c see ^c
	$Na_3Al(OH)(HPO_4)(PO_4)$	$Al(OH)_3$, $Na_2HPO_4 \cdot 2H_2O$, $NaH_2PO_4 \cdot 2H_2O$ (Na : P = 1.5)	600 ^d	—	20	133
$M^IM_3^{III}(OH)(HPO_4)(PO_4)$	$Na_3Al(OH)(HPO_4)(PO_4)$	Ga_2O_3 , $Na_2HPO_4 \cdot 2H_2O$, $NaH_2PO_4 \cdot 2H_2O$ (Na : P = 1.5)	600 ^d	—	20	133
	$Na_3Ga(OH)(HPO_4)(PO_4)$					

^a Slow cooling to 500 °C for 32 h; ^b slow cooling to 250 °C for 60 h; ^c unpublished data; ^d slow cooling to 500 °C for 66 h.

samples of $\text{MIn}(\text{OH})\text{PO}_4$ ($\text{M} = \text{K}, \text{Rb}$) in pure form failed. These samples contained unconsumed In_2O_3 even when the synthesis was carried out for 2–3 weeks. Under these conditions, the sodium analogue $\text{NaIn}(\text{OH})\text{PO}_4$ is not formed.

The hydrothermal synthesis of hydroxide phosphates of the leucophosphate group is characterised by a wide variety of the starting reagents. In a number of studies aimed at preparing porous organometallic phosphate compounds, hydroxide phosphates with composition $\text{M}^{\text{I}}\text{M}^{\text{III}}(\text{OH})(\text{PO}_4)_2 \cdot 2\text{H}_2\text{O}$ were synthesised.^{125, 128} Ammonium leucophosphate was prepared not only by the hydrothermal method with the use of aqueous solutions but also by the low-temperature synthesis from hydrogel ($T = 150^\circ\text{C}$, $\tau = 45$ h, pH of the final solution was 6.52).¹²⁴ The $\text{M}_{1.5}^{\text{I}}[\text{M}_2^{\text{III}}\text{O}_{0.5}(\text{OH})_{0.5}(\text{PO}_4)_2(\text{H}_2\text{O})] \cdot x\text{H}_2\text{O}$ compounds¹²⁹ ($\text{M}^{\text{I}} = \text{K}, \text{Rb}$), which are structurally similar to compounds of the leucophosphate group, are generated from mixtures of $\text{Al}(\text{OH})_3$ and $\text{M}^{\text{I}}\text{H}_2\text{PO}_4$ in the temperature range of $175\text{--}225^\circ\text{C}$. The $\text{NaAl}(\text{OH})\text{PO}_4$ and $(\text{NH}_4)\text{Al}_2(\text{OH})(\text{PO}_4)_2 \cdot 2\text{H}_2\text{O}$ compounds were prepared with the use of NaH_2PO_4 and $(\text{NH}_4)\text{H}_2\text{PO}_4$, respectively.^{130, 131} Hydroxide phosphates of this type are stable in weakly acidic and neutral media at pH 2.5–7.5.

The $\text{M}_4^{\text{I}}\text{M}^{\text{III}}(\text{OH})(\text{PO}_4)_2$ compounds ($\text{M}^{\text{I}} = \text{Na}$; $\text{M}^{\text{III}} = \text{Al}, \text{Ga}$)¹³² are formed as transparent elongated prismatic crystals in an alkaline medium (pH 10–12) under mild hydrothermal conditions in the presence of an excess of alkali cations ($\text{Na} : \text{Al} \geq 3$). The structurally related $\text{M}_2^{\text{I}}\text{M}^{\text{III}}(\text{OH})(\text{HPO}_4)(\text{PO}_4)$ compounds ($\text{M}^{\text{I}} = \text{Na}$; $\text{M}^{\text{III}} = \text{Al}, \text{Ga}$)¹³³ were prepared from weakly alkaline media at high temperatures (600°C) using stepwise cooling. The $\text{Na}_3\text{Al}(\text{OH})(\text{HPO}_4)(\text{PO}_4)$ and $\text{Na}_3\text{Ga}(\text{OH})(\text{HPO}_4)(\text{PO}_4)$ compounds crystallise as colourless prisms and thin platelet-like crystals, respectively.

2. Structures and properties

There is an obvious structural analogy between all hydroxide phosphates, except for compounds belonging to the $\text{M}^{\text{I}}\text{M}^{\text{III}}(\text{OH})\text{PO}_4$ group. The crystal chemistry of the latter compounds radically changes depending on the nature of the M^{I} and M^{III} cations.

Recent studies dealing with the determination of the crystal structures of complex hydroxide phosphates were aimed primarily at refining the assignment of a particular compound to the structural type (with a typical alternation of the cations and anions) and revealing the crystal-chemical features of the structures of the compounds synthesised.

Minerals with composition $\text{M}^{\text{I}}\text{M}^{\text{III}}(\text{OH})\text{PO}_4$, where $\text{M}^{\text{I}} = \text{Li}, \text{Na}$ and $\text{M}^{\text{III}} = \text{Al}, \text{Fe}$, are isomorphous. These compounds are characterised by high mobility of alkali atoms in the channels of the structures. The structural feature of this group of complex phosphates is the presence of chains built from the vertex-sharing FeO_6 or AlO_6 octahedra linked by OH groups (Table 14). Mixed frameworks containing such chains are also typical of kizerite ($\text{MgSO}_4 \cdot 2\text{H}_2\text{O}$), titanite (CaTiOSiO_4) and isostructural minerals (space group $C2/c$).⁸¹

In a manganese analogue of tavorite, *viz.*, $\text{LiMn}(\text{OH})\text{PO}_4$,¹³⁴ strong distortion of the $\text{MnO}_4(\text{OH})_2$ octahedra gives rise to a substantial ferromagnetic component although this compound

belongs to antiferromagnetics. The elongated $\text{Mn}-\text{O}$ bonds (O are the oxygen atoms of the PO_4 groups) make the main contribution to the direction of the vector of the magnetic moment. As a result, the vectors of the magnetic moments of the $\text{MnO}_4(\text{OH})_2$ octahedra belonging to the same chain are parallel, co-directed and virtually perpendicular to the $\text{M}-\text{OH}-\text{M}$ bond. This direction of the vectors of the magnetic moments is responsible for the ferromagnetic properties of the $\text{LiMn}(\text{OH})\text{PO}_4$ compound.¹³⁴

On going from iron- and manganese-containing compounds [$r_{\text{VI}}(\text{Fe}^{3+}) = 0.645 \text{ \AA}$, $r_{\text{VI}}(\text{Mn}^{3+}) = 0.65 \text{ \AA}$] to indium compounds [$r_{\text{VI}}(\text{In}^{3+}) = 0.79 \text{ \AA}$], the structural type changes attended with an increase in the symmetry from triclinic to orthorhombic and tetragonal (see Table 14). An increase in the ionic radius of alkali metal on going from potassium to rubidium also leads to an increase in the symmetry from orthorhombic to tetragonal. Complex indium hydroxide phosphates containing different monovalent cations have compositions in which the ratio $\text{M}^{\text{I}} : \text{M}^{\text{III}} : \text{PO}_4^{3-} = 1 : 1 : 1$ is retained. The structure of orthorhombic indium hydroxide phosphate $\text{KIn}(\text{OH})\text{PO}_4$ is based on helical chains of the $\text{InO}_4(\text{OH})_2$ octahedra sharing *cis* vertices.¹²⁷ These chains are extended along the *c* axis (Fig. 24*a*). The polyhedra about the potassium cations (KO_7) can be described as distorted trigonal antiprisms. In the structures of NH_4In and RbIn hydroxide phosphates, the presence of screw axes 4_3 leads to an ordered arrangement of the polyhedra in helical chains so that the channels of virtually square cross-section are formed along the $[001]$ direction (Fig. 24*b*). The NH_4^+ and Rb^+ ions are surrounded by nine oxygen atoms each.

In the structures of the $\text{M}^{\text{I}}\text{In}(\text{OH})\text{PO}_4$ compounds ($\text{M}^{\text{I}} = \text{Rb}$ and NH_4), the indium octahedra are almost non-distorted. Thus, the difference in the $\text{In}-\text{O}$ bond lengths is $0.003 \text{ \AA}$ and $0.059 \text{ \AA}$ in $(\text{NH}_4)\text{In}(\text{OH})\text{PO}_4$ (see Ref. 135) and $\text{RbIn}(\text{OH})\text{PO}_4$ (see Ref. 117), respectively. The crystallographically independent indium atoms alternate along the helical chains and are linked to each other through the bridging oxygen atoms of the hydroxy groups, which are not involved in hydrogen bonding with the nearest environment. The presence of independent OH groups in the structures was confirmed by IR spectroscopy ($\nu \approx 3520 \text{ cm}^{-1}$). Each PO_4 tetrahedron shares two vertices with the InO_6 octahedra belonging to the same chain and shares two other vertices with the octahedra from the adjacent chain. The chains are linked through the tetrahedra to form a framework whose large cavities are occupied by single-charged cations. The framework of the $\text{KIn}(\text{OH})\text{PO}_4$ compound is similar to that of $\gamma\text{-NaTiOPO}_4$.¹³⁶ The difference is observed in the positions of the alkali cations located in the tunnels of these structures.

The fact that indium and scandium have similar ionic radii [$r_{\text{VI}}(\text{Sc}^{3+}) = 0.745 \text{ \AA}$] as well as the fact that $\text{KIn}(\text{OH})\text{PO}_4$ and $\text{RbIn}(\text{OH})\text{PO}_4$ belong to different structural types indicate that related hydroxide phosphate $\text{KSc}(\text{OH})\text{PO}_4$ may occur. Apparently, the sodium-containing analogue with composition $\text{NaIn}(\text{OH})\text{PO}_4$ that is structurally similar to $\text{KIn}(\text{OH})\text{PO}_4$ does not occur. In this case, the steric factor is of considerable importance because the difference in the sizes of the potassium and sodium cations is much larger than that in the sizes of the potassium and rubidium cations.

Table 14. Crystallographic characteristics of the $\text{M}^{\text{I}}\text{M}^{\text{III}}(\text{OH})\text{PO}_4$ compounds.

Compound (mineral name)	Crystal system	Space group	<i>Z</i>	Unit cell parameters				Ref.
				<i>a</i> / $\text{\AA}$	<i>b</i> / $\text{\AA}$	<i>c</i> / $\text{\AA}$	α, β, γ / deg	
$\text{LiAl}(\text{OH})\text{PO}_4$ (montebrasite)	triclinic	$C\bar{1}$	4	6.713	7.708	7.019	91.31, 117.93, 91.77	81
$\text{LiFe}(\text{OH})\text{PO}_4$ (tavorite)	"	$P\bar{1}$	2	5.340	7.283	5.110	109.29, 97.86, 106.32	120
$\text{LiMn}(\text{OH})_{0.442}(\text{OH})_{0.558}\text{PO}_4$	"	$C\bar{1}$	4	6.719	8.187	7.123	89.5, 117.7, 86.4	134
$\text{KIn}(\text{OH})\text{PO}_4$	orthorhombic	$P2_12_12_1$	8	9.277	9.339	11.245	—	127
$\text{RbIn}(\text{OH})\text{PO}_4$	tetragonal	$P4_32_12$	8	9.400	—	11.179	—	117
$(\text{NH}_4)\text{In}(\text{OH})\text{PO}_4$	"	$P4_32_12$	8	9.423	—	11.177	—	135

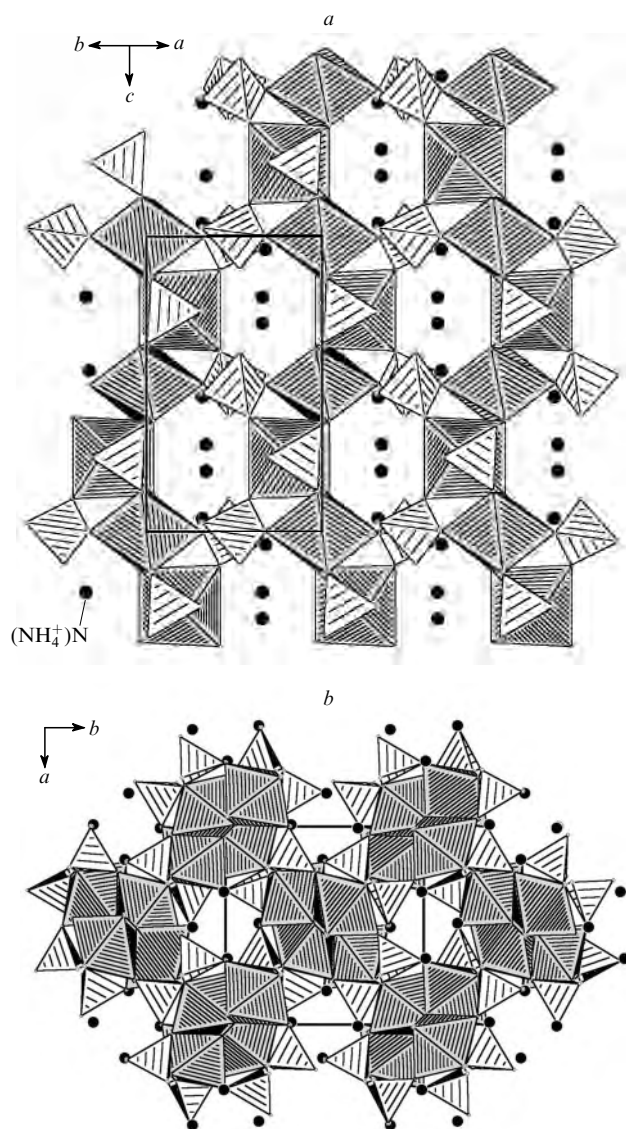


Figure 24. Chains of the $(\text{OH})_2$ octahedra in the structure of $(\text{NH}_4)\text{In}(\text{OH})\text{PO}_4$ along the $[110]$ direction (a) and the structure of $(\text{NH}_4)\text{In}(\text{OH})\text{PO}_4$ projected onto the ab plane (b).

Hence, analysis of the structural types in the morphotropic series $\text{M}^{\text{I}}\text{M}^{\text{III}}(\text{OH})\text{PO}_4$ demonstrates that the structures of these compounds are characterised by the presence of chains or ribbons, which are built from octahedra of the trivalent cations linked to each other through the OH vertices.

Taking into account the structural and compositional similarity, the $\text{M}^{\text{I}}\text{In}(\text{OH})\text{PO}_4$ compounds ($\text{M}^{\text{I}} = \text{K}, \text{Rb}$ and NH_4) can be compared with phases related to KTiOPO_4 . It is known that the TiO_6 octahedra in the structure of KTiOPO_4 are substantially distorted with alternation of short and long bonds along the $-\text{O}-\text{Ti}(1)-\text{O}-\text{Ti}(2)-\text{O}-$ chain. The differences between the long and short $\text{Ti}(1)-\text{O}$ and $\text{Ti}(2)-\text{O}$ bonds are 0.275 and 0.363 Å, respectively.¹¹⁶ These differences in the bond lengths are of importance in determining the nonlinear optical properties of the KTP-type $\text{A}^{\text{I}}\text{B}^{\text{IV}}\text{O}_x\text{V}_y\text{O}_4$ compounds. However, weak distortion of the $\text{M}^{\text{III}}\text{O}_6$ and $\text{M}^{\text{III}}\text{O}_x\text{F}_y$ octahedra in the structures of complex indium phosphates, such as $\text{M}^{\text{I}}\text{In}(\text{OH})\text{PO}_4$ ($\text{M}^{\text{I}} = \text{K}, \text{Rb}, \text{NH}_4$), KInFPO_4 and $\text{M}^{\text{I}}\text{InF}_{1-\delta}(\text{OH})_\delta\text{PO}_4$ ($\text{M}^{\text{I}} = \text{K}, \text{Rb}, \text{NH}_4$), and in the structures of $\text{M}^{\text{I}}\text{M}^{\text{III}}\text{F}_{1-\delta}(\text{OH})_\delta\text{PO}_4$ ($\text{M}^{\text{I}} = \text{K}, \text{NH}_4$; $\text{M}^{\text{III}} = \text{Ga}, \text{Fe}$) is responsible for the fact that these compounds do not exhibit nonlinear optical properties.

Two minerals, viz., wardite $\text{NaAl}_3(\text{OH})_4(\text{PO}_4)_2 \cdot 2\text{H}_2\text{O}$ ¹³⁷ and cyrilovite $\text{NaFe}_3(\text{OH})_4(\text{PO}_4)_2 \cdot 2\text{H}_2\text{O}$,¹²⁶ belong to hydroxide

phosphates with composition $\text{M}^{\text{I}}\text{M}^{\text{III}}(\text{OH})_4(\text{PO}_4)_2 \cdot 2\text{H}_2\text{O}$. These compounds crystallise in the tetragonal system (space group $P4_12_12$, $Z = 4$). The unit cell parameters of wardite ($a = 7.030$, $c = 19.040$ Å) are close to those of cyrilovite ($a = 7.313$, $c = 19.315$ Å). The structures of these minerals are composed of the layers located perpendicular to the $[001]$ direction. The layers consist of infinite chains of the alternating *cis*-linked $\text{M}(1)\text{O}_6$ and $\text{M}(2)\text{O}_6$ octahedra extended along the a and b axes (Fig. 25). In the $\text{M}(1)\text{O}_6$ octahedron, the M^{3+} cation is surrounded by three oxygen atoms of the PO_4 tetrahedra, two oxygen atoms of the OH groups and the oxygen atom of the water molecule. In the $\text{M}(2)\text{O}_6$ octahedron, the M^{3+} cation is surrounded by two oxygen atoms of the PO_4 groups and four oxygen atoms of the OH group. The $\text{M}(1)\text{O}_6$ octahedron is linked to two nearest $\text{M}(2)\text{O}_6$ octahedra through bridging hydroxy groups. The $\text{M}(2)\text{O}_6$ octahedron, in turn, is linked to four nearest strongly distorted $\text{M}(1)\text{O}_6$ octahedra through four hydroxy bridges. The cavities in the layers are occupied by sodium ions (coordination number is 8). The PO_4 tetrahedra share three vertices with three octahedra in the layer and one vertex with an octahedron from the adjacent layer, three vertices being involved in the $\text{M}(1)\text{O}_6$ octahedron and one vertex being involved in the $\text{M}(2)\text{O}_6$ octahedron.

In the mixed framework of the octahedra and tetrahedra, two types of channels are extended along the $[100]$ and $[010]$ directions. These channels are occupied by zeolite-type water molecules. The presence of water of crystallisation and bridging OH group in the structures was confirmed by IR spectroscopy. Analysis of the interatomic distances in the $\text{M}^{\text{III}}\text{O}_6$ polyhedra in the $\text{NaM}^{\text{III}}(\text{OH})_4(\text{PO}_4)_2 \cdot n\text{H}_2\text{O}$ compounds and the radii of the M^{III} cations demonstrated that the octahedral positions can be occupied not only by the Al and Fe cations but also by the gallium and vanadium cations with no changes in the crystal structure. The occurrence of potassium analogues is highly improbable because of the small sizes of the cavities in the layers.

Minerals of the leucophosphate of the general formula $\text{M}^{\text{I}}\text{M}_2^{\text{III}}(\text{OH})(\text{PO}_4)_2 \cdot 2\text{H}_2\text{O}$ ($\text{M}^{\text{I}} = \text{K}, \text{NH}_4$; $\text{M}^{\text{III}} = \text{Al}, \text{Fe}$) form a continuous series of low-temperature solid solutions. Three minerals of this series are known, viz., leucophosphate $\text{KFe}_2(\text{OH})(\text{PO}_4)_2 \cdot 2\text{H}_2\text{O}$, tinsleyite $\text{KAl}_2(\text{OH})(\text{PO}_4)_2 \cdot 2\text{H}_2\text{O}$ and speniscidite $(\text{NH}_4, \text{K})(\text{Al}, \text{Fe})_2(\text{OH})(\text{PO}_4)_2 \cdot 2\text{H}_2\text{O}$. Besides, the related synthetic KAl , NH_4Al , NH_4Ga and NH_4V analogues^{138–141} belong to this group (Table 15).

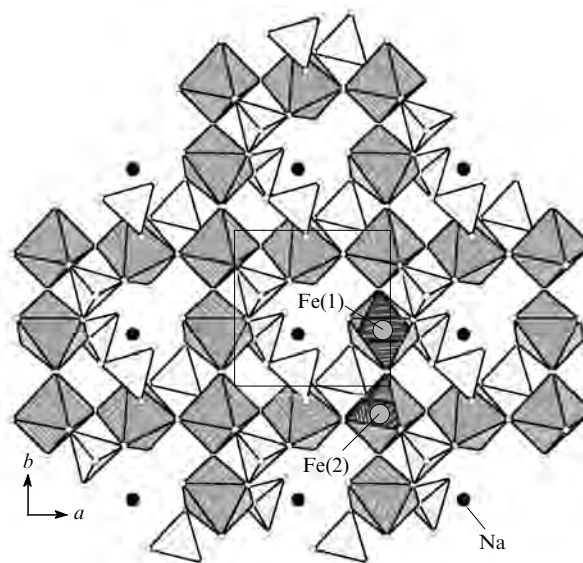


Figure 25. Structure of $\text{NaFe}_3(\text{OH})_4(\text{PO}_4)_2 \cdot 2\text{H}_2\text{O}$ projected onto the ab plane.

Table 15. Crystallographic characteristics of minerals of the leucophosphate group of the general formula $M^I M_2^{III}(\text{OH})(\text{PO}_4)_2 \cdot 2 \text{H}_2\text{O}$ and the $M_4 M^{III}(\text{OH})(\text{PO}_4)_2$ and $M_3 M^{III}(\text{OH})(\text{HPO}_4)(\text{PO}_4)$ compounds.

Compound (mineral)	Crystal system	Space group	Z	Unit cell parameters				Ref.
				$a / \text{\AA}$	$b / \text{\AA}$	$c / \text{\AA}$	β / deg	
$\text{KAl}_2(\text{OH})(\text{PO}_4)_2 \cdot 2 \text{H}_2\text{O}$	orthorhombic	$P2_12_12_1$	4	9.205	9.707	9.828	—	138
$\text{KAl}_2(\text{OH})(\text{PO}_4)_2 \cdot 2 \text{H}_2\text{O}$ (tinsleyite)	monoclinic	$P2_1/n$	4	9.602	9.532	9.543	103.16	123
$\text{K}_{1.5}\{\text{Al}_2\text{O}_{0.5}(\text{OH})_{0.5}(\text{PO}_4)_2(\text{H}_2\text{O})\} \cdot x \text{H}_2\text{O}$	"	$P2_1/n$	4	9.495	9.5589	9.4384	101.74	129
$(\text{NH}_4)\text{Al}_2(\text{OH})(\text{PO}_4)_2 \cdot 2 \text{H}_2\text{O}$	"	$P2_1/n$	4	9.553	9.577	9.614	103.6	130
$\text{KFe}_2(\text{OH})(\text{PO}_4)_2 \cdot 2 \text{H}_2\text{O}$ (leucophosphate)	"	$P2_1/n$	4	9.617	9.572	9.556	103.6	131
	"	$P2_1/n$	4	9.782	9.658	9.751	102.2	121
$(\text{NH}_4)\text{Fe}_2(\text{OH})(\text{PO}_4)_2 \cdot 2 \text{H}_2\text{O}$ (spheniscidite)	"	$P2_1/n$	4	9.756	9.664	9.769	102.4	122
	"	$P2_1/n$	4	9.819	9.737	9.874	102.8	124
$(\text{NH}_4)\text{Fe}_2(\text{OH})(\text{PO}_4)_2 \cdot 2 \text{H}_2\text{O}$ (spheniscidite)	"	$P2_1/n$	4	9.823	9.738	9.872	102.8	125
	"	$P2_1/n$	4	9.803	9.688	9.858	102.91	128
$(\text{H}_3\text{O})\text{Ga}_2(\text{OH})(\text{PO}_4)_2 \cdot 2 \text{H}_2\text{O}$	"	$P2_1/n$	4	9.68	9.64	9.77	102.7	139
$(\text{NH}_4)\text{Ga}_2(\text{OH})(\text{PO}_4)_2 \cdot 2 \text{H}_2\text{O}$	"	$P2_1/n$	4	9.689	9.703	9.788	102.80	140
$\text{LiNa}_2\text{HAl}(\text{OH})(\text{PO}_4)_2$	orthorhombic	$Pbcb$	4	6.948	14.089	14.065	—	141
$\text{Na}_4\text{Al}(\text{OH})(\text{PO}_4)_2$	"	$Pbcm$	8	15.279	14.660	6.947	—	132
$\text{Na}_4\text{Ga}(\text{OH})(\text{PO}_4)_2$	"	$Pbcm$	8	15.407	14.661	7.049	—	see ^a
$\text{Na}_3\text{Al}(\text{OH})(\text{HPO}_4)(\text{PO}_4)$	monoclinic	$C2/m$	4	15.277	7.054	7.041	96.73	133
$\text{Na}_3\text{Ga}(\text{OH})(\text{HPO}_4)(\text{PO}_4)$	"	$C2/m$	4	15.432	7.164	7.057	96.64	133

^a Our unpublished data.

The compounds of this groups are characterised by the presence of the $M_4^{III}(\text{OH})_2(\text{H}_2\text{O})_2(\text{PO}_4)_4$ island fragment formed from four octahedra of two types, viz., $M(1)\text{O}_4(\text{OH})_2$ and $M(2)\text{O}_4(\text{OH})(\text{H}_2\text{O})$. The central core of this fragment consists of two edge-sharing $M(1)\text{O}_6$ octahedra[¶] with two anchored hydroxo groups. The $M(1)\text{O}_6$ octahedra share edges containing two OH vertices with two $M(2)\text{O}_6$ octahedra (Fig. 26 *a, b*). The fragments consisting of four $M^{III}\text{O}_6$ octahedra are linked in a framework through the isolated PO_4 tetrahedra. The channels of the structure are occupied by monovalent cations and water molecules.

In each independent $M^{III}\text{O}_6$ octahedron, four oxygen atoms are at short distances from the M^{3+} ion (these distances differ by only 0.03–0.04 Å), whereas two oxygen atoms are far remote from M^{III} . This distortion of the octahedra results from the fact that the oxygen atoms of the OH groups and water molecules must satisfy the valence balance rule. The octahedral coordination of the M^{III} cations is retained but the $M^{III}-\text{O}$ distances change as the ionic radius increases in the series $\text{Al}-\text{Ga}-\text{V}-\text{Fe}$. Analysis of the interatomic $M^{III}-\text{O}$ distances in the $M^{III}\text{O}_6$ octahedra and the $M^I:M^{III}$ ratio showed that the compounds of all the above-mentioned trivalent cations ($M^{III} = \text{Al}, \text{Fe}, \text{V}, \text{Ga}$) in combination with rubidium can also crystallise in the structural type $M^I M_2^{III}(\text{OH})(\text{PO}_4)_2 \cdot 2 \text{H}_2\text{O}$. It is quite possible that In-containing analogues can also crystallise in this structural type. In all compounds with $M^I = \text{NH}_4$, the NH_4^+ cations are surrounded by four oxygen atoms giving rise to a tetrahedron within which two $\text{N}-\text{H}\cdots\text{O}$ hydrogen bonds occur (Fig. 26 *b*).

The water molecules in the structure of $M^I M_2^{III}(\text{OH})(\text{PO}_4)_2 \cdot 2 \text{H}_2\text{O}$ fulfil different functions. One H_2O molecule is involved in the first coordination sphere of the $M^{III}(2)\text{O}_6$ octahedron, whereas another water molecule is of a zeolite type and is not coordinated to any cation. As a result, the structural formula of these hydroxide phosphates can be written as follows $M^I\{M_2^{III}(\text{OH})(\text{PO}_4)_2(\text{H}_2\text{O})\} \cdot \text{H}_2\text{O}$.

It should be noted that the structures of all the above-considered minerals and their synthetic analogues are derived from the structure of $\text{GaPO}_4 \cdot 2 \text{H}_2\text{O}$.¹³⁹ In this structure, the positions of the hydroxonium ions correspond to the positions of the monovalent K^+ and NH_4^+ cations according to the structural formula $\text{H}_3\text{O}\{\text{Ga}_2(\text{OH})[\text{PO}_4]_2(\text{H}_2\text{O})\} \cdot \text{H}_2\text{O}$. The replacement of

¶ The presence of the edge-sharing $M^{III}\text{O}_6$ octahedra in these structures is responsible for the magnetic properties of iron-containing representatives of this group.

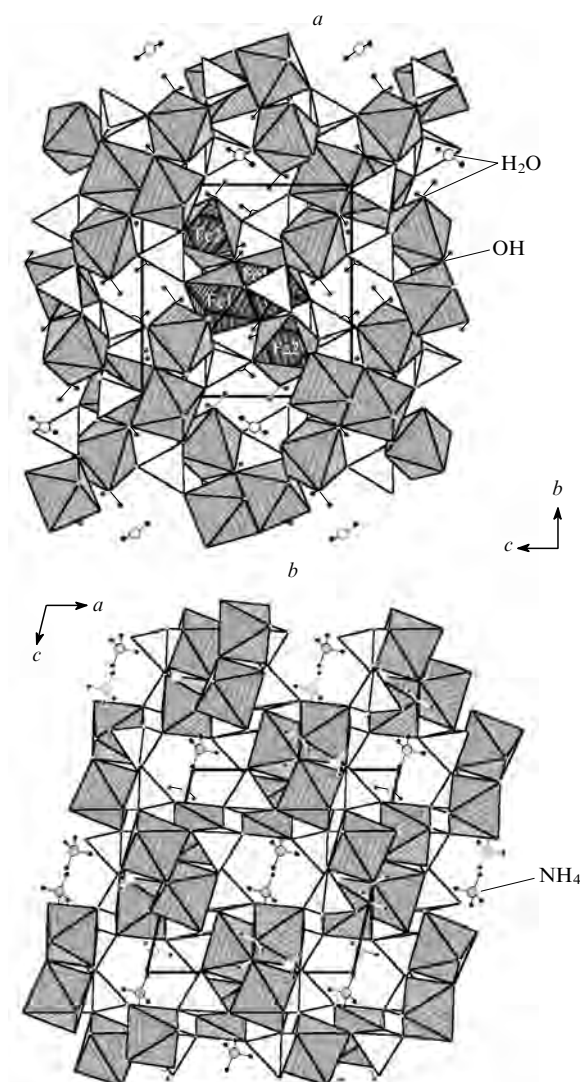


Figure 26. Structure of $(\text{NH}_4)\text{Fe}_2(\text{OH})(\text{PO}_4)_2 \cdot 2 \text{H}_2\text{O}$ projected onto the bc (*a*) and ac planes (*b*). The centrosymmetrical island fragments of the Fe octahedra are displayed (*a*); the positions of the NH_4^+ cations in the channels of the structure are shown (*b*).

one-half of the hydroxide ions in the $M^I\{M_2^{III}(OH)(PO_4)_2(H_2O)\} \cdot H_2O$ compounds by the oxide ions gives rise to compounds with compositions $M_{1.5}^I\{M_2^{III}O_{0.5}(OH)_{0.5}(PO_4)_2(H_2O)\} \cdot xH_2O$ ($M^I = K, Rb$; $M^{III} = Al$).¹²⁹

The presence of the $M_2^{III}O_4$ groups is common to hydroxide phosphates $M^IM_2^{III}(OH)(PO_4)_2 \cdot 2H_2O$ and their topological analogues deprived of OH groups, such as $(NH_4)Mo_2 \cdot P_2O_{10} \cdot H_2O$ ¹⁴² and $RbMo_2P_2O_{10} \cdot (1-x)H_2O$.¹⁴³ In the $Al_3(PO_4)_3 \cdot H_2O \cdot en$ and $Ga_3(PO_4)_3 \cdot H_2O \cdot en$ compounds (*en* is ethylenediamine), the $M_2^{III}O_4$ groups are involved in trigonal bipyramids and the organic cations (protonated ethylenediamine molecules) occupy the channels.¹⁴⁴ Due to the specific ion-conducting properties, these compounds can be used as molecular sieves.¹⁴⁵

Hydroxide phosphates with composition $Na_4M^{III}(OH)(PO_4)_2$ ($M^{III} = Al, Ga$) and the ratio $M^I : M^{III} = 4 : 1$ are also known (see Table 15). Let us consider the structures of these compounds using an aluminium compound as an example. The main structural elements of the $Na_4Al(OH)(PO_4)_2$ compound are the infinite $[Al(OH)(PO_4)_2]_{\infty}$ chains extended along the $[001]$ direction (Fig. 27*a*). In these chains, the $AlO_4(OH)_2$ octahedra are *trans*-linked to each other through the bridging oxygen atoms of the hydroxy groups (Fig. 27*b*). The adjacent octahedra in the chains are linked by two PO_4 groups. Each PO_4 group shares two vertices with the adjacent octahedra in the chain. The $[Al(OH)(PO_4)_2]_{\infty}^{4-}$ chains are held together primarily through interactions between two non-shared vertices of the phosphate groups and the sodium atoms located in the channels between the $[Al(OH)(PO_4)_2]_{\infty}^{4-}$ chains. The sodium atoms located between the PO_4 tetrahedra in *cis* positions with respect to the hydroxyl hydrogen atoms have a lesser effect on binding of the chains. The PO_4 tetrahedra and AlO_6 octahedra are only slightly distorted.

In the structure of $Na_4Al(OH)(PO_4)_2$, the sodium atoms have different coordination numbers depending on their positions with respect to the $[Al(OH)(PO_4)_2]_{\infty}^{4-}$ chains. Four of seven independent sodium atoms are involved in the NaO_6 octahedra. One NaO_{4+2} polyhedron is formed by four oxygen atoms located in the first coordination sphere (the $Na-O$ distances are ~ 2.495 Å) and two oxygen atoms at distances of $2.72-2.99$ Å. Finally, the coordination environment about two sodium atoms are five-vertex polyhedra with four short $Na-O$ bonds (~ 2.3 Å) and one abnormally large distance (~ 2.88 Å).

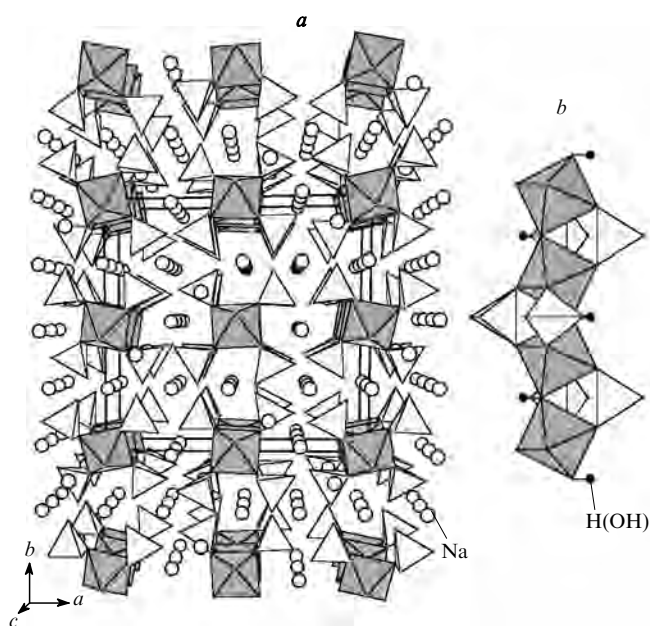


Figure 27. Structure of $Na_4Al(OH)(PO_4)_2$ projected along the $[001]$ direction (*a*) and the $[Al(OH)(PO_4)_2]_{\infty}^{4-}$ chain (*b*).

In the mineral tancoite $LiNa_2HAl(OH)(PO_4)_2$,¹⁴¹ the arrangement of the chains is analogous to that observed in the structure of $Na_4Al(OH)(PO_4)_2$. The slight differences in the positions of the Li and H atoms in the structure of tancoite as compared to the positions of the sodium atoms replacing these atoms in the structure of $Na_4Al(OH)(PO_4)_2$ cause changes in the symmetry of the structure, *viz.*, the parameter *a* is decreased, whereas the parameter *c* is doubled.

Taking into account the similarity of the ionic radii of aluminium, gallium and iron, gallium- and iron-containing analogues of $Na_4Al(OH)(PO_4)_2$ with the same structure would be expected to occur. Actually, we have recently prepared isostructural hydroxide phosphate $Na_4Ga(OH)(PO_4)_2$.

The structures of the $Na_3M^{III}(OH)(HPO_4)(PO_4)$ compounds ($M^{III} = Al, Ga$) are similar to that of $Na_4Al(OH)(PO_4)_2$ with the only difference that the sodium atoms are partially replaced by the hydrogen atoms of the HPO_4 groups (Fig. 28*a*).¹³³ The adjacent octahedra in the $[Al(OH)(HPO_4)(PO_4)_2]_{\infty}^{3-}$ chains are linked through the bridging HO groups and by the HPO_4 and PO_4 groups (Fig. 28*b*). The structure is additionally stabilised by hydrogen bonds involving the HPO_4 groups from the adjacent chains. The sodium atoms in the structure have different coordination environments, *viz.*, NaO_5 , NaO_6 and NaO_8 . The coordination polyhedron about the sodium atom with the coordination number of 8 is a distorted cube with four short, two medium and two long $Na-O$ distances. The average $M^{III}-O$ and $P-O$ bond lengths are comparable with the analogous distances in $Na_4Al(OH)(PO_4)_2$. For $Na_3Al(OH)(HPO_4)(PO_4)_2$, these bond lengths are 1.911 and 1.536 Å, respectively.

The chains consisting of the $[M(EO_4)_2X]$ groups (*X* is a non-specific ligand), which were found in the structures of $M_4^IM^{III}(OH)(PO_4)_2$ and $M_3^IM^{III}(OH)(HPO_4)(PO_4)_2$, are typical of a large group of phosphate, sulfate and silicate minerals.¹³² For example, in the structures of the minerals jahnsite $CaMnMg_2 \cdot [Fe(OH)(PO_4)_2]_2 \cdot 8H_2O$,¹⁴⁶ segelertite $CaMg[Fe(OH)(PO_4)_2] \cdot 4H_2O$ and overite $CaMg[Al(OH)(PO_4)_2] \cdot 4H_2O$ (see Ref. 147), the $[M(EO_4)_2X]$ chains are linked in layers through the $M^{II}O_2(H_2O)_4$ octahedra.

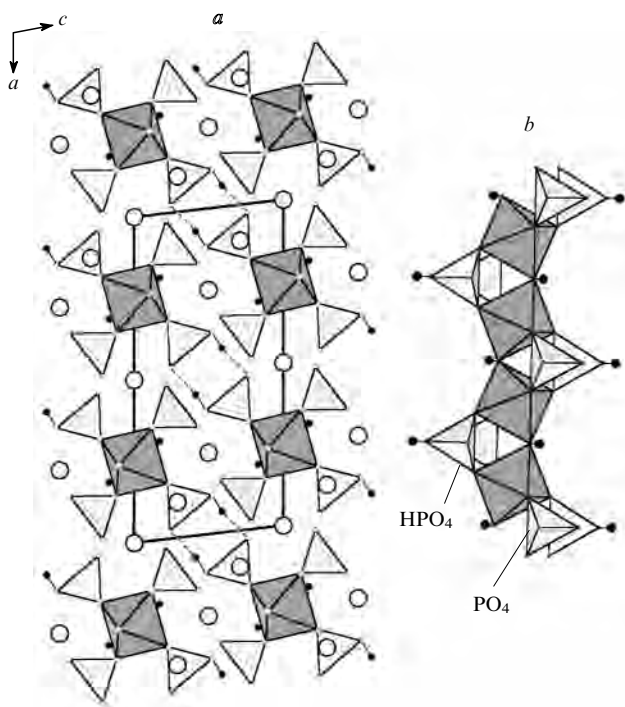


Figure 28. Structure of $Na_3Al(OH)(HPO_4)(PO_4)_2$ projected onto the *ac* plane (*a*) and the $[Al(OH)(HPO_4)(PO_4)_2]_{\infty}^{3-}$ chain (*b*).

Thermal stability of hydroxide phosphates containing mono- and trivalent cations depends on the mode of binding of water molecules in these structures. Thus, hydroxide phosphates $M^I\text{In}(\text{OH})\text{PO}_4$ ($M^I = \text{K}, \text{Rb}$) lose water of crystallisation in the temperature range of 500–700 °C. Decomposition of hydroxide phosphate $\text{KIn}(\text{OH})\text{PO}_4$ affords $\text{K}_3\text{In}(\text{PO}_4)_2$, InPO_4 and In_2O_3 . Hydroxide phosphate $(\text{NH}_4)\text{In}(\text{OH})\text{PO}_4$ decomposes in two steps at 180–490 °C and 535–690 °C. Crystallisation of InPO_4 starts at 620 °C. Dehydration of leucophosphite $\text{KFe}_2(\text{OH})_2(\text{PO}_4)_2 \cdot 2\text{H}_2\text{O}$ occurs in two steps at 300–575 °C. First, the zeolite-type water is removed and then the H_2O molecules located in the first coordination sphere about the iron atoms are eliminated. Dehydration of $\text{NaFe}_3(\text{OH})_4(\text{PO}_4)_2 \cdot n\text{H}_2\text{O}$ proceeds in one step. The temperature ranges of the removal of the zeolite-type water and water of crystallisation overlap (the maximum temperatures corresponding to the removal of these water molecules are 428 and 447 °C, respectively) and complete dehydration is achieved at 600 °C. In the case of the NH_4V analogue of leucophosphite, water of crystallisation is eliminated at a substantially lower temperature (in the range of 45–110 °C) and decomposition of the compound is completed at 320 °C. Dehydration of $\text{Na}_3\text{Al}(\text{OH})(\text{HPO}_4)(\text{PO}_4)$ proceeds in one step with a maximum at ~438 °C and ends in the formation of double aluminium phosphate $\text{Na}_3\text{Al}(\text{PO}_4)_2$.

A comparison of the data on the structures of complex hydroxide phosphates containing mono- and trivalent cations revealed the main structural features of these compounds. The coordination polyhedra about the M^{III} cations are without exception octahedra. The $M^{\text{III}}\text{O}_6$ octahedra are linked in infinite chains through the bridging hydroxy groups. Depending on the ratio between the M^I and M^{III} cations, the chains are either linked to each other through the phosphate tetrahedra or are held together by hydrogen bonds and $M^I \cdots \text{O}$ interactions[†] to form framework, layered or chain structures (Table 16).

For the above-considered compounds, two compositions with the ratios $M^I : M^{\text{III}} = 1 : 2$ or $1 : 1$ (in the case of the medium and large monovalent K^+ , Rb^+ , NH_4^+ cations) are preferential. The compositions with $1 : 3$ or $3 : 1$ (4 : 1), where M^{III} cations are either excessive or deficient with respect to M^I cations, are typical only of sodium-containing aluminium and gallium hydroxide phosphates, both the OH and HPO_4 groups being involved in compounds with the ratio $M^I : M^{\text{III}} = 3 : 1$. It should be noted that water molecules play an important role in the formation of structures containing an excess of M^{III} cations with respect to M^I . The H_2O molecules are involved in the formation of the first coordination sphere about the M^{III} cations and occupy the

channels and cavities in the structures as ‘guests’, which are not bound to any cations.

VI. Other complex phosphates containing mono- and trivalent cations

In addition to fluoride phosphates and hydroxide phosphates containing mono- and trivalent cations, other complex mixed-anion compounds are known. In such compounds, the PO_4^{3-} anion is combined with VO_4^{3-} , MoO_4^{2-} , SO_4^{2-} or $\text{S}_2\text{O}_3^{2-}$. It is expected that mixed-anion phosphates will exhibit improved properties (such as sorption ability, luminescence, *etc.*) as compared to monoanion phases. The replacement of the tetrahedral PO_4 group in the anion sublattices of complex phosphates by other groups enables one to vary not only the total negative charge of the compound, which makes it possible to change the number of cations, but also the size characteristics of the cavities in framework structures and of interlayer spaces in layered phases. Such structural changes may allow one to influence the catalytic properties and ionic mobility of compounds as well as ion exchange processes involving these compounds.^{148–152}

The partial replacement of the PO_4^{3-} anions in compounds with composition $\text{K}_3M^{\text{III}}(\text{PO}_4)_2$ ($M^{\text{III}} = \text{Y}, \text{La}, \text{Eu}, \text{Gd}, \text{Yb}$) by VO_4^{3-} gives rise to continuous or limited solid solutions based on one of the structural types (arcanite or glaserite) typical of non-substituted double phosphates $\text{K}_3M^{\text{III}}(\text{PO}_4)_2$ or vanadates $\text{K}_3M^{\text{III}}(\text{VO}_4)_2$. The lack of new compounds is associated with a small difference in the sizes of the PO_4^{3-} and VO_4^{3-} anions. The formation of limited or continuous solid solutions is determined by the dissimilarity or similarity of the structural types of the starting double phosphates and vanadates.²⁸

Phosphate vanadates $\text{K}_3M^{\text{III}}(\text{PO}_4)_x(\text{VO}_4)_{2-x}$ ($M^{\text{III}} = \text{Sc}, \text{Y}, \text{La} - \text{Lu}; x = 0 - 2$) exhibit sorption properties with respect to H_2O , CO_2 and organic compounds. The degree of sorption of H_2O and CO_2 from the gas phase depends on the $\text{PO}_4^{3-} : \text{VO}_4^{3-}$ ratio whose increase leads to preferential sorption of water molecules from a mixture of H_2O and CO_2 .¹⁵³ The degree of sorption correlates linearly with the conductivity and dielectric characteristics of the water-containing $\text{K}_3M^{\text{III}}(\text{PO}_4)_x(\text{VO}_4)_{2-x}$ phases.

Complex phosphate vanadates $\text{K}_3M^{\text{III}}_{1-y}\text{Eu}_y(\text{PO}_4)_x(\text{VO}_4)_{2-x}$ ($M^{\text{III}} = \text{Sc}, \text{Y}, \text{La}, \text{Gd}; x = 0 - 2; y = 0 - 1$) possess luminescent properties, which depend both on the concentration of the activator Eu^{3+} ions and the $\text{PO}_4^{3-} : \text{VO}_4^{3-}$ ratio. The formation of solid solutions, which crystallise in the same structural type, is evidenced by the similarity of their luminescence spectra. These spectra are characterised by the absence of complete concentration quenching of luminescence as the concentration of activator ions is increased. The maximum intensity of luminescence was observed at the Eu^{3+} concentration corresponding to $y = 0.3$.

[†] Considering the size factor, only sodium can serve as such monovalent cation.

Table 16. Characterisations of the structures of different types of complex hydroxide phosphates with M^I and M^{III} cations.

Type of compound	Ratio $M^I : M^{\text{III}}$	Crystal system	Space group	Building blocks	Structural type
$M^I M^{\text{III}}_3(\text{OH})_4(\text{PO}_4)_2 \cdot 2\text{H}_2\text{O}$ ($M^I = \text{Na}, M^{\text{III}} = \text{Al}, \text{Fe}$)	1 : 3	tetragonal	$P4_12_12$	$[\text{M}^{\text{III}}\text{O}_2(\text{OH})_4] \cup [\text{M}^{\text{III}}\text{O}_3(\text{OH})_2\text{O}_w]$ (chains) + $[\text{PO}_4]$	framework
$M^I M^{\text{III}}_2(\text{OH})(\text{PO}_4)_2 \cdot 2\text{H}_2\text{O}$ ($M^I = \text{K}, \text{NH}_4, M^{\text{III}} = \text{Al}, \text{Fe}, \text{Ga}, \text{V}$)	1 : 2	monoclinic	$P2_1/n$	$[\text{M}^{\text{III}}(\text{OH})_2(\text{H}_2\text{O})_2(\text{PO}_4)_4]_{3\infty}$ (island fragments)	"
$M^I M^{\text{III}}(\text{OH})\text{PO}_4$ ($M^I = \text{Li}, \text{Na}, \text{K}, \text{NH}_4, \text{Rb}; M^{\text{III}} = \text{Al}, \text{Fe}, \text{Mn}, \text{In}$)	1 : 1	triclinic orthorhombic tetragonal	$P\bar{1}, C\bar{1}$ $P2_12_12_1$ $P4_32_12$	$[\text{M}^{\text{III}}\text{O}_4(\text{OH})_2]_{\infty}$ (chains) + $[\text{PO}_4]$	"
$M^I_3 M^{\text{III}}(\text{OH})(\text{HPO}_4)(\text{PO}_4)$ ($M^I = \text{Na}, (\text{Li}, \text{Na}), M^{\text{III}} = \text{Al}, \text{Ga}$)	3 : 1	monoclinic	$C2/m$	$[\text{M}^{\text{III}}\text{O}_4(\text{OH})_2]_{\infty}$ (chains) + $[\text{PO}_4]$ and $[\text{HPO}_4]$	chain
$M^I_4 M^{\text{III}}(\text{OH})(\text{PO}_4)_2$ ($M^I = \text{Na}, M^{\text{III}} = \text{Al}, \text{Ga}$)	4 : 1	orthorhombic	$Pbcm$	$[\text{M}^{\text{III}}\text{O}_4(\text{OH})_2]_{\infty}$ (chains) + $[\text{PO}_4]$	"

Phosphate vanadates $K_3M^{III}_{1-j}Eu_j(PO_4)_x(VO_4)_{2-x}$ ($M^{III} = Sc, Y, Gd$) possessing bright red luminescence are promising photoluminescent and cathode-luminescent materials.^{154–156}

Complex molybdate phosphate $Na_2Y(PO_4)(MoO_4)$ ¹⁵⁷ was prepared by crystallisation from flux in the study of the $Y_2O_3-(NH_4)_2HPO_4-Na_2MoO_4$ system. This compound crystallises in the monoclinic system (space group $C2/c$, $Z = 8$, unit cell parameters $a = 13.928$, $b = 18.016$, $c = 6.847$ Å, $\beta = 119.62^\circ$). The structure of $Na_2Y(PO_4)(MoO_4)$ contains chains (along the c axis) of the edge-sharing YO_8 dodecahedra. The chains are linked in corrugated layers parallel to the ac plane through the PO_4 (shared edges) and MoO_4 (shared vertices) tetrahedra (Fig. 29 *a*). The sodium atoms are located in the interlayer space (Fig. 29 *b*). Molybdate phosphates of this type are unknown for REE.

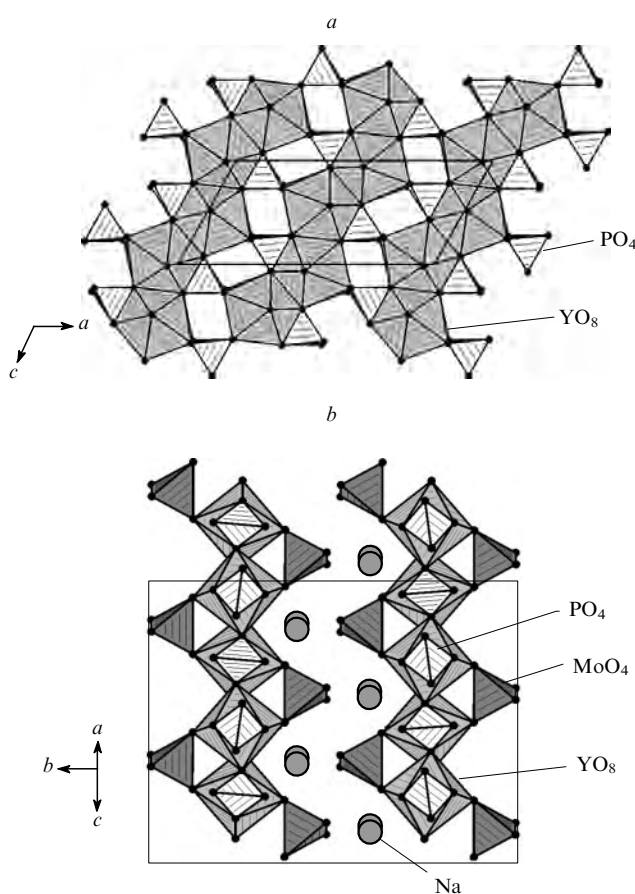


Figure 29. Structure of $Na_2Y(PO_4)(MoO_4)$ projected onto the ac plane (*a*) (MoO_4 tetrahedra are omitted) and the arrangement of the Na atoms in the structure (*b*).

Quite recently, sodium lanthanum phosphate thiosulfate with composition $Na_2La(PO_4)(S_2O_3)$ was prepared by the reaction of La_2O_3 with Na_3PO_3S in an excess of Na_2S_4 .¹⁵⁸ This compound crystallises in the monoclinic system (space group $P2_1/c$, $Z = 4$, unit cell parameters $a = 13.779$, $b = 5.336$, $c = 9.356$ Å, $\beta = 89.97^\circ$). In the crystal structure of $Na_2La(PO_4)(S_2O_3)$, the LaO_7S_2 polyhedra are linked in chains through the apical sulfur atoms of the thiosulfate groups. The chains are linked in layers by the PO_4 and S_2O_3 tetrahedra (Fig. 30 *a, b*). The negatively charged $[La(PO_4)(S_2O_3)]^{2-}$ fragment is the major building block of each layer. The $[La(PO_4)(S_2O_3)]_n$ layers are parallel to the bc plane. The terminal sulfur atoms of the thiosulfate ions are located within these layers. The structure contains three types of sodium atoms. The Na(1) and Na(2) atoms are located in the interlayer space occupying the centres of the octahedra, which are formed by the oxygen atoms belonging only either to the phosphate $[Na(1)]$ or

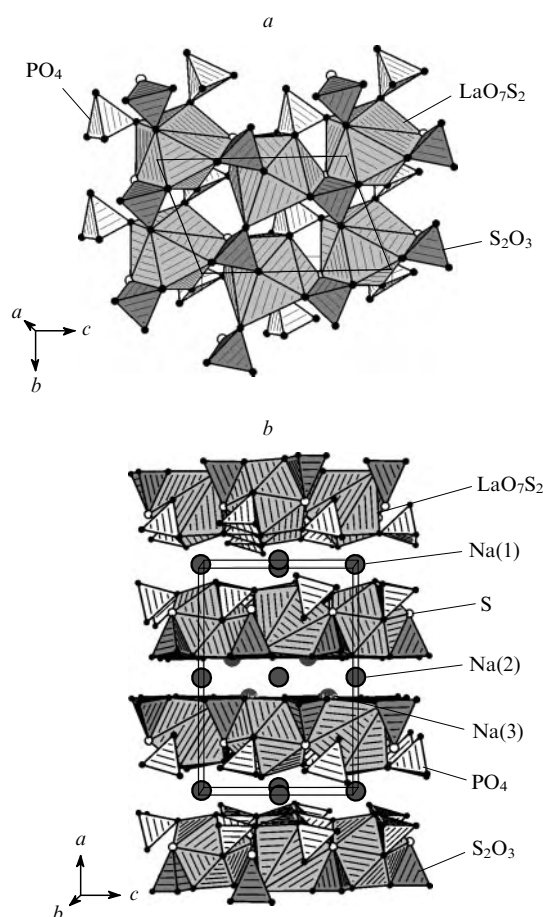


Figure 30. Structure of $Na_2La(PO_4)(S_2O_3)$ projected onto the bc plane (*a*) and the chains of the LaO_7S_2 polyhedra linked through the PO_4 and S_2O_3 tetrahedra (*b*).

thiosulfate $[Na(2)]$ groups. The Na(3) atoms are in an octahedral environment formed by the oxygen atoms belonging to four $S_2O_3^{2-}$ anions and one PO_4^{3-} anion.

A new structural type for the $Na_2La(PO_4)(S_2O_3)$ compound would be expected to occur by analogy with the $Na_2Y(PO_4)(MoO_4)$ compound combining the PO_4^{3-} and MoO_4^{2-} anions. However, analysis of the polyhedra demonstrated that the structure of $Na_2La(PO_4)(S_2O_3)$ is derived from glaserite $K_3Na(SO_4)_2$. The difference is that one-half of positions, which are occupied by the alkali-metal cations in the structures of glaserite-like double phosphates [for example, in $K_3M^{III}(PO_4)_2$, where $M^{III} = Lu, Sc$], are vacant in the structure of $Na_2La(PO_4)(S_2O_3)$. These changes in the cation composition lead to the appearance of a superstructure in $Na_2La(PO_4)(S_2O_3)$ resulted from doubling of the unit cell parameter a corresponding to the parameter c in the glaserite structure. In addition, the incorporation of the $S_2O_3^{2-}$ ion into complex phosphate has a substantial effect on thermal stability of the $Na_2La(PO_4)(S_2O_3)$ compound. Thus, the decomposition temperature of the $Na_2La(PO_4)(S_2O_3)$ compound is $313^\circ C$, whereas this temperature for $Na_3La(PO_4)_2$ is much higher ($1000^\circ C$). The data from powder X-ray diffraction analysis and the results of IR and Raman spectroscopy for the decomposition product of $Na_2La(PO_4)(S_2O_3)$ (after TGA) demonstrated that sodium lanthanum phosphate thiosulfate decomposes to form a compound of unknown composition containing the PO_4^{3-} and SO_4^{2-} ions in the anion sublattice.

Recently, a series of new phases with composition $Li_{3-x}Fe_2(PO_4)(SO_4)_2$ were prepared.¹⁵⁹ In these compounds, x depends on the content of iron in oxidation states 2+ and 3+. The redox potential of the $LiFe_2(PO_4)(SO_4)_2$ compound (3.4 eV) is higher than that of its monoanion precursor $Li_3Fe_2(PO_4)_3$

(2.8 eV), and this compound is a promising electrodic material for recharging lithium batteries.

The above-considered examples demonstrate that the $M^I M^{III}(\text{PO}_4)(\text{EO}_4)_2$ compounds possess new or improved properties (important for technical applications) as compared to monoanion complex phosphates. The total negative charge of the anionic portion of the compound can be changed by replacing the PO_4 groups in the anion sublattices of complex phosphates by the tetrahedral EO_4 groups ($E = \text{V}, \text{Mo}, \text{S}$), which allows one to change the number of cations and size characteristics of the cavities of framework structures and of the interlayer spaces in layered phases.

VII. Conclusion

A comparison of the crystal structures of different groups of complex phosphates containing mono- and trivalent cations not only reveals the similarity of formal characteristics (composition, simplest structural polyhedra) among these compounds but also enables one to establish their structural features depending on the size factors (ionic radii of the M^I and M^{III} cations), nature of the cations and anions, combinations of different anions, presence of water molecules and OH groups and hydrogen bonding.

Compositions with the ratio $M^{III}:\text{PO}_4^{3-}$ or $M^{III}:(\text{PO}_4^{3-} + \text{EO}_4^{2-})$ equal to 1:2, for example, $M^I M^{III}(\text{PO}_4)_2$, $M^I M^{III}(\text{HPO}_4)_2$ and $M^I M^{III}(\text{PO}_4)(\text{EO}_4)$, are typical of simple double phosphates, hydrogen phosphates and phosphates whose anionic portions contain the PO_4 groups together with other EO_4 tetrahedra ($\text{EO}_4 = \text{MoO}_4, \text{S}_2\text{O}_3$). Simple hydroxide phosphates and fluoride phosphates have related structures corresponding to the formulas $M^I M^{III}(\text{OH})\text{PO}_4$ and $M^I M^{III}\text{FPO}_4$. A limited number of compositions and structural types are known for simple double phosphates. A complication of the anionic portion of double phosphates and the presence of water molecules in these compounds lead to the formation of complex phosphates of different types (fluoride phosphates, hydrogen phosphates containing different $\text{H}_n\text{PO}_4^{3-n}$ anions and hydroxide phosphates), which differ both in composition and structure. In most representatives of complex phosphates containing mono- and trivalent cations, the ionic radius of the M^{III} cation is no larger than 0.8 Å (Al, V, Fe, Cr, Sc, Ga, In). Compounds containing REE or Y are known only for double phosphates and fluoride phosphates.

Changes in the ionic radii of the M^I and M^{III} cations (particularly, in the REE series) both in compositionally different and analogous groups of compounds are accompanied by a change in the structural type. In the case of sodium derivatives, which are most prone to polymorphism, the structural changes associated with a change in the size of the M^{III} cation and synthesis conditions are most pronounced (see Fig. 1 and Table 3).

The structures of complex phosphates of all the above-considered types are built from the $M^{III}\text{O}_x$, $M^{III}\text{O}_x(\text{H}_2\text{O})_y$ or $M^{III}\text{O}_{x-y}[\text{F},(\text{OH})]_y$ polyhedra ($x = 6-8$ and $y = 2-4$) and the PO_4 or H_nPO_4 polyhedra (the EO_4 tetrahedra can partially replace the PO_4 tetrahedra). The polyhedra about the M^{III} cations with the ionic radii $r \leq 0.8$ Å are octahedra distorted to a greater or lesser extent. The vertices of the octahedra are occupied by the oxygen atoms of the PO_4 , H_nPO_4 , EO_4 or OH groups or water molecules. In the case of fluoride phosphates, the F atoms can also be involved in the coordination polyhedra. In the structures of double REE phosphates and fluoride phosphates, the REE atoms adopt the coordination numbers of 7, 8 and 9.

The partial replacement of the PO_4^{3-} anions by the $\text{H}_n\text{PO}_4^{3-n}$ ($n = 1, 2$), EO_4^{2-} , F^- or OH^- anions and changes in the ratios $r(M^I):r(M^{III})$, $M^I:M^{III}$ and $M^{III}:\text{PO}_4$ ($\text{H}_n\text{PO}_4^{3-n}$, $n = 0-2$) lead to the formation of more complex structural ensembles based on either framework or layered constructions. Layered structures are typical of compounds with a high content of the M^I (or $M^I + \text{H}^+$) cations with respect to the M^{III} cations. This relationship is observed in most of the group of compounds considered above, viz., in double phosphates $M^I M^{III}(\text{PO}_4)_2$, fluoride phosphates

$M^I M^{III}\text{F}_2(\text{PO}_4)_2$, hydrogen phosphates $M^I M^{III}(\text{H}_2\text{PO}_4)_6 \cdot (\text{HPO}_4)_2$ and phosphates containing an EO_4 tetrahedron along with the PO_4 tetrahedron, for example, in $\text{Na}_2\text{Y}(\text{PO}_4)(\text{MoO}_4)$ and $\text{Na}_2\text{La}(\text{PO}_4)(\text{S}_2\text{O}_3)$. One-dimensional motifs are observed in compounds characterised by a high content of alkali-metal cations and the presence of hydroxy groups, for example, in $M^I M^{III}(\text{OH})(\text{HPO}_4)(\text{PO}_4)$ and $M^I M^{III}(\text{OH})(\text{PO}_4)_2$.

A decrease in the $M^I:M^{III}$ ratio results in the formation of framework structures typical of most of representatives of these groups of compounds, in particular, of $M^I M^{III}(\text{PO}_4)_3$, $M^I M^{III}(\text{HPO}_4)_2$, $M^I M^{III}(\text{OH})(\text{PO}_4)$, $M^I M^{III}\text{FPO}_4$ and $M^I M^{III}\text{F}_3(\text{PO}_4)_2$. In framework structures, the $M^{III}\text{O}_x$ or $M^{III}\text{O}_{x-y}[\text{F},(\text{OH})]_y$ polyhedra are linked to each other through either tetrahedral groups (in double and hydrogen phosphates) or fluoride and hydroxy groups (in fluoride phosphates and hydroxide phosphates, respectively).

The character of the structures depends substantially on the presence of the $\text{H}_n\text{PO}_4^{3-n}$ cations, OH groups and H_2O molecules in the coordination sphere about the M^{III} cation, which is associated with the involvement of these groups and molecules in the formation of rather strong hydrogen bonds.

Complex phosphates can be used in the design of polyfunctional materials. Compounds of REE and Sc containing the PO_4^{3-} anions together with the VO_4^{3-} anions are of particular interest. The formation of solid solutions based of double REE- and Sc-containing phosphates and vanadates allows one to vary the luminescent, sorption and other properties of the materials rather accurately by changing the $\text{PO}_4^{3-}:\text{VO}_4^{3-}$ ratio. Phosphate vanadates selective absorb H_2O , CO_2 and various organic molecules from the gas phase. Europium-doped compounds of this type containing Sc, Y and REE possess luminescent properties. It is also highly probable that REE fluoride phosphates and phosphate vanadates will exhibit catalytic properties. Phosphate vanadates of REE can be used also in the construction of nonlinear optical materials.

Phosphates with composition $M^I M^{III}_2(\text{PO}_4)_3$ ($M^I = \text{Li}, \text{Na}$; $M^{III} = \text{Sc}, \text{In}, \text{Fe}$) are ionic conductors. Some representatives of hydrogen phosphates possess proton conductivity. A number of these compounds (with zeolite-type structures) are of interest as new ion exchange phases. The fact that most of the complex phosphates belong to dielectric compounds provides the basis for the preparation of dielectric materials for different purposes.

* * *

When this review was already in preparation, new data on the synthesis, crystal structures and properties of two groups of complex phosphates, viz., $M^I M^{III}(\text{HPO}_4)_2$ and $M^I M^{III}(\text{OH})(\text{PO}_4)_2 \cdot 2\text{H}_2\text{O}$, were reported. Thus, we have expected that indium hydrogen phosphates $M^I\text{In}(\text{HPO}_4)_2$ ($M^I = \text{Li}, \text{Na}, \text{Ag}, \text{Rb}$),¹⁶⁰ scandium hydrogen phosphates $M^I\text{Sc}(\text{HPO}_4)_2$ ($M^I = \text{K}, \text{Rb}, \text{NH}_4$) and iron hydrogen phosphate $\beta\text{-RbFe}(\text{HPO}_4)_2$ would occur, and this assumption was confirmed. All these compounds, except for $\text{KSc}(\text{HPO}_4)_2$ (space group $Pnma$), crystallise in the monoclinic system (space group $P2_1/c$). The above-listed hydrogen phosphates either widen the range of representatives of the known structural type $\beta\text{-RbV}(\text{HPO}_4)_2$ (see Ref. 62), for example, $\beta_1\text{-RbIn}(\text{HPO}_4)_2$, $\beta\text{-RbFe}(\text{HPO}_4)_2$ and $M^I\text{Sc}(\text{HPO}_4)_2$, where $M^I = \text{K}, \text{Rb}, \text{NH}_4$, or form unique framework structures, for example, $M^I\text{In}(\text{HPO}_4)_2$, where $M^I = \text{Li}, \text{Na}, \text{Ag}$. Our assumption that the structural group of the mineral leucophosphate must involve also rubidium hydroxide phosphate $\text{RbGa}_2(\text{OH})(\text{PO}_4)_2 \cdot 2\text{H}_2\text{O}$ was also confirmed.¹⁶¹

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^c — *Dokl. Chem. (Engl. Transl.)*

^d — *Crystallogr. Rep. (Engl. Transl.)*

^e — *Inorg. Mater. (Engl. Transl.)*

Barium borate β -BaB₂O₄ as a material for nonlinear optics

P P Fedorov, A E Kokh, N G Kononova

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Abstract. Data on the structure, polymorphism, phase equilibria, growth techniques, properties and applications of single crystals of the low-temperature modification of barium borate are analysed. The bibliography includes 201 references.

I. Introduction

Barium borates possess many interesting and valuable properties. Interest in these compounds is due to not only pure research aspects, but also the possibility of modern technological applications. Currently, barium borates are used in production of ceramic glazes, luminophors, oxide cathodes as well as additives to pigments for aqueous emulsion paints.^{1–8} The BaO–B₂O₃ system (a constituent of the BaO–B₂O₃–SiO₂ system) serves as the basis when synthesising special optical glasses.^{9–14}

The history of studies of barium borate, BaB₂O₄, can be divided into two periods. The pioneering communication concerning the synthesis of BaB₂O₄ single crystals dates back to the 19th century.^{1,2} The structure of anions in crystalline borates was established by X-ray structural analysis in the 1950s.^{3,4,15} The crystal structures of a number of barium borates including the high-temperature modification of BaB₂O₄ were established in the 1960s;^{16–18} however, these results were of low reliability.

Two crystalline modifications[†] of BaB₂O₄, *viz.*, the high-temperature (α) and the low-temperature (β) forms were described and characterised by X-ray diffraction analysis by Levin and McMurdie.¹²

In the anions, oxygen atoms surrounding borons can form two types of coordination environment, *viz.*, a tetrahedral and a trigonal coordination environment corresponding to the *sp*³- and *sp*²-hybridisation of the electron orbitals of the B atom, respectively.¹⁹ As a rule, both of them are realised in borate ions. Both the BO₃ triangles and BO₄ tetrahedra can form fused structures by sharing their vertices (bridging oxygen atoms), thus forming polyanions. The presence of polymeric anions in borate melts is responsible for hysteresis of properties (in particular, viscosity) and the glass-forming ability.⁸

The second period of studies of BaB₂O₄ dates back to the 1980s and is associated with the discovery of nonlinear optical properties in the single crystals of the low-temperature modification of barium borate, β -BaB₂O₄ (BBO)[‡] (see Refs 20–25). Its crystals are non-centrosymmetric, which is responsible for a number of specific properties of the compound.^{26,27} This form of barium borate combines excellent nonlinear optical characteristics [large effective second harmonic generation (SHG) coefficient, which is nearly 6 times higher than that of potassium dihydrophosphate crystals; large birefringence; wide transparency region (190–3500 nm), high laser damage threshold], good mechanical properties and very low hygroscopicity. Comparison of the properties of BBO with those of other optically active nonlinear crystals shows that barium borate is the best candidate for fabrication of solid-state UV lasers operating at a wavelength of 200 nm. BBO single crystals are used in optoelectronics for laser radiation-to-radiation frequency conversion (in particular, visible-to-UV frequency upconversion) by the SHG and higher harmonic generation (up to the fifth harmonic) mechanisms.

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[†] In the literature, the high-temperature and the low-temperature modifications of barium borate are, as a rule, designated as α -BaB₂O₄ and β -BaB₂O₄, respectively (in this review, we also use these notations). However, quite the reverse notations are sometimes used.

[‡] The terminology is somewhat ambiguous. The compound having a composition BaO·B₂O₃ is usually treated as a salt, Ba(BO₂)₂, of metaboric acid (HBO₂) and called barium metaborate;² sometimes, the same compound is called barium diborate (see, *e.g.*, Ref. 4). However, barium diborate has another composition, namely, BaO·2 B₂O₃.² To match the crystal structure of BBO, it is more correct to represent its composition as Ba₃(B₃O₆)₂.

Recently, frequency conversion by the stimulated Raman scattering (SRS) mechanism using BBO-crystal oscillators has been studied.^{28–30}

In the last decade, new crystals possessing nonlinear optical properties (including borates) were synthesised.^{31–39} These are, *e.g.*, LiB_3O_5 (LBO)⁸ (see Ref. 31), $\text{KBe}_2\text{B}_3\text{O}_7\text{F}_2$ (KBBF),³² $\text{Sr}_2\text{Be}_2\text{B}_2\text{O}_7$ (SBBO),³³ $\text{LiCsB}_6\text{O}_{10}$ (CLBO),³⁴ $\text{Ba}_2\text{Be}_2\text{B}_2\text{O}_7$ (TBO) and $\text{K}_2\text{Al}_2\text{B}_2\text{O}_7$ (KABO)³⁵ and BiBO_3 (BIBO);³⁶ however, BBO remains of considerable value.

Nonlinear optical properties of various borate single crystals are due to electron delocalisation^{37,38,40–43} in complex boron–oxygen anions. The simplest examples of such anions are provided by the $[\text{BO}_3]^{3-}$ triangles and by two types of ring trimers, *viz.*, the $[\text{B}_3\text{O}_6]^{3-}$ units constructed of three BO_3 triangles with two of the three vertices shared and the $[\text{B}_3\text{O}_7]^{5-}$ units (two BO_4 tetrahedron). They are shown in Fig. 1. Peculiarities of the electronic structure of borate crystals determine high polarisability of these compounds, which is comparable to that of aromatics. These crystals also have good mechanical properties and high laser damage threshold, which is typical of inorganic crystals.⁴⁴

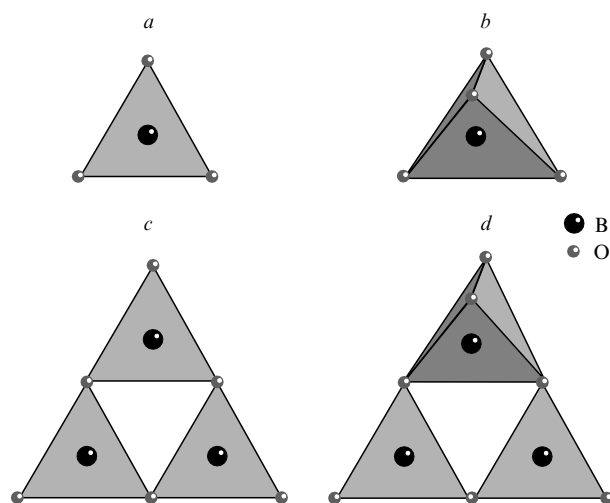


Figure 1. Structural units present in borate crystals. BO_3 (a); BO_4 (b); B_3O_6 (c) and B_3O_7 (d).

Solid-state optoelectronics (photonics) requires high-quality crystals that contain no inclusions, twins and inhomogeneities, are free from thermal strain and variations of the refractive index, have a definite crystallographic orientation and are, as a rule, rather large (of the order of a centimetre). BBO single crystals can be grown by melt-solution (high-temperature flux) technique using the modified Kyropoulos and Czochralski methods^{45,46} or by direct crystallisation from supercooled melts. Crystal growth is complicated by high viscosity and glass-forming ability of melts. The polymeric structure of borate melts can be to some extent controlled by shifting the acid–base equilibria.^{47,48} Low yield of materials suitable for practical applications, undesired variations of the properties of BBO crystals and high cost of optical elements are due to the fact that growing such crystals is a technologically sophisticated procedure.

Recently, interest to centrosymmetric single crystals of the high-temperature α -modification of BaB_2O_4 has quickened.⁴⁹ These crystals are characterised by large birefringence, broad optical transparency region (190–3500 nm) and can compete with calcite crystals that are widely used in linear optics.

An extensive literature on BBO crystals has evolved. Despite this fact, a number of topical problems concerning both the basic

(nonstoichiometry, polymorphism, phase equilibria, thermodynamics) and applied (elucidation of the reasons responsible for characteristic optical and structural inhomogeneities of BBO crystals, optimisation of crystal growth conditions) aspects of the investigation and growth of these crystals are still to be solved.

II. Barium borates. The $\text{BaO} - \text{B}_2\text{O}_3$ system

Studies of the phase equilibria in the $\text{BaO} - \text{B}_2\text{O}_3 - \text{H}_2\text{O}$ system at 30 °C (Fig. 2) revealed the existence of barium metaborate tetrahydrate, $\text{BaO} \cdot \text{B}_2\text{O}_3 \cdot 4\text{H}_2\text{O}$, and barium triborate heptahydrate, $\text{BaO} \cdot 3\text{B}_2\text{O}_3 \cdot 7\text{H}_2\text{O}$.^{2,50} Some other hydrated barium borates were reported in the early studies.² More recently,⁴ $\text{BaO} \cdot \text{B}_2\text{O}_3 \cdot 5\text{H}_2\text{O}$ was synthesised, which is formed in dilute solutions and is thought to be metastable,⁵ as well as $\text{BaB}_2\text{O}_4 \cdot 1.67\text{H}_2\text{O}$.⁵¹ Determination of the crystal structures of $\text{BaO} \cdot \text{B}_2\text{O}_3 \cdot 4\text{H}_2\text{O}$ (see Ref. 52) and $\text{BaO} \cdot \text{B}_2\text{O}_3 \cdot 5\text{H}_2\text{O}$ (see Refs 53 and 54) revealed the presence of isolated tetrahedral $\text{B}(\text{OH})_4$ groups in these crystals; therefore, the formulae of the compounds can be written as $\text{Ba}[\text{B}(\text{OH})_4]_2$ and $\text{Ba}[\text{B}(\text{OH})_4]_2 \cdot \text{H}_2\text{O}$, respectively.

The crystalline compounds $\text{Ba}_2[\text{B}_5\text{O}_{18}(\text{OH})_2]\text{OH}$, $\text{Ba}[\text{B}_5\text{O}_{18}(\text{OH})] \cdot \text{H}_2\text{O}$ and $\text{Ba}_5[\text{B}_{20}\text{O}_{33}(\text{OH})_4] \cdot \text{H}_2\text{O}$ were hydrothermally synthesised in the $\text{BaO} - \text{B}_2\text{O}_3 - \text{M}_2\text{O} - \text{H}_2\text{O}$ ($\text{M} = \text{K}, \text{Rb}, \text{Cs}$) systems at 280 °C under a pressure of 70 atm.^{55–58}

The melting diagram of the $\text{BaO} - \text{B}_2\text{O}_3$ system was studied by thermal analysis.^{59,60} Using the ‘composition–property’ curve, six congruently melting compounds were found. These are $3\text{BaO} \cdot \text{B}_2\text{O}_3$, $2\text{BaO} \cdot \text{B}_2\text{O}_3$, $\text{BaO} \cdot \text{B}_2\text{O}_3$, $\text{BaO} \cdot 2\text{B}_2\text{O}_3$,

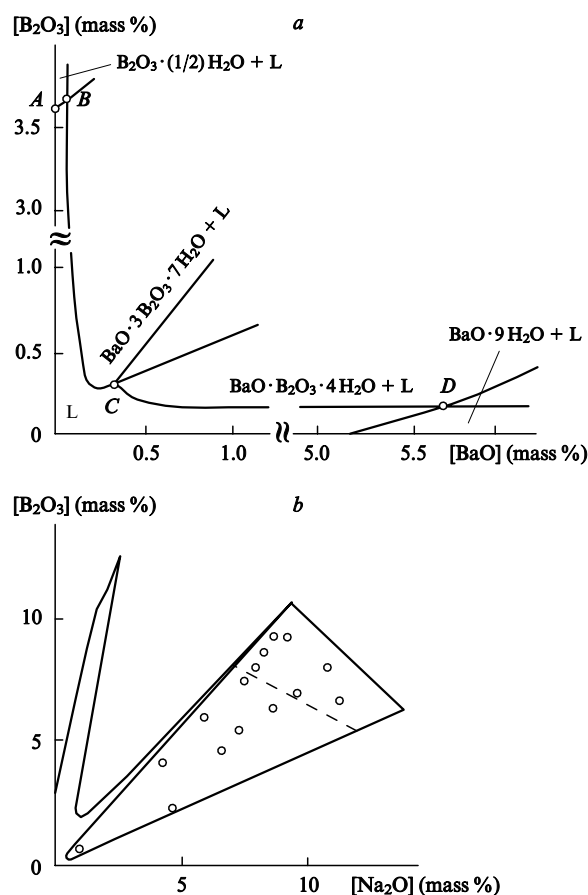


Figure 2. Phase equilibria in the $\text{BaO} - \text{B}_2\text{O}_3 - \text{H}_2\text{O}$ system at 30 °C (a)^{2,50} and crystallisation field of $\text{BaB}_2\text{O}_4 \cdot n\text{H}_2\text{O}$ (open circles) in sodium borate solutions at 25 °C (b).⁵ Points B, C and D denote eutonics (a); the dashed line designates the boundary between the tetrahydrate and pentahydrate regions (b).

§ The notations widely used in the literature are given in parentheses.

BaO $\cdot$ 3 B₂O₃ and BaO $\cdot$ 4 B₂O₃ (for the generalised phase diagram of the BaO–B₂O₃ system, see Ref. 2). It is believed that super-cooling of melts occurred in these studies.

Phase equilibria in the BaO–B₂O₃ system have been studied in detail¹² by annealing and quenching techniques and by the X-ray phase and thermal analyses. Only four congruently melting compounds were found, namely, 3 BaO $\cdot$ B₂O₃, BaO $\cdot$ B₂O₃, BaO $\cdot$ 2 B₂O₃ and BaO $\cdot$ 4 B₂O₃. A melt immiscibility region was observed near the boron oxide composition.

Barium metaborate, BaO $\cdot$ B₂O₃, melts congruently at 1095 °C and forms eutectics at 905 and 889 °C.¹² In addition to the high-temperature α -modification of BaO $\cdot$ B₂O₃, the low-temperature β -modification was found and characterised by X-ray powder diffraction. No transition temperature was reported;¹² it was only assumed to lie between 100 and 400 °C. More recently, in studies of the BaO–B₂O₃–SiO₂ ternary system¹³ the temperatures of a number of phase transformations in the BaO–B₂O₃ system were corrected (increased by ~ 10 °C) while the melting temperature of BaO $\cdot$ B₂O₃ was found to be 1105 °C.

The generalised phase diagram of the BaO–B₂O₃ system (Fig. 3), which was proposed by Levin and reported in a handbook,¹⁰ has been commonly accepted by crystal growth researchers (see, e.g., Refs 11, 27, 46). Following Feigelson *et al.*,⁴⁶ in Fig. 3 we added a horizontal line (dash-and-dot line) corresponding to the polymorphic transformation of BaO $\cdot$ B₂O₃ at 925 °C (see below). It should be noted that the boundaries of the immiscibility region (dashed line) do not match those reported earlier.¹² The coordinates of the upper critical point of the immiscibility dome (1931 °C, 6.6 mol.% BaO) were determined in a thorough study by Hageman and Oonk.⁶¹

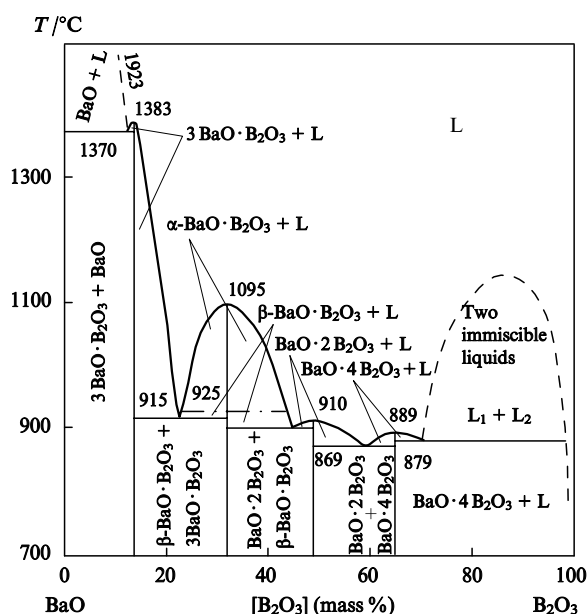


Figure 3. Phase diagram of the BaO–B₂O₃ system.¹⁰

The middle part of the phase diagram of the BaO–B₂O₃ system was revised by Hübner⁶² who showed that not only the above-mentioned compounds, but also 2 BaO $\cdot$ 5 B₂O₃, 2 BaO $\cdot$ B₂O₃ and 4 BaO $\cdot$ B₂O₃ are formed in the system. All of the newly found compounds were characterised by X-ray powder diffraction. The congruent melting temperature of 2 BaO $\cdot$ B₂O₃ (920 ± 5 °C) is close to the temperature of the eutectic between BaO $\cdot$ B₂O₃ and 3 BaO $\cdot$ B₂O₃.^{12,13} The temperature of the polymorphic transformation of BaO $\cdot$ B₂O₃ is 925 ± 5 °C. Hübner proposed the existence of homogeneity regions for both modifications of BaO $\cdot$ B₂O₃ and suggested that this region for the high-temperature form is especially broad (Fig. 4). According to this

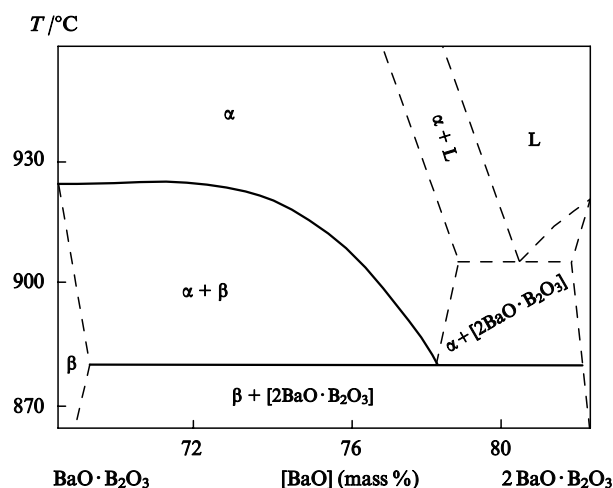


Figure 4. Middle part of the phase diagram of the BaO–B₂O₃ system.⁶²

version of the phase diagram, the low-temperature modification of β -BaB₂O₄ is not in the equilibrium with the B₂O₃-enriched melt; however, this contradicts the results obtained more recently.^{63,64}

Hübner⁶⁵ also studied the phase equilibria in the BaO–B₂O₃–Al₂O₃ system and reported the formation of continuous solid solutions in the composition range between 2 BaO $\cdot$ B₂O₃ and the low-temperature modification of BaO $\cdot$ B₂O₃ at 700 °C (Fig. 5). The formation of individual compound 2 BaO $\cdot$ B₂O₃ was established based on the X-ray diffraction data obtained in melt crystallisation studies in a number of ternary systems.⁶⁶ Compound 2 BaO $\cdot$ B₂O₃ crystallises in the monoclinic crystal system (Table 1) and its unit cell parameters are close to those of β -BaB₂O₄ in the monoclinic setting (the difference consists in doubling the parameter *c*). This structural type is possible only if barium and oxygen ions are inserted into the β -BaB₂O₄ lattice, which is accompanied by a dramatic increase in density.

Single crystals of the 2 BaO $\cdot$ 5 B₂O₃ (Ba₂B₁₀O₁₇) phase found by Hübner⁶² were grown by Stone *et al.*⁶⁸ by slowly cooling a stoichiometric melt. The solid-phase synthesis was carried out at 750 °C and the melting temperature of the compound was reported to be 901 °C. The melt undergoes a glass transition on cooling with ease.

The crystal structures of compounds BaO $\cdot$ 2 B₂O₃ (Ba₄O₇), BaO $\cdot$ 4 B₂O₃ (Ba₈O₁₃) and 2 BaO $\cdot$ 5 B₂O₃ (Ba₂B₁₀O₁₇) were established (see Table 1).^{16,18,68} At 700 °C, compound BaO $\cdot$ 4 B₂O₃ undergoes a phase transition from the low-temperature orthorhombic to the high-temperature tetragonal modification which is stable up to the congruent melting temperature (889 °C).⁶⁷ The heat of the transition is 2100 J mol^{–1}. The phase transition is accompanied by twinning of crystals.

An IR spectroscopic study⁷⁵ revealed the presence of isolated BO₃ triangles in the structure of compound 3 BaO $\cdot$ B₂O₃ which is thus an orthoborate.

The generalised phase diagram of the BaO–B₂O₃ system is shown in Fig. 6. Since the melting temperature of compound Ba₂B₁₀O₁₇ (see Ref. 68) is somewhat higher than the liquidus temperature for this composition (see Ref. 12), this compound seems to be stable. According to the version of the phase diagram proposed by Levin and McMurdie,¹² an eutectic corresponding to the crystallisation of BaO $\cdot$ 2 B₂O₃ and BaO $\cdot$ 4 B₂O₃ should occur in this concentration range; however, no eutectic effects were observed. Probably, they simply overlooked the compound 2 BaO $\cdot$ 5 B₂O₃. Earlier,⁶⁰ a congruently melting compound of other stoichiometric composition was found in this concentration range.

The ‘interrelation’ between compounds 2 BaO $\cdot$ B₂O₃ and BaO $\cdot$ B₂O₃ is still a moot question. The melting temperature of 2 BaO $\cdot$ B₂O₃ reported by Hübner is much lower than the liquidus

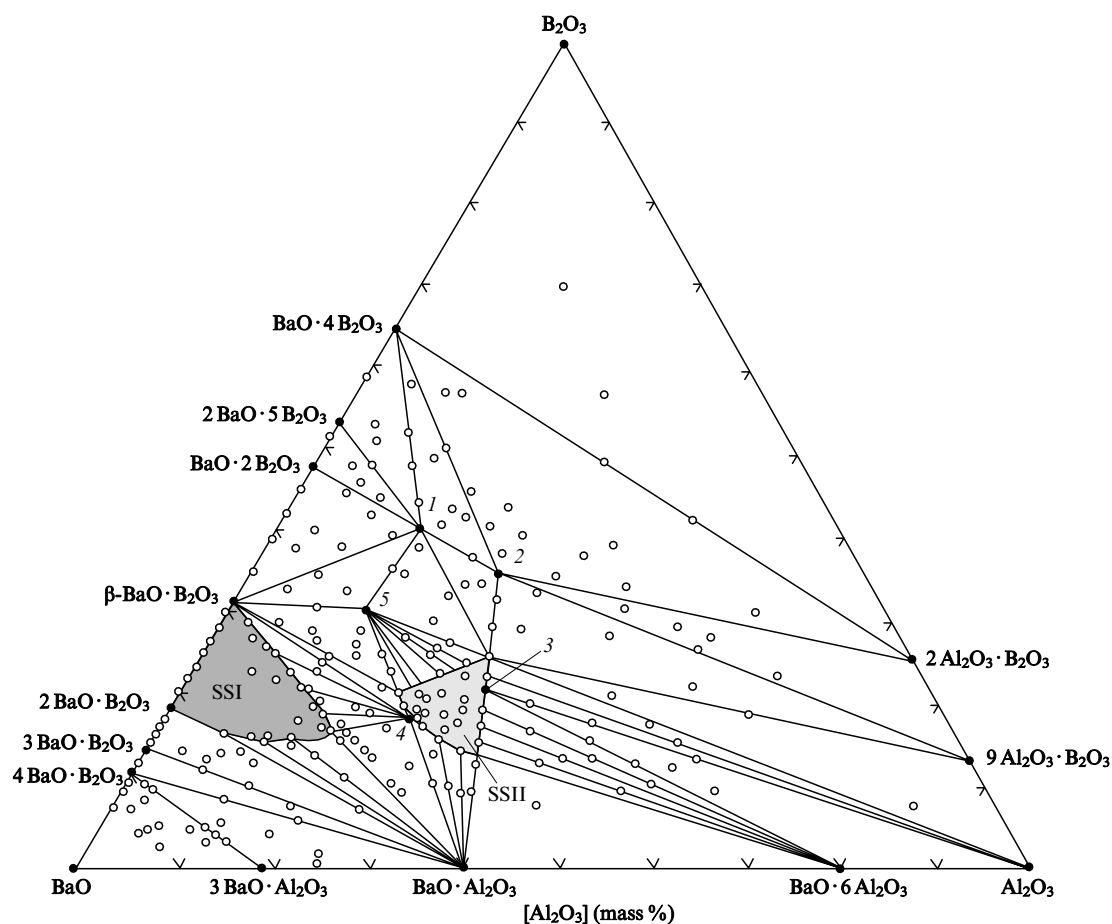


Figure 5. Phase equilibria in the BaO–B₂O₃–Al₂O₃ system at 700 °C.⁶⁵

Open circles denote the compositions studied; full circles denote compounds; SSI and SSII designate the regions of solid solutions; 2 BaO·4 B₂O₃·Al₂O₃ (1), BaO·2 B₂O₃·Al₂O₃ (2), BaO·B₂O₃·Al₂O₃ (3), 3 BaO·2 B₂O₃·2 Al₂O₃ (4) and 5 BaO·6 B₂O₃·2 Al₂O₃ (5).

Table 1. Crystallographic characteristics of anhydrous barium borates.

Compound	Crystal system	Space group	Unit cell parameters					Density /g cm ^{−3}	Ref.
			<i>a</i> /Å	<i>b</i> /Å	<i>c</i> /Å	<i>α, β, γ</i> /deg	<i>Z</i>		
BaB ₈ 13	orthorhombic	<i>P</i> 222 ₁	8.56	17.38	13.20		8	2.91	18
			8.55	17.352	13.21		8	2.927	67
	tetragonal ^a		8.630		13.268		4	2.899	67
BaB ₄ 7	monoclinic	<i>P</i> 2 ₁ / <i>c</i>	10.56(1)	8.20(1)	13.01(1)	<i>β</i> = 104.95(17)	8	3.57	16
Ba ₂ B ₁₀ 17	triclinic	<i>P</i> 1	9.858(1)	9.990(1)	6.706(1)	<i>α</i> = 96.79(1) <i>β</i> = 106.64(1) <i>γ</i> = 76.89(1)	2	3.54	68
β-BaB ₂₄	trigonal	<i>R</i> 3 <i>c</i>	12.532		12.717		18	3.74	22
			12.529		12.731		18	—	69
			12.519		12.723		18	—	70
			12.547(6)		12.736(9)		18	—	44
			12.500(3)		12.6875(9)		18	—	71
			12.517(3) ^b		12.708(3) ^b		18	—	72
α-BaB ₂₄	trigonal	<i>R</i> 3̄ <i>c</i>	7.2188(10)		39.000(4)		18	3.734	17
			7.2351		39.192		18	3.751	73
Ba ₂ B ₂₅	monoclinic	<i>P</i> 2, <i>Pm</i> or <i>P</i> 2/ <i>m</i>	11.014(6)	12.684(5)	16.856(7)	<i>β</i> = 99.82(3)	19	5.07	62
	trigonal	—	21.70 ^c		12.74 ^c				
Ba ₃ B ₂₆	orthorhombic	—	13.82	14.81	13.43		16	5.11	74

^a At 725 °C. ^b Doped with neodymium. ^c Recalculated by the authors of this review using Hübner's data.⁶²

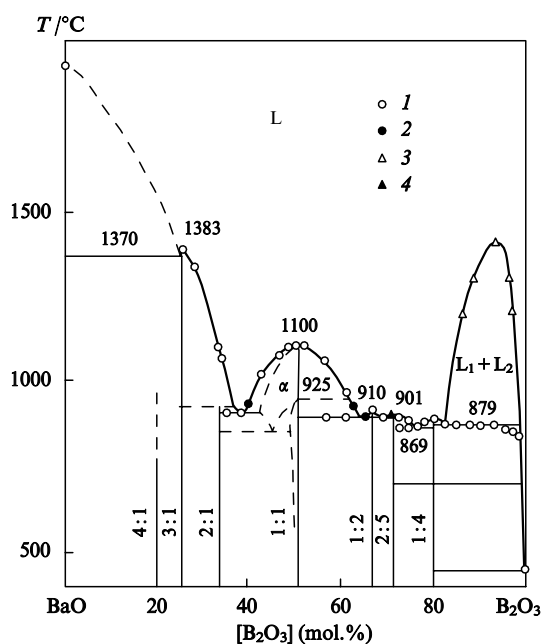


Figure 6. Generalised phase diagram of the BaO–B₂O₃ system. The data were taken from Ref. 12 (1), Ref. 64 (2), Ref. 61 (3) and Ref. 68 (4).

temperatures determined earlier^{12,59} and, hence, cannot correspond to the equilibrium congruent melting of this compound. However, it is rather close to the eutectic temperature. The authors of this review suggest incongruent melting of 2 BaO·B₂O₃ following a peritectic reaction (see Fig. 6).

Hübner's assumption⁶² of the presence of the homogeneity region based on BaO·B₂O₃ is in agreement with the absence of eutectic effect in this concentration range.¹² Figure 6 presents a version of the phase diagram containing the regions of solid solutions based on α -BaB₂O₄ and β -BaB₂O₄ shown according to Hübner. The presence of these regions suggests a strong non-stoichiometry of BaB₂O₄. If this is the case, the maximum on the liquidus curve should not coincide with the point corresponding to the 1:1 composition. It should also be noted that the densities of both the α - and β -modifications of BaB₂O₄ are much lower than the average density obtained by linear approximation of the data for compounds in the BaO–B₂O₃ system. This anomaly can be to some extent compensated for by the formation of interstitial solid solutions. This issue as well as the thermal stability of 4 BaO·B₂O₃ call for further investigation.

III. Glass formation in the BaO–B₂O₃ system

Melt cooling in the BaO–B₂O₃ system causes glass formation.^{9,11,14} The most stable glasses (ingots up to 50 g by mass) are fabricated by solidification of melts containing from 16 mol.% to 40 mol.% BaO, *i.e.*, in the region of existence of the low-melting compounds BaO·2 B₂O₃, 2 BaO·5 B₂O₃ and BaO·4 B₂O₃ (see Fig. 6). As the cooling rate increases, the region of glass formation extends (up to 60.5 mol.% BaO for ingots of mass 0.1 g) and includes the composition BaB₂O₄. No transparent homogeneous glasses are formed on cooling of B₂O₃-enriched melts. At temperatures that are somewhat higher than the liquidus temperature, the equilibrium melt represents two immiscible liquids of different compositions. Similarly to the melt, on cooling each of the liquids can undergo a glass transition.

Boron oxide can undergo a spontaneous glass transition.⁹ Glassy boron oxide can be readily obtained from boracic acid which melts at 176 °C. Long-term heating is accompanied by slow removal of water from the melt; however, trace amounts of water are hard to remove. The content of the residual water after heating

at 1200 °C for 19 h is 0.127 mass %. Pumping anhydrous dinitrogen through the melt over a period of 5 h reduces the content of water down to 0.025 mass %. A nearly completely dehydrated material was prepared by long-term heating at a pressure of 1 Torr in a platinum crucible and then in a graphite crucible. The viscosity of the melt depends on the content of water; as this parameter decreases from 0.248 mass % down to 0.025 mass %, the temperature corresponding to a viscosity of 10⁴ P increases from 537 to 550 °C.

It is noteworthy that the viscosity of B₂O₃ at 450 °C (melting temperature) is much lower than that of silica at 1710 °C; however, glassy boron oxide is much more hard to crystallise compared to glassy silica. This was assumed to be due to abnormally high ratio of the bond energy to the melting temperature of glassy B₂O₃. No spontaneous devitrification of B₂O₃ at an atmospheric pressure was observed. Crystallisation of boron oxide requires heating at 225–250 °C over a period of several days in a loosely plugged vessel. The sample slowly loses water and is transformed into a solid finely crystalline aggregate characterised by a density of 2.42 g cm^{−3} and a melting temperature lying between 460 and 470 °C. The content of B₂O₃ in the material thus obtained is 99.4% while the rest seems to be the bound water.

An X-ray study of glassy B₂O₃ showed that its structure is a disordered network of [BO₃]^{3−} triangles (in which each oxygen atom is linked to two boron atoms) or distorted [BO₄] tetrahedra.

Glass formation is also typical of the systems comprising B₂O₃ and alkali metal oxides. The Na₂O–B₂O₃ system is characterised by two glass formation regions¹⁴ corresponding to the concentration ranges 0 mol.%–8 mol.% (or 0 mol.%–30 mol.%) and 66.5 mol.%–71.5 mol.% Na₂O. The second glass formation region coincides with the region of existence of low-melting compositions in the vicinity of the NaBO₂–Na₄B₂O₅ eutectic. A 'belt'-like glass formation region was found in the Na₂O–BaO–B₂O₃ system at the B₂O₃ concentration of greater than 60 mol.%.⁷⁶

IV. Methods of preparation of BaB₂O₄

There are four groups of methods for preparation of BaB₂O₄. These are precipitation of crystal hydrates from aqueous solutions followed by dehydration; hydrolysis of alkoxides; anhydrous solid-phase syntheses (possibly) followed by melting and melt-solution syntheses. The last-named group also includes various single-crystal growth techniques which can be considered as specific methods of synthesis.

1. Precipitation of BaB₂O₄·*n* H₂O from aqueous solutions

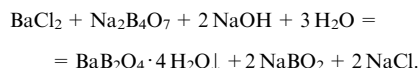
Methods for the synthesis of barium borate based on precipitation of crystal hydrates BaB₂O₄·*n* H₂O from aqueous solutions (aqueous methods) have been known for long.^{2–8} However, they are rarely employed for the preparation of charge that is used as raw material for the crystal growth.

Aqueous methods for the synthesis of different metal borates share a number of features. During precipitation from aqueous solutions the borates are isolated as crystal hydrates. The content of the bound water depends on the reaction conditions. In addition, metal borates can be isolated in the amorphous state. Such borates are intermediate products of many syntheses; nevertheless, they can undergo a transition into the crystalline state under particular conditions. Amorphous borates are, as a rule, highly reactive.

Borates can contain water in the form of both hydroxyl ion and solvate molecules. This allows one to rationalise a complex process of dehydration of borates at elevated temperatures which involves elimination of individual solvate water molecules and hydroxyl groups, which is due to association of boron-containing anions. Usually, removal of water occurs in a stepwise manner in the temperature range from 100 to 200 °C. The residual water can be removed only at very high temperatures (~1000 °C and above). Often, dehydration of borates is accompanied by a specific

effect of borate rearrangement⁷⁷ which was first reported by Nikolaev.⁷⁸ Namely, dehydration causes a complete destruction of the crystal lattice and transition of the compound under study into the amorphous state; further heating leads to crystallisation accompanied by exothermic effect, which can be detected on thermograms.

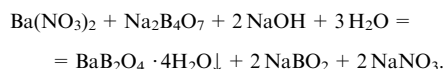
The synthesis of BaB_2O_4 by precipitation from aqueous solutions should be carried out in a strongly basic medium ($\text{pH} > 11$) provided that variations of the pH value during crystallisation are small. This can be done by performing a reaction between a solution of boric acid and a solution of $\text{Ba}(\text{OH})_2$ (see Ref. 4) or BaCl_2 .⁵¹ However, it is more convenient to use barium chloride and a mixture of sodium tetraborate and sodium hydroxide.



To maintain the pH value at the desired level, a nearly twofold excess of the precipitating agent is required. The reaction results in a flaky precipitate which is transformed into crystalline $\text{BaB}_2\text{O}_4 \cdot 4\text{H}_2\text{O}$ after several hours.

The crystallisation fields of $\text{BaB}_2\text{O}_4 \cdot 4\text{H}_2\text{O}$ and $\text{BaB}_2\text{O}_4 \cdot 5\text{H}_2\text{O}$ in sodium borate solutions at 25 °C for the reaction presented above were studied by Gode.⁵ The possibility of nearly complete precipitation of boron (in the form of barium borate) from solutions was demonstrated (see Fig. 2b). A drawback of this method consists in poisoning the precipitate by sodium and chlorine impurities.

The synthesis of barium borate from barium nitrate was proposed⁸

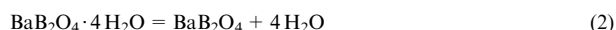
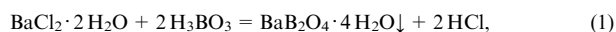


It was proposed to remove the chloride (impurity in NaOH) and sodium ions using an ammonia solution (to prevent transformation into polyborates). Drying at 400–650 °C for 30 min resulted in an anhydrous product.

To transform non-crystalline barium borate into the crystalline $\text{BaO} \cdot \text{B}_2\text{O}_3 \cdot 4\text{H}_2\text{O}$, it was recommended⁶ to grind the material in a boric acid solution in the presence of KOH. The yield of the desired product was low (~20%).

Dehydration of the tetrahydrate $\text{BaO} \cdot \text{B}_2\text{O}_3 \cdot 4\text{H}_2\text{O}$ begins at 70 and is completed at 140 °C, while dehydration of the pentahydrate $\text{BaO} \cdot \text{B}_2\text{O}_3 \cdot 5\text{H}_2\text{O}$ occurs in the temperature range from 50 to 450 °C.⁴ It should be noted that the melting temperatures of the dehydrated products (1015 and 925 °C, respectively)⁴ are much lower than the equilibrium melting temperatures. Probably, this is due to the influence of the residual water. According to Lehmann *et al.*,⁵¹ dehydration of $\text{BaO} \cdot \text{B}_2\text{O}_3 \cdot 1.67\text{H}_2\text{O}$ occurs in the temperature range 90–170 °C.

Precipitation of the tetrahydrate $\text{BaB}_2\text{O}_4 \cdot 4\text{H}_2\text{O}$ from solution followed by thermal decomposition following the reactions



was employed^{79–82} for the synthesis of BaB_2O_4 that is used as raw material (charge) for the melt growth of β - BaB_2O_4 crystals (the so-called chloride technique). Remelting or sintering BaB_2O_4 at 1095 °C for 3 h results in a coarse-grained material of higher purity grade compared to the charge obtained by solid-phase synthesis from barium carbonate. A thermogram exhibiting a clearly seen peak corresponding to the melting at 1100 °C has been reported.⁸²

It should be noted that the synthesis of BaB_2O_4 by thermolysis of crystal hydrates allows reliable preparation of a product of stoichiometric composition. In addition, it seems that aqueous solutions favour purification of barium-containing reagents

(removal of impurities including strontium and calcium that strongly affect the stability of the crystalline modifications of BaB_2O_4).

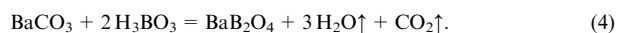
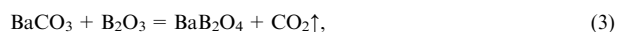
2. Syntheses using ‘soft chemistry’ methods

Recently, the so-called ‘soft chemistry’ methods have been used for the synthesis of inorganic materials (see, *e.g.*, Ref. 83). These methods can also be employed to synthesise barium borate. For instance, a stoichiometric mixture of boron triethoxide and barium isopropoxide was slowly hydrolysed with distilled water.⁸⁴ The powder dried *in vacuo* at 60 °C was found to be a new γ -modification of BaB_2O_4 .

3. Anhydrous high-temperature syntheses

Compound BaB_2O_4 can be directly synthesised by melting BaO and B_2O_3 at 1150 °C for 1 to 2 h.⁸⁵ According to the results of differential thermal analysis (DTA) study, the reaction begins at 1060 °C.

Barium borate (the starting material for the synthesis of single crystals) is usually prepared from a mixture of BaCO_3 and B_2O_3 (see Refs 86–89) or H_3BO_3 .^{64, 80, 90–92} The syntheses are conducted using the following reaction equations

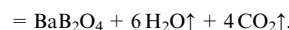
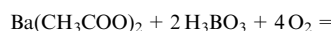
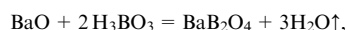


Powder mixtures taken in the stoichiometric ratios are mechanically mixed and then heated until sintering and melting. In the case of reaction (3) the powders are sintered at 800 °C for 10 h, melted at 1200 °C for 10 min and then zone melted (both processes are carried out in a graphite boat in an argon atmosphere)⁸⁸ or are melted in air at 1150 °C for 5 h. For the reaction with H_3BO_3 it was recommended⁹² to use a stepwise synthesis with allowance for the reaction mixture to stay at 150 and 700 °C.

Usually, syntheses are performed in platinum crucibles; however, graphite crucibles can also be used in an inert atmosphere (argon).⁸⁸

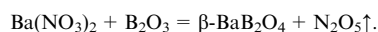
It seems likely that one can synthesise BBO from barium carbonate according to Berzelius by boiling a barium carbonate suspension in an aqueous boric acid (analogously to the synthesis of lead borate⁴). However, this synthetic route was not studied experimentally.

Barium borate BaB_2O_4 is also synthesised using other barium compounds (*e.g.*, barium oxide,⁷⁹ barium acetate^{90, 91} and barium nitrate^{12, 82}) as starting reagents.



The reaction with barium acetate was carried out in a platinum crucible using stepwise heating;^{91, 92} finally, the product was kept at 1150 °C for 50 h. The reaction proceeds in air; however, it does not always happen that the reaction goes to completion under the crystal growth conditions. This leads to poisoning the growing crystals with carbon. In the reaction with barium nitrate the ground mixture of reagents was heated to 700 °C for 2 h and then repeatedly heated above this temperature.¹²

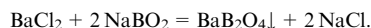
The following reaction was conducted⁸²



A ground mixture of reagents was repeatedly heated from 700 to 850 °C. It was also found that the reactions of BaCO_3 or BaO with H_3BO_3 do not result in products that are suitable for the Czochralski growth of β - BaB_2O_4 .

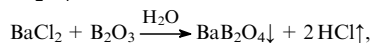
4. Melt-solution crystallisation

Barium borate can be synthesised by exchange reactions in melts. The first successful synthesis dates back to 1874.^{1,79} The following reaction was used



Sodium chloride having a lower melting temperature acts as solvent that is removed with water after cooling.

Reactions analogous to the processes underlying the aqueous methods of synthesis^{93,94} can also be used for the synthesis of β -BaB₂O₄



The excess barium chloride acts as flux. The reaction was carried out in a platinum crucible at 1000 °C for 2 h.⁹³ The driving force of the synthesis of BaB₂O₄ is the difference between the heat of reaction and the energy of pyrohydrolysis of barium chloride (~ 78 kcal).

A method of fabrication of a seed rod necessary for melt-solution growth of single crystals is as follows.⁹⁴ BaB₂O₄ polycrystals precipitated in the reaction with boric acid are ground, moulded, sintered in an oxygen atmosphere at 730–850 °C, re-ground and then re-sintered at 850–1095 °C.

An extensive literature on the synthesis of single crystals using the systems of the BaB₂O₄–S or, more generally, BaO–B₂O₃–S types (S is the melt playing the role of solvent) has evolved. Both equilibrium and nonequilibrium melt crystallisations are possible (the former corresponding to the primary crystallisation region of β -BaB₂O₄ in the phase diagrams). Among various solvents, Na₂O is most widely used at present (see below).

Melt-solution growth of single crystals is strongly affected by the impurities coming into the crystal from the solvent. These are the melt components (first of all, sodium), impurities contained in the starting reagents and accumulated within the growing crystal (*e.g.*, potassium or strontium) and ‘extra’ impurities that come from the material the crucible is made of (platinum).

V. Polymorphism and the crystal structure

In addition to the high- and low-temperature modifications of BaB₂O₄ (these two were mentioned above) there are some indications of the existence of at least one unstable low-temperature modification designated as T-BaB₂O₄ (see Ref. 51), or γ -BaB₂O₄.^{84,95} The X-ray diffraction patterns of the samples reported in Refs 51, 84 and 95 are close but not identical. The samples of this phase were obtained by dehydration of BaB₂O₄ · 1.67 H₂O (see Ref. 51) and by the interaction of boron triethoxide and barium isopropoxide. According to Yamaguchi *et al.*,⁸⁴ γ -BaB₂O₄ undergoes an irreversible transformation into α -BaB₂O₄ on heating to ~ 600 °C. An IR spectroscopic study of γ -BaB₂O₄ showed that, in contrast to the structure of the α - and β -forms of BaB₂O₄ (see below), the structure of this modification comprises infinite anionic chains constructed of [BO₄] tetrahedra with their vertices shared (calcium, strontium and lithium metaborates have an analogous structure).[†]

The crystal structure of α -BaB₂O₄ was established by Mighell and Perloff.¹⁷ It was found that the crystal is characterised by the trigonal system and centrosymmetric space group $R\bar{3}c$ (Fig. 7).

According to Hübner,⁶² β -BaB₂O₄ single crystals have a monoclinic unit cell with the parameters $a = 11.133$, $b = 12.67$, $c = 8.381$ Å and $\beta = 100.04^\circ$; the space group is $C2/c$ and $Z = 12$. Coincidence of the results of X-ray powder diffraction studies^{12,62} indicates that the same modification of barium borate was investigated in both cases.

However, Hübner's⁶² choice of the unit cell was questioned.⁶⁹ According to Liebertz and Stahr,⁶⁹ β -BaB₂O₄ crystals are uniaxial and trigonal (the crystallographic parameters are listed in Table 1). This discrepancy is of fundamental nature, since the space group $C2/c$ is centrosymmetric while the space group $R\bar{3}c$ is non-centrosymmetric. Frohlich⁷⁰ established the crystal structure of β -BaB₂O₄ and confirmed the results obtained by Liebertz and Stahr.⁶⁹ Lu *et al.*²² also reported similar results; however, they believed that the β -BaB₂O₄ crystal is characterised by the space group $R\bar{3}$. The results obtained by Lu *et al.*²² were used in the interpretation of the Raman spectra of β -BaB₂O₄ crystals.⁹⁷ Re-determination of the crystal structure^{44,71} and the results of piezoelectric and electro-optical measurements^{38,98} and Raman spectroscopy studies^{99,100} confirmed that the low-temperature modification of barium borate is characterised by the space group $R\bar{3}c$.

A thorough study⁸⁵ of BaB₂O₄ single crystals confirmed the lack of central symmetry and revealed a slight monoclinic distortion of the trigonal lattice. The parameters of the trigonal lattice of β -BaB₂O₄ obtained by different authors are slightly different (see Table 1).

The high- and low-temperature modifications of barium borate exhibit pronounced structural similarity, *viz.*, both of them have layered structures, contain nearly planar boron–oxygen [B₃O₆]^{3–} ring groups arranged perpendicular to the three-fold axis while their lattice parameters are related by simple formulae $a_\alpha \approx \sqrt{3}a_\beta$, $c_\alpha \approx (1/3)c_\beta$, $Z_\alpha = Z_\beta$.

The [B₃O₆]^{3–} groups are constituents of the structure of only one out of the three known crystalline modifications of metaboric acid, namely, metastable orthorhombic HBO₂-III with a melting temperature of 176 °C.³ Therefore, the α - and β -modifications of BaB₂O₄ are salts of this acid.

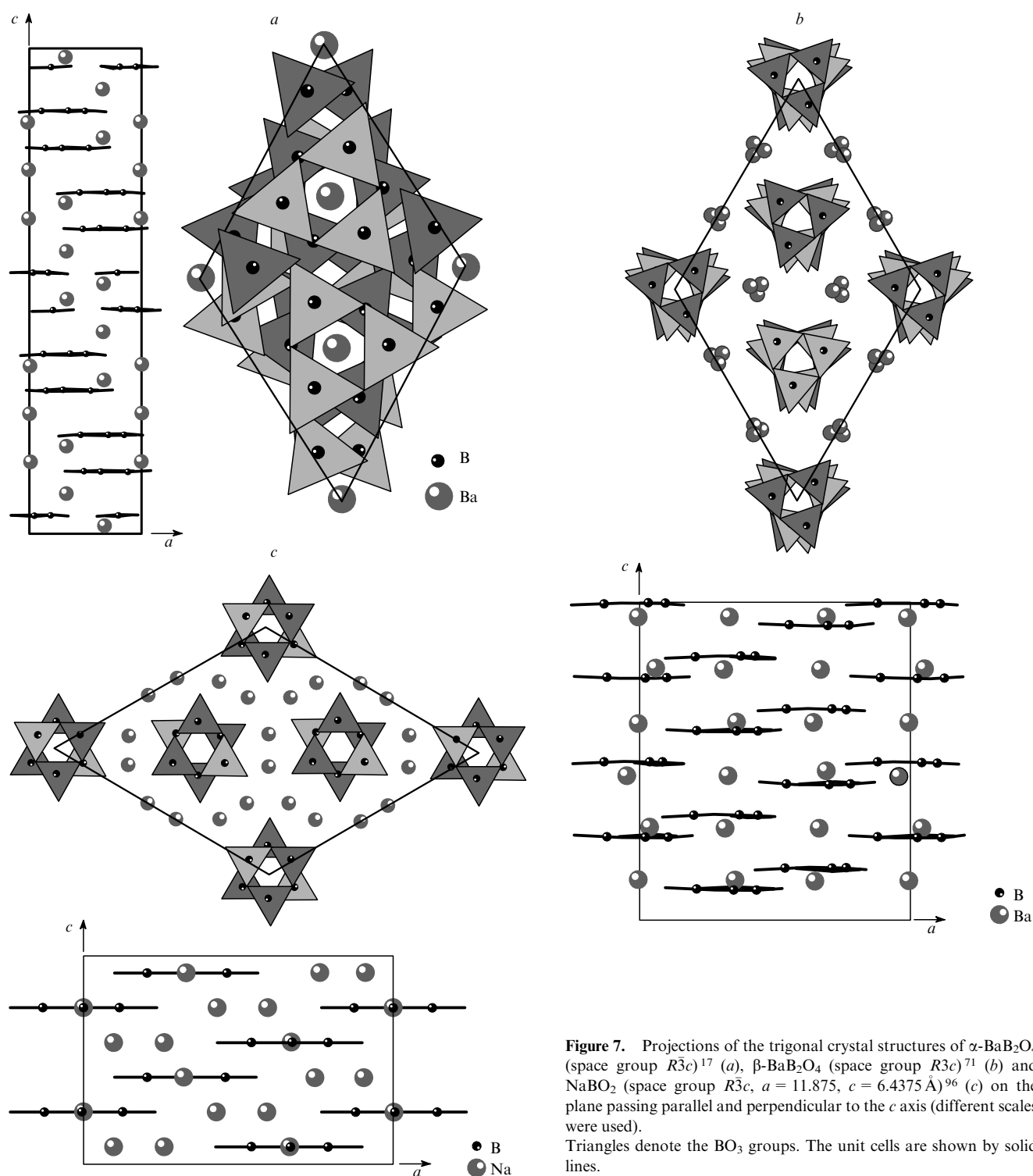
High-temperature Raman spectroscopy studies^{99,100} of the α - and β -forms of BaB₂O₄ revealed a change in the number of spectral lines in the frequency range of internal vibrations of the [B₃O₆]^{3–} anions corresponding to the D_{3h}^6 and C_{3v}^6 symmetry, respectively. The B–O distances in and out of the ring are ~ 1.40 and 1.32 Å, respectively.

The structures of the α - and β -modifications of BaB₂O₄ are characterised by different types of coordination environment of barium ions. In the high-temperature α -modification there are two types of barium atoms. The coordination number of barium atoms occupying the first position is 6 while for Ba atoms in the second position it equals 9. In the low-temperature β -modification the Ba atoms are in irregular environment of eight oxygen atoms shared by three ring borate anions. The Ba–O distances, $d(\text{Ba–O})$, lie between 2.613 and 3.025 Å. The X-ray powder diffraction patterns of the α - and β -modifications of BaB₂O₄ are presented in Fig. 8.

Investigation of the nonlinear optical properties of BBO is a topical problem. In this connection it is appropriate to briefly outline the nature of chemical bonding in this compound.^{38,40–43,97} In the [B₃O₆]^{3–} ring anions, the sp^2 -hybridised boron atoms form σ -bonds with oxygen atoms. The filled orbitals of the oxygen atoms and the vacant orbitals of the boron atoms involved in the rings interact with one another, thus forming the π -bonds. Positively charged Ba²⁺ ions and negatively charged [B₃O₆]^{3–} groups interact electrostatically. In addition, the intermolecular interaction occurs between electrically neutral layers. A number of the first-principle studies of the electronic structure and nonlinear optical susceptibilities of BBO have been reported.^{42,43} The results of calculations are in good agreement with the experimental data. The energy states of the atoms constituting the [B₃O₆]^{3–} anions contribute to both the upper part and the bottom of the conduction band.

Different temperatures of the phase transition between the β - and α -modifications of BaB₂O₄ have been reported (100–400 °C,¹² 880 °C,¹⁰³ ~ 900 °C⁴⁴ and 917 °C¹⁰⁴). Currently, a value of 925 ± 5 °C reported by Hübner⁶² and confirmed

[†] In addition, two unstable modifications of BaB₂O₄ were obtained during crystallisation of glasses in the BaO–B₂O₃–Al₂O₃ system.⁶⁵



in the annealing and quenching studies^{23, 105} has been commonly accepted.

The phase transition in question is strongly hindered. An X-ray diffraction pattern obtained after annealing of coarse-grained (40–50 μm), single-phase (β -phase) crystalline BBO at 940 °C for 4 h exhibited only traces of the α -phase.⁸⁷ Annealing at higher temperatures is accompanied by gradual decrease in the intensity of the reflections of the β -phase and by simultaneous increase in the intensity of the reflections of the α -phase. After annealing at 960 °C for 2 h nearly ~50% of the initial β -phase transformed into the α -phase. Analogous studies were carried out using single-phase (α -phase) crystalline BBO. After annealing at ~800 °C for 7 h nearly ~30% of the initial α -phase transformed

into the β -phase. At lower temperatures, the phase transformation occurred very slowly.

During measurements¹⁰⁶ of the thermal expansion coefficients the BBO single crystals were overheated up to 983 °C at a heating rate of 1 deg min⁻¹ and to 1010 °C at a heating rate of 0.1 deg min⁻¹. Transition into the α -phase occurred after reaching these temperatures.

According to Kimura and Feigelson,¹⁰⁷ the $\beta \rightarrow \alpha$ transformation takes only 5 min on heating above 1000 °C. It should be noted that the samples studied contained Sr (~0.05%) and Ca (~0.03%); it is thought that Ca impurity causes stabilisation of the α -phase.¹⁰⁸

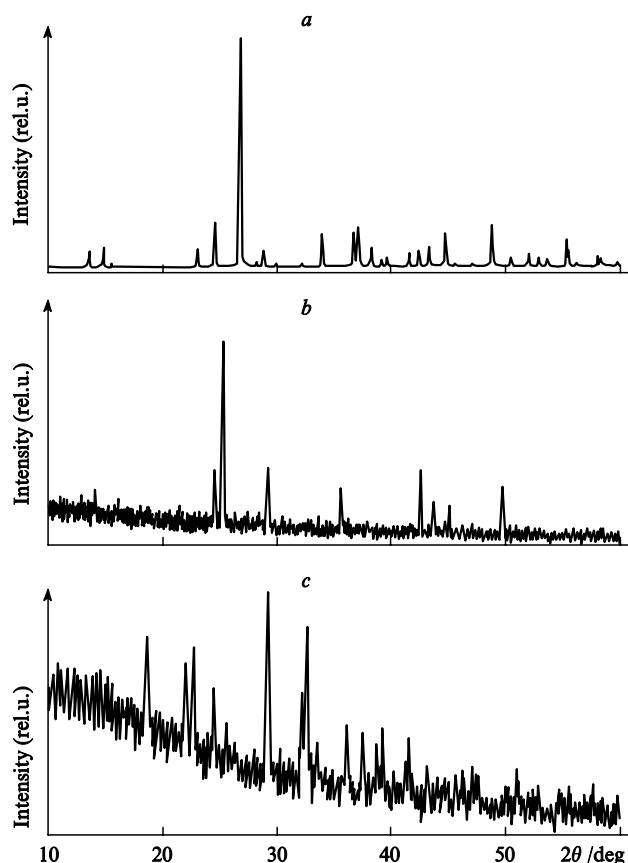


Figure 8. X-Ray powder diffraction patterns (CuK α radiation) of α -BaB₂O₄ (a), β -BaB₂O₄ (b) and NaBaBO₃ (c).^{101, 102}

A number of *in situ* studies of the $\beta \rightleftharpoons \alpha$ transformation by high-temperature X-ray powder diffraction have been reported.^{82, 84, 106} Kozuki and Itoh¹⁰⁶ heated BBO powder to 1050 °C but no phase transition was observed. Yoshimoto and Kimura⁸² also did not observe the $\beta \rightarrow \alpha$ and $\alpha \rightarrow \beta$ phase transitions upon heating to 1000 °C. According to Yamaguchi *et al.*,⁸⁴ transformation of β -BaB₂O₄ prepared by heating from the γ -modification into α -BaB₂O₄ begins at 870 °C and is completed at 940 °C. The kinetics of this transformation have been studied.

The most surprising results were reported by Kouta *et al.*⁸⁰ who studied the transition in question and did not observe even minor indications of the phase transformation after heating β -BaB₂O₄ powder at 1090 °C for 5 h and subsequent cooling of the sample. The results of DTA study⁸⁰ showed that both modifications of BaB₂O₄ melt at nearly the same temperature, namely, 1100 ± 0.5 °C (α -phase) and 1099 ± 0.5 °C (β -phase).

A special study concerning the influence of the heating and cooling rates ($v = 3.75, 5.0, 7.5, 10.0, 15.0$ deg min⁻¹) on both the transition temperatures and reversibility of the phase transformations has been reported.¹⁰⁴ It was shown that the temperatures of the polymorphic transition of the low-temperature modification of BaB₂O₄ into the high-temperature form (917 °C) and the melting temperature of the latter (1092 °C) are virtually independent of the heating rate, whereas the reverse is observed on cooling.

VI. Peculiarities of crystallisation of BaB₂O₄ melts

BBO melts are characterised by high viscosity, tendency to supercooling and by hysteresis of properties. The physical properties of BBO have been studied recently.^{81, 109} The viscosity of the melt

monotonically increases from 20 to 61 mPa cm⁻¹ as the temperature decreases from 1463 to 1271 K and is ~ 30 mPa cm⁻¹ at the melting temperature. The activation energy of the viscous flow for the melt is 0.95 eV. The time taken to achieve the equilibrium viscosity of the melt at 1463 K is nearly 10 h. The density of the melt is a linear function of the temperature in the range between 1463 and 1271 K; it is described by the following equation

$$\rho = (4.453 - 0.000545)T$$

It was found that $\rho = 3.707$ g cm⁻³ at the melting temperature. The thermal expansion coefficient of the melt is 1.5×10^{-4} K⁻¹. The surface tension at the melting temperature is 0.35 N m⁻¹ (see Ref. 89).

According to the results of our experiments data and to Itoh *et al.*⁷⁹, the degree of supercooling of the melt (ΔT) in a platinum crucible can be as high as 250 °C at cooling rates spanning the range from 4 to 15 deg min⁻¹. In this case crystallisation of β -BaB₂O₄ can occur at temperatures that are much higher than the temperature of the polymorphic transition. Crystallisation occurs randomly; there is a wide spread of the melt crystallisation temperature values but no correlations between this temperature and the cooling rate are observed. Mention has been made that the degree of supercooling of the melt can be as high as 300 °C.¹¹⁰ The problem of crystallisation of BBO (spontaneous crystallisation, seed crystallisation using α -BaB₂O₄ and β -BaB₂O₄ and crystallisation on a platinum wire) has been the subject of numerous studies.

In a study¹⁰⁴ the degree of supercooling of the melt was 170–200 °C. On cooling ($v = 3.75, 5.0, 7.5, 10.0, 15.0$ deg min⁻¹), crystallisation occurred only at the temperature of the polymorphic transition or at lower temperatures and resulted in the low-temperature modification of BaB₂O₄. The crystallisation temperatures were found to be $T_c = 917$ °C at $v = 3.75$ and 5 deg min⁻¹, $T_c = 887$ °C at $v = 7.5$ deg min⁻¹ and $T_c = 857$ °C at $v = 15$ deg min⁻¹.

BBO melts can exist without any changes in the metastable state for long at temperatures that are higher than the temperature of the polymorphic transition and lower than the melting temperature. However, seeding causes rapid crystallisation the rate of which increases with temperature. If α -BaB₂O₄ is used as seed, the same modification of barium borate crystallises. Seeding with β -BaB₂O₄ causes crystallisation of the β -modification despite its instability under these conditions.

Experiments on platinum seeded crystal growth showed⁸⁷ that co-crystallisation of β -BaB₂O₄ and α -BaB₂O₄ begins if $\Delta T \geq 40$ °C. At smaller ΔT values, crystallisation of the α -phase occurs, whereas β -BaB₂O₄ mainly crystallises at temperatures below 1030 °C (*i.e.*, at $\Delta T \geq 70$ °C).⁸²

The degree of supercooling achievable using graphite crucibles is substantially lower compared to platinum crucibles; in addition, crystallisation of both the α - and β -modifications of BaB₂O₄ in graphite crucibles is possible.¹⁰⁷ This is thought to be due to some similarity between the trigonal structures of graphite and BBO.

Thermodynamically, the possibility of direct melt crystallisation of the low-temperature phase can be rationalised by taking into account strong supercooling of the melt and the existence of the temperature of metastable melting of the low-temperature phase (at this temperature the curves of the temperature dependences of the Gibbs thermodynamic potentials of the low-temperature phase and the melt intersect). The corresponding scheme is presented in Fig. 9. The temperature of metastable melting, T_β , of the low-temperature modification lies between the temperature of equilibrium melting, T_α , of the high-temperature modification and the temperature of polymorphic transformation, T_l . For the crystallisation of the β -phase to begin the melt temperature should be lower than T_β .

Ignoring the difference between the heat capacities of the α - and β -modifications of BaB₂O₄, the following relationship is valid:¹¹⁰

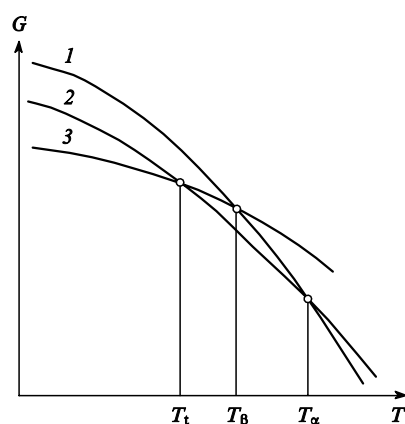


Figure 9. Temperature dependences of the Gibbs thermodynamic potentials (G) of the melt (1) and of the α - (2) and β -modifications (3) of BaB_2O_4 .¹⁰⁶

T_t is the temperature of polymorphic transformation, T_β is the temperature of metastable melting of the low-temperature modification and T_α is the temperature of the equilibrium melting of the high-temperature modification.

$$T_\beta = \frac{\Delta H_t + \Delta H_\alpha}{\Delta S_t + \Delta S_\alpha} = \frac{\Delta H_\beta}{\Delta S_\beta},$$

where ΔH and ΔS are the enthalpies and entropies of the reactions. By denoting

$$\delta = \frac{\Delta H_t}{\Delta H_\alpha},$$

one gets¹¹¹

$$T_\beta = \frac{(\delta + 1)T_\alpha T_t}{\delta T_\alpha + T_t}.$$

The estimates of the T_β value are strongly different (Table 2).

From the standpoint of polymorphism, BaB_2O_4 presents a unique phenomenon, since both modifications (α and β) of this compound have virtually equal melting enthalpies and melting temperatures, while the enthalpy (and, correspondingly, entropy) of the $\alpha \rightleftharpoons \beta$ transition is very low.^{80, 82} On the other hand, here we deal with the first-order phase transition characterised by significantly different crystal structures, volumes and densities (in the temperature range from 20 to 1000 °C) of both phases. In this case, a correct thermodynamic description of the phase transformations requires that the heat capacities be taken into account (they must be measured) and, hence, the approximate relationships listed above cannot be used. Under the conditions in question the mutual stability of the polymorphous modifications strongly depends on the presence of impurities, defects, as well as on the mechanical strain and surface energy, so that the possibility of melt crystallisation of a particular modification is first of all determined by the kinetic considerations.

Table 2. Melting temperatures (°C) and enthalpies (kJ mol^{-1}) of the α - and β -modifications of BaB_2O_4 .

T_α	T_β	ΔH_α	ΔH_β	Ref.
1095	1078	67.784	74.562	111
1100	1050	—	—	106
1100 ± 0.5	1099 ± 0.5	—	—	80
—	—	109.45	110.00	82

Hindered melt crystallisation of BBO can be rationalised based on structural considerations. The results of high-temperature Raman spectroscopy studies^{99, 100, 112} of barium borate point to a dramatic difference between the spectra of the melt and crystalline $\beta\text{-BaB}_2\text{O}_4$. The spectrum of supercooled melt exhibited not only narrow lines of $[\text{B}_3\text{O}_6]^{3-}$ anions, but also a number of broad bands corresponding to internal vibrations of long-chain $[\text{BO}_2]_n^{n-}$ anions. The contribution of the $[\text{B}_3\text{O}_6]^{3-}$ anions near the melting temperature is small; however, it increases as the degree of supercooling of the melt increases. Probably, melting of BBO is accompanied by rearrangement of the boron–oxygen complexes (transformation of the $[\text{B}_3\text{O}_6]^{3-}$ ring anions into long anionic chains). Crystallisation is accompanied by the reverse rearrangement.

High viscosity of barium borate melts and their tendency to glass formation are due to the presence of long anionic chains. The hysteresis of viscosity (see above)^{81, 109} seems to be associated with polymerisation–depolymerisation of $[\text{B}_3\text{O}_6]^{3-}$ anions.

Structural rearrangement of the melt on heating was studied experimentally (by X-ray powder diffraction) and theoretically (by the molecular dynamics method).^{113, 114}

It was found⁸² that self-melt crystallisation of $\beta\text{-BaB}_2\text{O}_4$ single crystals is possible if the starting material used for the preparation of the melt corresponded to the β -phase and no melt overheating occurred. The character of crystallisation of the melt can be affected by the presence of fine particles and structural fragments of crystalline phases that play the role of nucleation and crystallisation centres.⁸⁷ Overheating causes destruction of these centres. Graphite particles present in the melt can also play the role of crystallisation centres.¹⁰⁷

Information on the influence of atmosphere on the character of crystallisation of BBO melts was questioned by some authors. However, an increase in the degree of supercooling of the melt in the case of crystallisation in an argon atmosphere compared to the crystallisation in air has been reported recently.¹¹⁵

VII. Growth of $\beta\text{-BaB}_2\text{O}_4$ single crystals

Peculiarities of crystallisation of BBO melts determine two most widely used methods for the growth of $\beta\text{-BaB}_2\text{O}_4$ single crystals. These are the supercooled self-melt growth (under nonequilibrium conditions) and melt-solution growth techniques. In the latter case, both single crystal growth from the equilibrium primary crystallisation region and nonequilibrium crystallisation are possible. The schemes of a number of most widely used single crystal growth techniques are presented in Fig. 10.

1. Self-melt growth of single crystals

Self-melt growth techniques of $\beta\text{-BaB}_2\text{O}_4$ single crystals have the advantages that the growing crystals are not poisoned with flux and the crystallisation rates are high (by an order of magnitude higher compared to melt-solution crystal growth). However, in these cases crystallisation occurs under nonequilibrium conditions at large temperature gradients, which causes development of mechanical strain in and cracking of the crystal. In addition, the crystal quality strongly depends on the procedure employed for the preparation of the starting reagents and on the crystallisation conditions. These methods have not received wide application so far.

Single crystals of $\beta\text{-BaB}_2\text{O}_4$ were Czochralski grown using a platinum wire seed.^{79, 80} Noteworthy is that only the α -modification was melt crystallised if the starting reagents were prepared by the carbonate technique [see reactions (3) and (4)]. The process using the starting reagents synthesised by the chloride method [see reactions (1) and (2)] led to direct crystallisation of the β -phase in a narrow range of the temperature gradient (G) values at the crystallisation front ($G = 150\text{--}125 \text{ deg cm}^{-1}$). Variation of G (an increase up to 175 deg cm^{-1} and a decrease down to 50 deg cm^{-1}) resulted in the crystallisation of the α -phase. A cracked single-crystal boule 7 mm in diameter and 18 mm

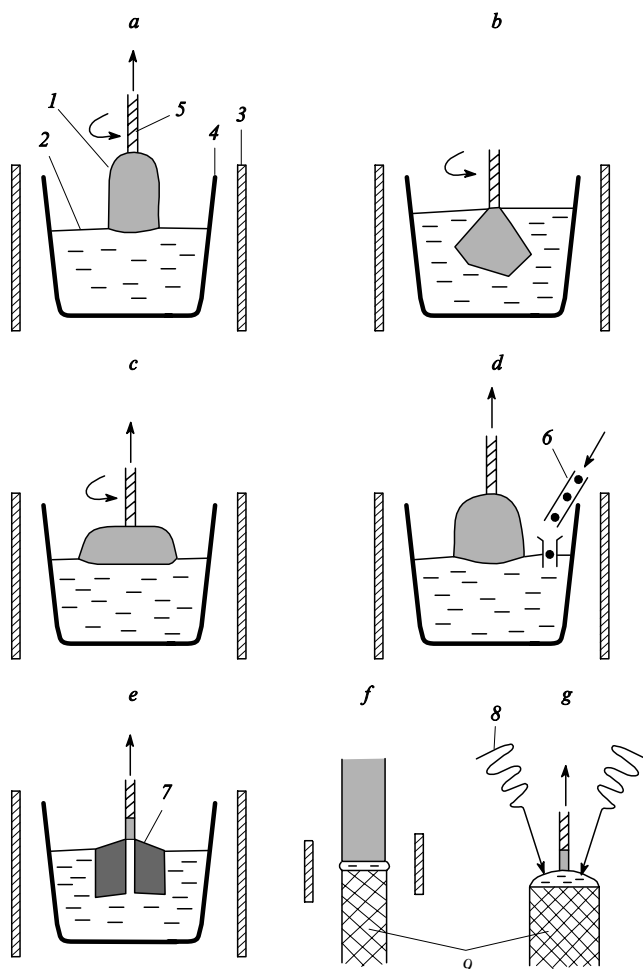


Figure 10. Schematic illustrations of the most widely used experimental techniques for the melt and melt-solution growth of single crystals. Czochralski technique, $T = \text{const}$ (a); Kyropoulos technique (immersion-seeded solution growth, ISSG), T decreases (b); top-seeded solution growth (TSSG) technique, T decreases (c); melt feed Czochralski technique (d); Stepanov technique, $T = \text{const}$ (e); zone melting technique (f) and laser assisted pulling from pedestal (g). Crystal (1); melt (2); heater (3); crucible (4); seed (5); feeding charge (6); shape-forming element (7); laser heating (8) and polycrystal (9).

long was obtained at a seed rotation rate of 20 rpm and a pulling speed of 0.6 mm h^{-1} .⁷⁹ Improvement of the growth technique allowed obtaining single crystals 15 mm in diameter and 40 mm long without cracks at a seed rotation rate of 14 rpm and a pulling speed of 4 mm h^{-1} .⁸⁰

According to Kozuki and Itoh,¹⁰⁶ the upper critical temperature for stable Czochralski self-melt growth of β -BaB₂O₄ crystals is 1050°C . The starting material (charge) is prepared from barium nitrate and boron oxide. A single crystal 15 mm in diameter and 7 mm long was grown at a seed rotation rate of 10 rpm and a pulling speed of 3 mm h^{-1} . The vertical temperature gradient was only 10 deg cm^{-1} ; however, a strong influence of the radial temperature gradient was revealed (in this case, the optimum value was 77 deg cm^{-1} , see Ref. 116).

Yet another example of the Czochralski growth of β -BaB₂O₄ crystals has been reported.⁸⁹ A β -BaB₂O₄ seed of specified orientation was placed in a platinum pipe 2 or 4 mm in diameter. The charge was prepared from barium carbonate. The predominant impurity was platinum (30 ppm). The temperature gradient was 300 deg cm^{-1} . Crystals 7 mm in diameter and 20 mm long were grown at a seed rotation rate of 15 rpm and a pulling speed of 5 mm h^{-1} . The same technique was also used for the crystallisa-

tion of solid solutions β -Ba(B_{1-x}R_x)₂O₄ ($R = \text{Al, Ga}$, $0 \leq x \leq 0.1$).¹¹⁶

2. Melt-solution growth of single crystals[†]

a. Choice of solvent

An appropriate solvent (flux) must provide a rather extended primary crystallisation region of the low-temperature modification of BaB₂O₄ and reduce the viscosity and glass-forming ability of the melt. As a consequence, the melts should exhibit a lower degree of polymerisation of the boron–oxygen chains and an increased proportion of the $[\text{B}_3\text{O}_6]^{3-}$ ring anions. The solvent must be of low volatility, possess stable properties and provide very weak interaction with the crystal to exclude the possibility of poisoning. The melt should also not be an aggressive medium towards the material the crucible is made of.

A melt growth technique of β -BaB₂O₄ single crystals from the starting reagents using a shift from the stoichiometric composition towards an excess of BaO or B₂O₃ (the so-called self-flux) has been reported.^{63,103} However, the temperature ranges suitable for crystal growth in this manner are narrow (less than 20°C). More often, an excess of B₂O₃ is used;^{120,121} however, in this case the crystal growth is hampered due to high viscosity of the melt.

A large number of compounds and their combinations have been considered as candidates for solvents. These are, e.g., Li₂O,^{62,103} BaCl₂,^{103,121} BaF₂,^{66,103,121,122} NaF,^{66,90,91,123} LiF,⁶⁶ NaCl,^{66,124–126} NaCl–Na₂O,¹²⁵ PbO,¹²⁷ Na₂O–Nd₂O₃,^{72,120} LiNbO₃,¹²⁰ PbF₂–B₂O₃,¹²⁰ CaF₂¹²⁴ and Na₂SO₄.¹²⁴

Usually, the solvent is chosen based on the phase diagrams of corresponding systems. Some known regions of the phase diagrams are presented in Fig. 11. The BaB₂O₄–NaCl, BaB₂O₄–

[†] For basic principles of the methods for melt-solution (flux) crystal growth, see Refs 117–119.

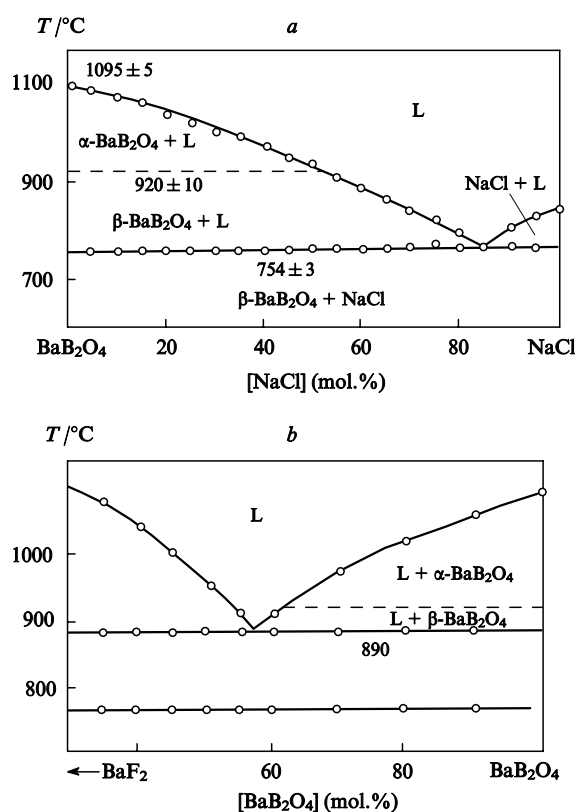
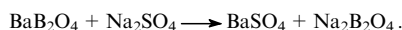


Figure 11. Phase equilibria in the systems BaB₂O₄–NaCl (see Ref. 124) (a) and BaB₂O₄–BaF₂ (see Ref. 122) (b).

NaF and BaB_2O_4 – BaF_2 sections seem to be quasi-binary. The BaB_2O_4 – Na_2SO_4 section is unstable, since in this case an exchange reaction occurs



The temperatures of the eutectic in the BaB_2O_4 – NaCl system, determined by different authors,^{124,125} virtually coincide (see Fig. 11 a); however, the compositions of the eutectic are appreciably different. Correspondingly, the concentration ranges of the growth of β - BaB_2O_4 crystals in this system are also different. Data on the phase equilibria along the BaB_2O_4 – NaF (see Refs 66 and 123) and BaB_2O_4 – BaF_2 sections (see Refs 103 and 122) are contradictory.

All solvents studied have certain drawbacks. The systems containing Li_2O (see Ref. 103) and BaF_2 (see Ref. 122) exhibit very narrow crystallisation regions of β - BaB_2O_4 , while no such region at all was found in the system containing CaF_2 .¹²⁴ The system with BaCl_2 is characterised by fast hydrolysis. If fluoride melts are used, pyrohydrolysis also occurs in air,¹²⁸ either relatively fast (BaF_2) or slow (NaF). A number of additives (e.g., MgF_2 and BaF_2) do not favour reduction of the melt viscosity; besides, the melt containing MgF_2 is prone to glass formation.⁶⁶ The use of lead-containing compounds^{120,127} favours stabilisation of the α -modification of BaB_2O_4 .⁴⁹ Potassium fluoride additives cause significant changes in the lattice parameters of BBO crystals, which seems to be due to isomorphous incorporation of potassium.⁶⁶

The BaO – B_2O_3 – BaF_2 system is used as flux in the growth of rare-earth ferrite single crystals.¹²⁹

Sodium fluoride is considered as candidate for flux. The BaB_2O_4 – NaF section and the BaO – B_2O_3 – NaF system are characterised by broad regions of primary crystallisation of β - BaB_2O_4 ⁶⁶ and by substantial reduction of the viscosity of the melt, which permits crystallisation at higher rates. However, to make the best use of these advantages, the crystals should be grown in an inert gas atmosphere. Slow pyrohydrolysis of NaF in air during crystallisation causes a gradual transformation of the BaB_2O_4 – NaF system into the BaB_2O_4 – Na_2O system.

Na_2O ^{45,46,64,86,90,91,101–103,105,121,124,130–146} is, at present, most widely used for melt-solution growth of β - BaB_2O_4 single crystals. Melt-solution growth of single crystals in the BaB_2O_4 – $\text{Na}_2\text{B}_2\text{O}_4$ system has also been reported.¹⁰³ The process is complicated by high viscosity of the melt and its tendency to supercooling. A number of studies concerning variation of the melt composition in the BaO – B_2O_3 – Na_2O system are available.^{64,134–137,143,144}

Phase equilibria in the BaB_2O_4 – Na_2O system were first studied by DTA¹⁰⁵ (cited according to Refs 46 and 130). A compound $\text{Na}_2\text{BaB}_2\text{O}_5$ was identified, which congruently melts at 846 °C. The temperatures of the eutectics are 755 and 573 °C. The phase diagram constructed by Huang and Liang¹⁰⁵ was used for the choice and ‘tuning’ of the growth regimes of BBO crystals.

Kaplun *et al.*¹³³ proposed yet another version of the phase diagram of the BaB_2O_4 – Na_2O system. In this case, the liquidus curve in the BBO crystallisation region and the eutectic position match those reported by Huang and Liang;¹⁰⁵ however, the compound $\text{Na}_2\text{O} \cdot \text{BaB}_2\text{O}_4$ was assumed to be incongruently melting at 830 ± 3 °C following a peritectic reaction resulting in a refractory compound that melts at temperatures above 1300 °C (this compound was assumed¹³³ to have a composition $3 \text{ BaO} \cdot \text{B}_2\text{O}_3$). An analogous interpretation of the phase equilibria in this system was reported in other studies.^{143,144} The generalised phase diagram of the BaB_2O_4 – Na_2O system is shown in Fig. 12.

The region of primary crystallisation of β - BaB_2O_4 in the BaO – B_2O_3 – Na_2O ternary system (Fig. 13) has been thoroughly studied by Nikolov and Peshev.⁶⁴

The contradiction between the results of studies^{105,133} was solved recently.¹⁰² In an investigation of the BaB_2O_4 – Na_2O section by DTA and visual-polythermal analysis (VPA) it was found (see Fig. 12) that both strong thermal effects (ascribed¹⁰⁵ to

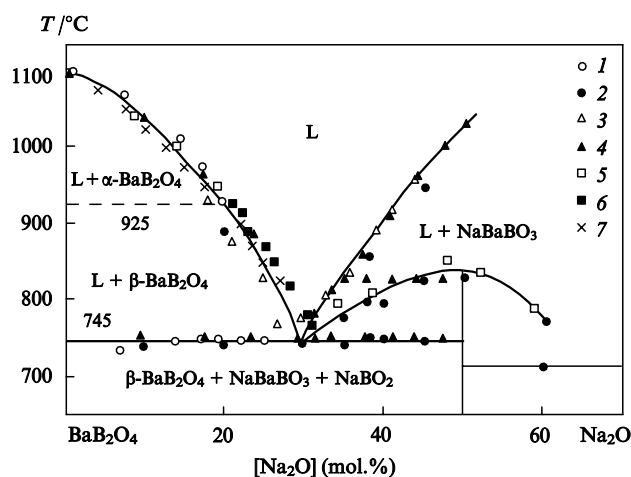


Figure 12. Phase equilibria along the BaB_2O_4 – Na_2O section.¹⁰²

The data were obtained by DTA, the mixtures were prepared by successive addition of Na_2CO_3 to remelted BaB_2O_4 (1); the data were obtained by DTA, the samples were prepared by solid-phase synthesis (2); the data were obtained by visual-polythermal analysis (3); other data were taken from Ref. 133 (4), Ref. 105 (5), Ref. 64 (6) and Ref. 72 (7).

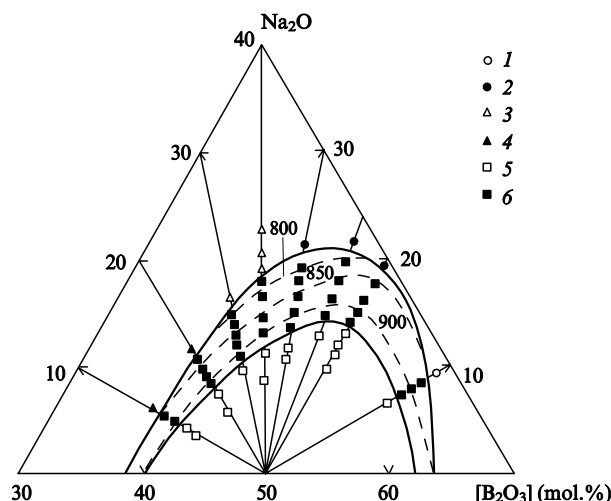


Figure 13. Primary crystallisation region of the α - and β -modifications of BaB_2O_4 in the BaO – B_2O_3 – Na_2O ternary system.⁶⁴

Primarily crystallising phases: $\text{Na}_2\text{BaB}_2\text{O}_5$ (1), NaBO_2 (2), $\text{Na}_2\text{BaB}_2\text{O}_5$ (3), $\text{Ba}_3\text{B}_2\text{O}_6$ (4), α - BaB_2O_4 (5) and β - BaB_2O_4 (6). The dashed lines denote isotherms.

the melting of $\text{Na}_2\text{BaB}_2\text{O}_5$) and high-temperature equilibrium crystallisation (liquidus curve) manifest themselves in the concentration range from 30 mol.% to 50 mol.% Na_2O . These results are in agreement with those reported by Kaplun *et al.*¹³³ The medium-temperature effects were found¹⁰² to be concentration dependent (this contradicts the results reported earlier¹³³), which is impossible in the case of stable quasi-binary section.

X-Ray diffraction and Raman spectroscopy studies showed that the reaction of BaB_2O_4 with Na_2O results in barium orthoborate, NaBaBO_3 , whose structure comprises isolated $[\text{BO}_3]$ triangles and that compound $\text{Na}_2\text{O} \cdot \text{BaB}_2\text{O}_4$ does not exist. Single crystals of compound NaBaBO_3 were grown by spontaneous crystallisation from melts of different compositions including a melt containing 62 mol.% BaB_2O_4 and 38 mol.% Na_2O using a platinum loop seed. The compound melts at 1270 °C and undergoes a rapid degradation in air, being a good absorbent of water and carbon dioxide. The X-ray diffraction pattern of NaBaBO_3 is

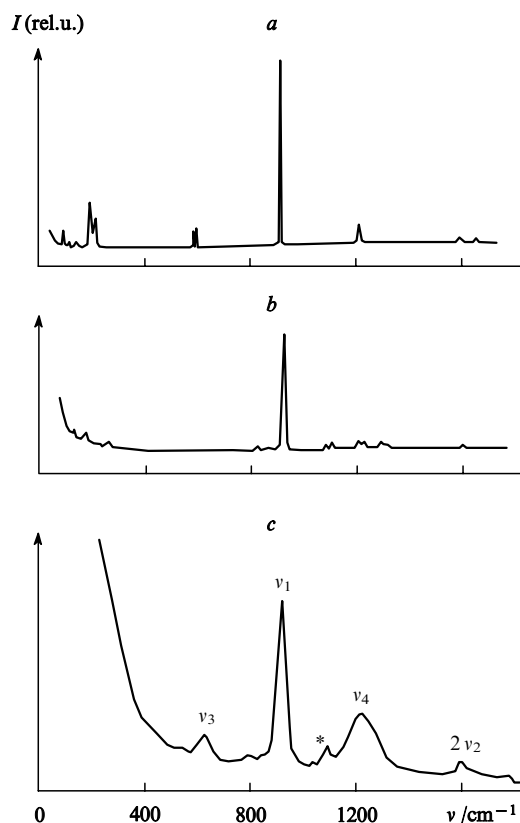


Figure 14. Raman spectra of a NaBaBO₃ single crystal (*a*), Na₃BO₃ powder (*b*) and 3 Na₂O · B₂O₃ melt (*c*).¹⁰² The fundamental vibration of the impurity carbonate ion is asterisked.

shown in Fig. 8*c* and its Raman spectrum is presented in Fig. 14*a*.

Both the α - and β -modifications of BaB₂O₄ have nearly identical thermodynamic characteristics.^{80, 82} This means that the liquidus curve (surface) corresponding to the polymorphic transformation of BaB₂O₄ should exhibit no kinks.

The projection of the liquidus surfaces of a part of the BaO–B₂O₃–Na₂O system on the concentration triangle is shown in Fig. 15. In this system, compound NaBaBO₃ is assumed to be congruently melting and the BaB₂O₄–NaBO₂, NaBaBO₃–NaBO₂ and, probably, BaB₂O₄–NaBaBO₃ sections are thought to be of eutectic character (the eutectics lie at 28 mol.% BaO, 50 mol.% B₂O₃, 22 mol.% Na₂O, 826 °C and at 22 mol.% BaO, 39 mol.% B₂O₃, 39 mol.% Na₂O, 830 °C). The region of primary crystallisation of NaBaBO₃ can be determined by analysing the morphology of the primary (spontaneously grown) crystals. The primary crystals are isometric individuals in contrast to needle-shaped BaB₂O₄ and NaBO₂ crystals. The ternary eutectic occurs at 745 °C and lies at 41 mol.% BaO, 41 mol.% B₂O₃, 18 mol.% Na₂O (or 70 mol.% BaB₂O₄, 30 mol.% Na₂O). The results obtained by different authors^{64, 102} are in good agreement.

By chance, the BaB₂O₄–Na₂O section passes nearly exactly through the ternary eutectic in the BaB₂O₄–NaBaBO₃–NaBO₂ ternary system. Therefore, the left part of the BaB₂O₄–Na₂O section looks like a binary system. It seems likely that weak high-temperature effects were overlooked¹⁰⁵ and that the non-variant effect of the L + NaBaBO₃ + NaBO₂ binary eutectic was interpreted to be the melting of a compound BaB₂O₄ · Na₂O, while the co-crystallisation (co-melting) curve of NaBaBO₃ + NaBO₂ was considered to be the liquidus curve.

Studies of the phase diagram of the BaO–B₂O₃–Na₂O system are complicated by high reactivity and hygroscopicity of melts, by their ability to absorb carbon dioxide and by the

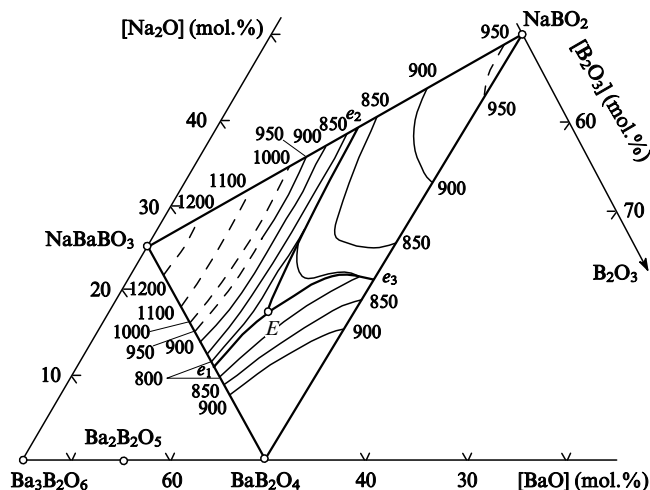


Figure 15. Projections of the liquidus surfaces in the BaB₂O₄–NaBaBO₃–NaBO₂ system on the concentration triangle.¹⁰² The eutectics are labelled *e*₁–*e*₃ and the ternary eutectic is labelled *E*.

corroding action of the melts on the platinum crucibles. High viscosity of the melts and their tendency to supercooling, glass formation and appearance of metastable equilibria present a particular problem.^{102, 143–145}

According to the phase diagram of the BaB₂O₄–Na₂O section (see Fig. 12), the temperature range of crystallisation of β -BaB₂O₄ is ~ 170 °C. The compositions suitable for growth of the low-temperature phase lie in the range 22 mol.%–30 mol.% Na₂O. Usually, the composition with the Na₂O content between 20 mol.% and 22 mol.% is used as charge. However, supercooling of the melt allows growth of large β -BaB₂O₄ crystals at a Na₂O content of less than 5 mol.% at ~ 1050 °C.¹²¹

The volatility of the melt increases along the BaB₂O₄–Na₂O section, whereas its viscosity decreases as the concentration of Na₂O increases.^{121, 132, 145}

b. Crystal growth techniques

The driving force of the melt-solution growth of BBO crystals is due to temperature reduction. Usually, vaporisation of the solvent is not used as a method for the preparation of a supersaturated solution.^{117–119} The process can be performed using various equipment.

Schematic illustrations of a number of crystal growth techniques are shown in Fig. 10.

Only a few studies are concerned with the growth of (i) BBO single crystals by the travelling solvent method (a version of zone melting technique),¹³¹ (ii) single-crystal filaments by laser-assisted pulling from pedestal¹²⁰ and (iii) plates using the Stepanov technique.^{85, 92}

The so-called top-seeded solution growth (TSSG) technique is most widely used.^{45, 46, 66, 86, 121, 130, 137–140, 146} It allows bulk BBO crystals (up to 60 mm in diameter and more than 10–15 mm long) to be grown (Fig. 16). Several versions of this method are known. If crystal growth occurs on slow cooling of the melt without pulling the seed, one deals with the Kyropoulos technique. The Czochralski method involves pulling of the seed-growing crystal under isothermal conditions (see Fig. 10).

In the case of melt-solution crystallisation the composition of the crystal differs from that of the melt; therefore, a feature of the Czochralski technique is continuous change in the composition of the melt and, correspondingly, in the crystallisation conditions. To avoid variations of the melt composition and other parameters and to maintain steady-state growth conditions, a method involving melt feed with BBO charge was proposed.¹³²

Often, a combination of the two above-mentioned growth techniques is employed. In this case, a slow pulling of the crystal is

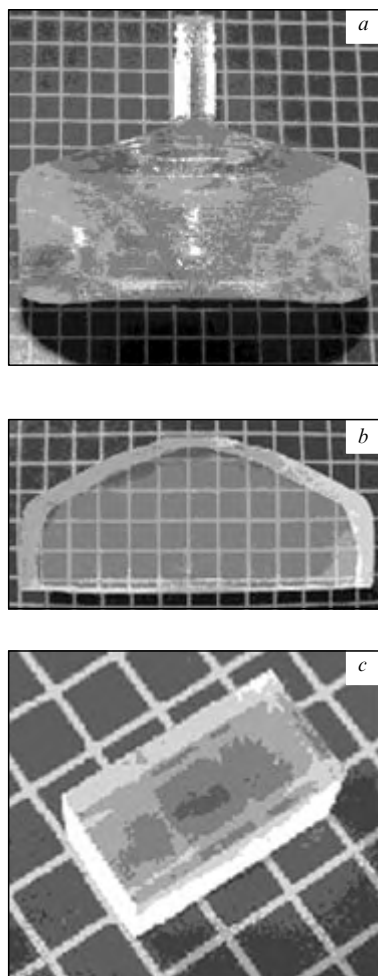


Figure 16. Photographs of a BBO crystal (*a*), axial slice 8 mm thick (*b*) and a nonlinear optical element of dimensions $8 \times 8 \times 15 \text{ mm}^3$ (*c*). Paper cell size is $5 \times 5 \text{ mm}$. The crystal was grown by the authors of this review at the Crystal Growth Laboratory, Institute of Mineralogy and Petrography, Siberian Branch of the Russian Academy of Sciences.

combined with slow cooling of the melt. The major advantages of the TSSG technique with pulling of the crystal compared to analogous technique without pulling are as follows:

- higher crystal growth rate;
- the possibility of growing thick crystals in smaller crucibles;
- prevention the crucible walls from touching with the growing crystal, which causes seed failure.

Seed growth of bulk $\beta\text{-BaB}_2\text{O}_4$ crystals of good quality with and without pulling from Na_2O flux has been reported.¹²¹ The seed rotation rate varied from 2 to 60 rpm while the pulling speed was $0.01\text{--}0.02 \text{ mm h}^{-1}$. The high seed rotation and crystal pulling rates cause undesired changes in the shape of the interface from a convex interface to a concave one. Inclusion-free BBO crystals were grown at low pulling rates (of the order of 0.5 to 1.0 mm per day).

As a rule, a melt of composition 75 mol.% BBO–25 mol.% Na_2O was used. The liquidus temperature for this composition is $\sim 886^\circ\text{C}$. The starting reagents (BaCO_3 , H_3BO_3 and Na_2CO_3) were weighed, mixed and placed in a platinum crucible 75 mm in diameter. Then the crucible was heated to $\sim 1110^\circ\text{C}$ over a period of several hours until complete decomposition of carbonates. Seed crystals with different orientations were used for crystal growth. Orientation of the seed crystal affects not only the rate and quality of growth, but also the shape of the BBO crystal. A high

anisotropy of the growth rate of BBO crystals was reported. The rates of growth along the *a* and *b* axes were found to be higher than the rate of growth parallel to the *c* optical axis. Crystals grown parallel to the *a* and *b* axes or in other directions that strongly deviate from the *c* axis usually undergo spontaneous cracking in the (001) cleavage plane. This is due to anisotropy of the thermal expansion. The thermal expansion and thermal conductivity coefficient of BBO crystals measured along the *c* axis are by nearly an order of magnitude larger than those measured in the perpendicular direction.³⁹

The radial and axial temperature gradients and the shape of the liquid–solid interface are important parameters that define quality of the crystal. Crystals of the best quality are usually grown if the interface is flat or slightly convex. The shape of the interface depends on both the pulling speed and the seed rotation rate. Obtaining a flat or slightly concave interface requires that the pulling speed and the seed rotation rate be 0.5–1.0 mm per day and 4–8 rpm, respectively. As the seed rotation rate increases, the contribution of forced convection gradually becomes much larger than that of natural convection. If the pulling speed seed is too high, the growing crystals can lose contact with the solution.

Search for methods of control of convective heat and mass transfer always has received considerable attention, since it is these processes that in most cases provide the possibility of growing particular types of crystals with preset properties. All methods of control can be divided into contact methods and contactless ones. The former are based on the action of a physical body placed in contact with the melt, solution or another crystallisation medium. Most of these methods involve mechanical rotation of the crystal and/or crucible, the use of various diaphragms, stirrers, shape-forming elements, *etc.* A number of contact methods have been applied to the growth of BBO crystals.^{139, 147, 148} Extreme sophistication of the mechanical devices gave an impetus to search for simpler methods of control of the heat and mass transfer processes. This approach had some success.

Contactless techniques are based on the action of physical fields (gravitational, electromagnetic and thermal) on the heat and mass transfer processes.

In practice, all crystal growth techniques include (sometimes, unconsciously) a certain pattern of the heat field. In most cases these are static heat fields characterised by the symmetry axis of an infinite order, L_∞ , and particular values of the axial and radial temperature gradients. Traditionally, crystals are grown in tube heating furnaces with cylindrical heat field symmetry L_∞ (excluding the edge effects). With the advent of precision heating furnaces (PHF),¹⁴⁹ the possibility of controlling the heat field and the heat and mass transfer during the crystal growth appeared. This is achieved by changing the heat field symmetry and by rotating the heat field. A version of dynamic control of the heating elements (HE) in such a furnace has been reported.^{150–153} In practice, the growth of crystals under conditions of static, azimuthally distributed heat field in the PHF is also of considerable interest.¹⁴⁰ These conditions are created by either commutation or regular arrangement of the HE around the PHF muffle, which provides a radially distributed pattern for power delivered to the muffle walls and, hence, to the walls of the growth crucible.

Experiments on the growth of BBO crystals¹⁴⁰ were carried out using a heating furnace with a total of 18 HE arranged evenly around the quartz muffle 110 mm in diameter with walls 4 mm thick. Switching on all series-connected HE in the furnace produced a heat field of cylindrical symmetry L_∞ . Strictly speaking, in this case the heat field symmetry should be L_{18} ; however, it was considered as L_∞ (within the limits of experimental error) due to the choice of an optimum distance between the HE and taking into account the effect of the heat field smoothing by the muffle and the crucible walls. Switching off each third HE changed the heat field symmetry in the furnace to six-fold symmetry L_6 . If three HE arranged at an angle of 120° with respect to one another were switched off, the heat field symmetry reduced to L_3 . In

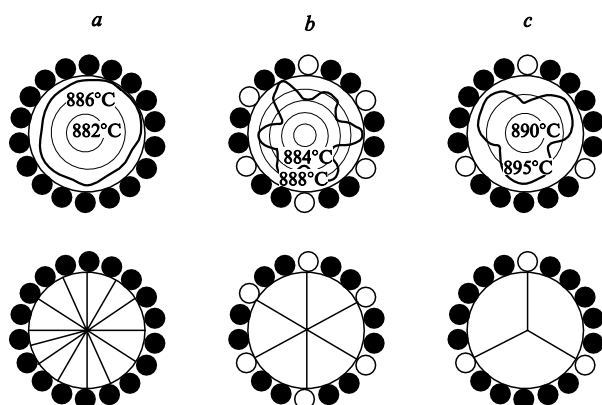


Figure 17. Polar diagrams of the heat fields of symmetry L_∞ (a), L_6 (b) and L_3 (c) used for the growth of BBO crystals (at the top) and the corresponding convective patterns (at the bottom). The open circles denote the switched off heating elements.

Fig. 17, we present the horizontal sections of the growth furnace and the polar diagrams of the heat fields of symmetry L_∞ , L_6 and L_3 , as well as the typical convective patterns on the melt-solution surface, formed under the action of the heat fields of different symmetry.

BBO crystals were grown on a 4×4 mm seed oriented parallel to the optical axis c . The growth procedure consisted in search for an equilibrium temperature by seed touching the melt-solution surface in the place where the rays of the convective star are brought to a point. After the seed started to spontaneously dissolve, the temperature in the furnace was lowered by 1–2 degrees. The next touching of the melt surface was performed after 2–3 h. After prolonged (12–24 h) liquid–seed contact the crystal was allowed to grow on cooling the furnace at a rate of 1–3 degrees per day. The seed was rotated at 1–2 rpm and moved upward at a rate of 0.3–0.4 mm per day. The growth process continued until the crystal became visually much less transparent. This was interpreted as an indication of the constitutional supercooling, which induced a cellular crystal growth.

The experimental data on the growth of BBO crystals under the action of steady-state heat fields of different symmetry are listed in Table 3. As can be seen, a change in the heat field symmetry from L_∞ to L_6 led to a slight increase in the ‘yield’ coefficient (from 1.22 ± 0.02 to 1.27). However, the ‘yield’ coefficient increased by a factor of 1.7 to 2.07 g (kg deg)^{−1} on going to L_3 symmetry [cf. a theoretical value of ~ 2.52 g (kg deg)^{−1} obtained according to the liquidus equilibria in the BaB₂O₄–Na₂O system].

Table 3. Experimental data on BBO crystals grown in a crucible 100 mm in diameter at initial charge of 1.5 kg in heat fields of different symmetry.¹⁴⁰

Run No.	Heat field symmetry	ΔT /°C	Pulling /mm	Crystal mass /g	‘Yield’ coefficient ^a /g (kg deg) ^{−1}
1	L_∞	117.5	12.6	212	1.20
2	L_∞	122.9	10.3	227	1.23
3	L_∞	106.4	16.7	198	1.24
4	L_6	94.2	14.2	179	1.27
5	L_3	103.0	14.4	319	2.07

^a The ‘yield’ (or ‘mass production’) coefficient is an increase in the mass of a crystal grown upon 1 °C temperature reduction at initial crucible charge of 1 kg.

The changes in the ‘yield’ coefficient as function of the heat field symmetry and the observed character and evolution of convective flows on the melt surface were interpreted as follows.¹⁴⁰ As the heat field with L_3 symmetry was created in the growth furnace, the convective regime in the bulk of the melt changed fundamentally. The fluid body divided into three azimuthally distributed convective cells in which the thermal-gravitational flows moved up and down, thus ‘enveloping’ nearly the whole bulk of the liquid phase and forming three intense surface flows merging at the centre. This convective regime provided a permanent renewal of the melt in the region near the crystallisation interface, thus substantially delaying the onset of constitutional supercooling. In this case the ‘yield’ coefficient amounted to 82% of its maximum theoretical value. This, in a way, characterises the extent of involvement of the fluid body in the convection.

BBO crystals thus obtained were found to have a very small central defect region. These crystals can be used for fabrication of relatively large (up to 20 mm and more) nonlinear optical elements and electro-optical cells oriented parallel to the optical axis c .

Feigelson *et al.*¹³⁰ reported the ‘yield’ coefficients of 2.01 and 2.13 g (kg deg)^{−1} obtained in the growth of BBO crystals from a crucible 55 mm in diameter with the corresponding initial charges of 380 and 290 g. An increase in the charge to 470 g caused reduction of the ‘yield’ coefficient to 1.6 g (kg deg)^{−1}. This points to significant difference between the convective regimes in the crucibles 55 and 100 mm in diameter at comparable temperature gradients in the growth furnace.

Recently,¹⁵⁴ pioneering results concerning the growth of BBO crystals in rotating heat fields of different symmetry have been reported.

VIII. Defects and impurities in crystals

Information on intrinsic nonstoichiometry and impurity defects in BBO crystals is scarce.¹⁵⁵ Three types of radiation defects that exhibit UV absorption at 210, 250 and 310 nm were identified in γ -irradiated BBO crystals. The formation of these defects is assumed to be associated with both cleavage of the B–O bonds and atomic displacements from the equilibrium positions.¹⁵⁶

Growth defects were studied by chemical etching, optical microscopy, microprobe technique, X-ray topography and laser scanning tomography.^{46, 86, 121, 130, 157, 158} The main types of defects found in BBO crystals were inclusions (usually, they are interpreted as flux inclusions) and inclusion-induced dislocations. The appearance of gas bubbles is associated with the presence of trace amounts of non-decomposed carbonates in the charge.⁸⁶ High density of dislocations due to solvent trapping was pointed out.¹²¹ It is assumed that removal of inclusions must favour a substantial improvement of the quality and optical characteristics of BBO crystals.

The content of sodium in β -BaB₂O₄ crystals grown under different conditions (from melt-solution and from a stoichiometric melt according to Czochralski) can vary from 120 to 680 ppm (0.012 mass %–0.068 mass %).¹⁵⁹ Transparent inclusion-free crystals contain from 0.012 mass % to 0.023 mass % Na. At a sodium content of greater than 0.035 mass %, the crystals are semi-transparent until becoming opal. Sodium impurity was found to be responsible for thermoluminescence of BBO crystals.^{159, 160}

Among other impurities, an increased concentration of strontium was pointed out.¹⁶¹ Probably, this impurity incorporates into the BBO crystals from barium-containing starting reagents. Lead impurity causes stabilisation of the α -modification of BaB₂O₄.⁴⁹

A feature of BBO crystals is accumulation of sodium and potassium impurities.¹⁰¹ The critical concentration of sodium is 0.021 mass %. As the content of sodium exceeded this value, inclusions of the second phase and the scattering centers appear.¹⁰¹ The effective distribution coefficient of sodium between the crystal and melt is $(2.5–4.4) \times 10^{-3}$.

From crystal chemical considerations it follows that alkali metal impurities can incorporate into the structure of β -BaB₂O₄. As can be seen in Fig. 7, BaB₂O₄ and a sodium compound NaBO₂ are structurally similar. They contain identical structural fragments (boron – oxygen [B₃O₆]³⁻ anions) stacked perpendicular to the *c* axis of the trigonal lattice and exhibit a similar packing motif. The difference is in the arrangement of cations; the number of sodium ions that provide electrostatic compensation of charge is twice as large as the number of barium ions. The trigonal unit cells also have close parameters (see Table 1). This suggests the possibility of heterovalent isomorphism simply described as Ba $\rightleftharpoons$ 2Na and incorporation of extra sodium ions into the β -BaB₂O₄ lattice. The authors of this review also assume that the major type of intrinsic point defects in β -BaB₂O₄ crystals are Frenkel pairs characterised by displacement of Ba ions from the equilibrium positions to the interstitial ones. Close values of the unit cell parameters allow epitaxial growth of NaBO₂ on the β -BaB₂O₄ crystals.

Even better is agreement between the lattice parameters of β -BaB₂O₄ and potassium metaborate, KBO₂, which is isostructural to the sodium-containing analogue. Potassium ions are readily incorporated into the BBO lattice (potassium fluoride melt was used as flux).⁶⁶

The distribution coefficient of sodium in BBO crystals is small, therefore this impurity can be removed by zone melting with ease.⁸⁸ Low efficiency of this technique in the removal of strontium impurity from BBO crystals¹⁰⁷ indicates that the corresponding distribution coefficient approaches a unity.

Inclusions in BBO crystals were found to be sodium enriched.^{46, 130} Identification of the phase that is formed at the crystallisation interface, thus blocking the process of crystal growth, by X-ray powder diffraction failed.⁶⁶ However, a recent X-ray powder diffraction study of the particles with inclusions, picked up with a microscope, showed¹⁰² that this phase has a composition NaBaBO₃.

IX. Constitutional supercooling

Morphological instability of the crystallisation front (Fig. 18) occurs in a certain stage of melt-solution growth of BBO crystals (usually, as the crystal becomes ~ 15 mm thick). It involves the development of a characteristic cellular substructure with quasi-hexagonal cells, which is accompanied by trapping of inclusions and the formation of a protrusion.^{46, 66, 130} The appearance of cellular substructure is the major reason for forced termination of the process of crystal growth. This phenomenon is associated with specific features of heat transfer during the growth process.^{130, 143} However, usually the morphological instability is due to the

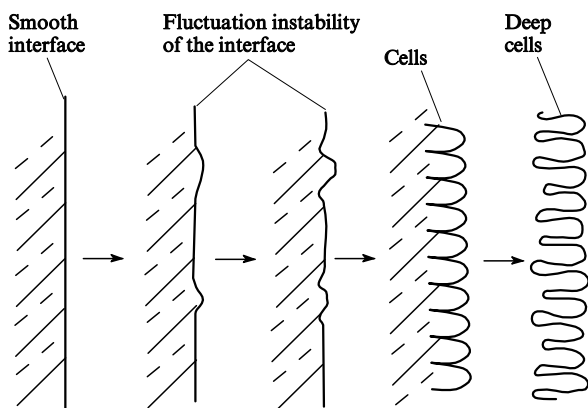


Figure 18. Qualitative picture of the development of morphological instability of the crystallisation front and the formation of cellular substructure.

constitutional supercooling which has been studied in detail for binary systems.^{162–166}

Consider the growth of BBO crystals from a Na₂O melt-solution. In this case, sodium piles up near the solidification front, thus causing the loss of its stability. Figure 19 presents a scheme illustrating the distribution of the melt components in the region adjacent to the solidification front for a steady-state growth of BBO crystals from Na₂O melt-solution at the rate *R*. Since the amount of sodium incorporated into the crystal is very small, it is displaced by the growing crystal and is accumulated near the liquid – solid interface. The sodium concentration jump appeared at the crystallisation front induces a diffusion flow of sodium ions in the melt, which is directed away from the liquid – solid interface. The content of barium and boron in the melt is somewhat lower than in the crystal; therefore, these components are trapped by the crystal. This leads to the appearance of a region depleted of Ba and

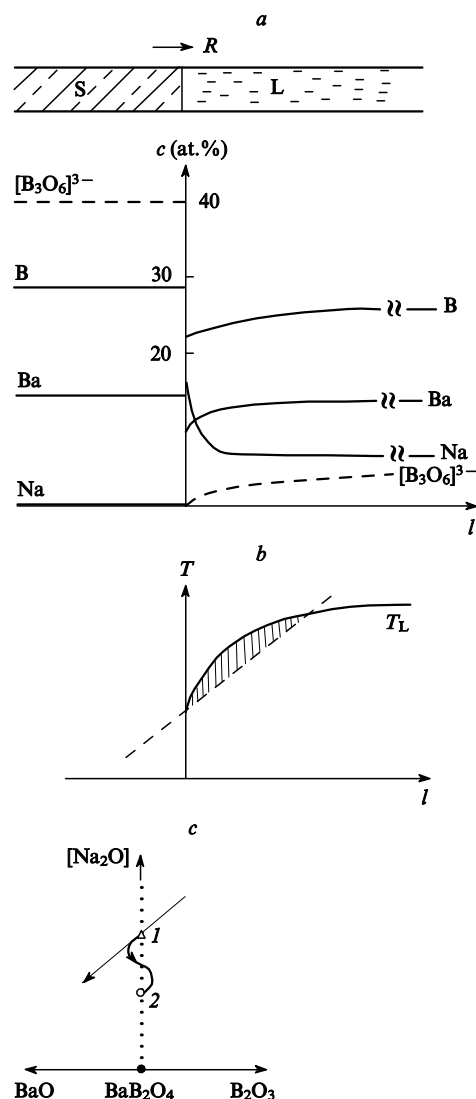


Figure 19. Schemes illustrating the distributions of the B, Ba, Na and [B₃O₆]³⁻ ring ion concentrations in the crystal – melt system for a steady-state directional crystallisation occurring at a rate *R* (a), of the equilibrium crystallisation temperature of β -BaB₂O₄ (solid line) and of actual change in the temperature (dashed line) (b), and the hypothetical change in the melt composition with the distance from the solidification front (diffusion path) during the growth of BBO crystals (c).¹⁰⁴

Shown are the constitutional supercooling region (b, hatched), the melt composition at the solidification front (c, 1) and the starting composition of the melt (c, 2).

B near the crystallisation front and induces diffusion flows directed from the bulk of the melt towards the interface. Accumulation of the excess sodium should reduce the equilibrium liquidus temperature. The integrated distribution curve of the equilibrium crystallisation temperature is presented in Fig. 19b while the possible shift of the figurative point corresponding to the melt composition for actual crystallisation is shown in Fig. 19c. Since the BaB₂O₄–Na₂O section is unstable, the line corresponding to the change in the melt concentration with distance from the solidification front (diffusion path) should deviate from this section, thus forming a zig-zag curve on the concentration triangle.¹⁶⁷

More detailed analysis of the situation requires a consideration of different forms of boron present in the melt. As mentioned above, melting of BaB₂O₄ causes destruction of the [B₃O₆]^{3–} ring anions (*i.e.*, this crystal is a typical example of compound which nearly completely dissociates on melting).^{99, 100, 112} According to the molecular dynamics calculations,¹⁶⁸ the addition of Na₂O to the melt leads to shortening of the [BO₂]_{*n*}[–] polymer chains formed by [BO₃]^{3–} triangles and to an increase in the proportion of isolated [BO₃]^{3–} triangles, dimeric [B₂O₅]^{4–} units, three-membered [B₃O₇]^{5–} fragments and [B₃O₆]^{3–} ring anions. Nevertheless, one can state that it is the low concentration of the [B₃O₆]^{3–} ring anions near the crystallisation front that is the limiting factor for the growth of BBO crystals.

It should be noted that steady-state melt-solution growth of BBO crystals can be performed using the Czochralski method with melt feed¹³² or by floating zone technique.¹³¹ Experiments carried out according to Kyropoulos (with slow cooling of the system) represent a kind of non-steady-state processes characterised by accumulation of sodium near the solidification front (Fig. 20).

The simplest constitutional supercooling criterion for solidification front stability is provided by the Tiller–Chalmers criterion

$$\frac{GD}{R} < \frac{mC_0(1-k)}{k},$$

where G is the temperature gradient in the melt at the solidification front, D is the diffusion coefficient of the solute, R is the crystal growth rate, m is the slope of the liquidus curve, C_0 is the concentration of the solute in the solution and k is the partition coefficient. This criterion was proposed for steady-state processes in dilute binary systems^{162, 163} and cannot be applied to the crystallisation of BBO. This criterion is equivalent to the boundary condition at the crystallisation interface while the integrated curve describing the increase in the equilibrium crystallisation temperature (liquidus temperature) with the distance from the solidification front of BBO follows the same pattern as in the case of binary systems. Therefore, the criterion for morphological stability of the solidification front of BBO (heat transfer is assumed negligible) can be written as follows

$$\frac{G}{R} D^* < m\Delta C,$$

where D^* is the function of the diffusion coefficients of the components of the system in the melt (it varies from one composition to another), m is the directional derivative of the liquidus temperature taken along the tangent to the diffusion path at the point corresponding to the melt composition at the solidification front (this point is labelled l in Fig. 19c) and ΔC is the change in the composition at the interface. An analogous expression proposed¹⁶⁶ for binary systems can also be used for non-steady-state processes.

In any case the most important factors improving the stability of the solidification front against constitutional supercooling are an increase in the temperature gradient at the crystallisation front and a decrease in the crystal growth rate.

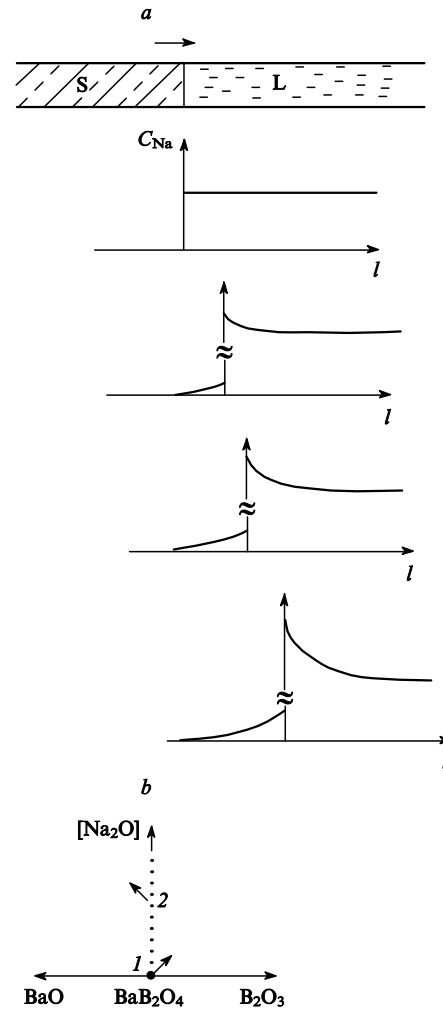


Figure 20. Schemes illustrating successive accumulation of sodium ahead of the crystallisation front for a non-steady-state growth of BBO crystal (a) and the change in the sodium content in the crystal (l) and in the melt (2) (b).

There are two reasons for deterioration of the optical quality of flux grown BBO crystals. These are (i) the attainment of critical supersaturation with respect to sodium near the crystallisation front and (as a consequence) the appearance of a cellular structure with trapped inclusions and (ii) accumulation of sodium impurity above the equilibrium solubility (limiting concentration) in BBO followed by crystallisation of the second phase on cooling of the crystal. In both cases mixing of the melt for not only control of the heat convection, but also homogenisation of the melt composition is of paramount importance.

X. Properties and fields of application of β -BaB₂O₄ crystals

Crystals of the non-centrosymmetric low-temperature modification, β -BaB₂O₄, are widely used in nonlinear optics as nonlinear-optical crystals possessing large birefringence for the generation of optical harmonics and sum frequencies of laser radiation in the visible and UV regions. Widespread use of this material in quantum electronics is to a great extent due to relatively high optical damage threshold. Numerous applied^{30, 169–195} and materials science studies^{156, 157, 196–201} of BBO were reported in the last decade.

Development of compact solid-state sources of tunable UV, visible and IR radiation is topical. Currently, BBO-crystal para-

metric light oscillators (OPOs) pumped by the second and third harmonics of Nd:YAG lasers are most widely used. These devices generate tunable radiation in the 2628 and 3036 nm regions, respectively.¹⁹² The tuning range of BBO-crystal OPOs is limited to strong absorption of the idler wave radiation in the spectral region from 2200 to 3000 nm.⁴⁴ The pioneering study of the characteristics of a BBO-crystal OPO pumped by the fourth harmonic of a Nd:YAG laser ($\lambda = 266$ nm) was reported by Bosenberg *et al.*¹⁹³ A BBO-crystal OPO 25 mm long generated radiation in the spectral region between 330 and 1370 nm at a pulsed pump intensity exceeding 23 MW cm^{-2} . Another BBO-crystal OPO pumped by the fourth harmonic of a single-mode Nd:YAG laser generated radiation in the region 302–2248 nm at a pulsed pump energy of 20 mJ with a conversion efficiency of 6.3% at a wavelength of 340.2 nm at quadruple the oscillation threshold.¹⁹²

The characteristics of a BBO-crystal Type-I OPO pumped by the fourth harmonic of a multimode Nd:YAG laser have been studied.¹⁹⁴ The output was tunable over the region 300–2340 nm. The efficiency ranged up to 15% near the peak of the tunability curve at double the oscillation threshold. The OPO configuration was based on a BBO crystal (aperture 6×8 mm, length 14 mm) cut for Type-I phase matching at an angle (θ) of 38.3° with respect to the optical axis of the crystal.

The above-mentioned applications of BBO crystals were based on the second-order optical nonlinearity. However, $\beta\text{-BaB}_2\text{O}_4$ also possesses third-order optical nonlinearity.³⁰ In particular, it was found that picosecond laser pump of BBO at 1 μm excites efficient Stokes and anti-Stokes Raman parametric generation (RPG) and allows simultaneous SHG and multicomponent RPG in the visible and near IR regions. In particular, a BBO-crystal active element 15 mm long [excitation configuration $a(cc)a$] pumped at 1 μm re-emitted to all RPG components more than 35% of the energy (~ 1 mJ), the first Stokes line ($\lambda = 1.1414 \mu\text{m}$) accounting for $\sim 20\%$. The efficiency of picosecond RPG from $\beta\text{-BaB}_2\text{O}_4$ was also illustrated by an extended (up to the thirteenth component with $\lambda = 0.5661 \mu\text{m}$) wing of the multicomponent anti-Stokes spectral region. Based on high SHG efficiency of BBO crystals, an SRS experiment with the optically active element oriented parallel to the Type-I phase matching direction ($ee-o$) was carried out.³⁰ The experiments showed the possibility of simultaneous conversion of the 1 μm pump of BBO into both the Stokes and anti-Stokes components and the second harmonic. It was found that excitation of the multicomponent RPG induced by the second harmonic generated by the BBO crystal occurs at a lower pump power, which is due to high SHG efficiency from BBO crystals and to dispersion of the Raman amplification coefficient of BBO. This discovery — simultaneous manifestation of the second- and third-order optical nonlinearities in BBO crystals — can be used for creation of novel types of $\beta\text{-BaB}_2\text{O}_4$ -based laser frequency converters.

Electro-optical application of BBO crystals as Pockels cells in the UV spectral region should be emphasised.¹⁹⁵

Recently, BBO crystals have been on the commercial market. A large body of valuable information on the physicochemical properties of BBO crystals can be found in the Internet at URLs <http://www.crystaux.com/betabbo.htm> (website of DLK Crystal) and <http://www.clevelandcrystals.com/BBOLOBO.shtml> (website of Cleveland Crystals, Inc.). The principal properties of BBO crystals are listed in Table 4.

XI. Conclusion

Based on the aforesaid, the following conclusions can be drawn.

Polymorphism of BaB_2O_4 is a unique phenomenon. On the one hand, the high- and low-temperature modifications of this compound have substantially different structures. On the other hand, their thermodynamic characteristics are nearly identical. Studies of the mutual stability of these modifications and of the influence of different factors on their crystallisation and kinetics

Table 4. Properties of BBO single crystals.

Parameter	Value
Optical transmission /nm (50% transmission at a thickness of 3 mm)	0.196–2.2
Indices of refraction ^a at λ	
0.2660 nm	1.7571; 1.6146
0.4358 nm	1.6868; 1.55638
0.5461 nm	1.6738; 1.5547
0.6328 nm	1.6673; 1.5500
1.0642 nm	1.6551; 1.5425
Absorption coefficients α (cm^{-1}) at λ	
0.266 nm	0.04–0.15
1.0 nm	0.001–0.002
2.09 nm	0.0085; ^b 0.07 ^c
Laser damage threshold / GW cm^{-2} at $\lambda = 1.0642$ nm	
10 ns pulse	0.0046
0.1 ns pulse (2.3 J)	15
Nonlinear optical susceptibility / pm V^{-1}	2.3; ^d < 0.1 ^e
Phasematching range (λ /nm)	
Type I SHG	0.4096–3 +
Type II SHG	0.53–3 +
Phasematching angle ^f (deg) at maximum nonlinear optical susceptibility and 25°C	
0.532 nm, type I SHG	47.6; 90
0.532 nm, type II SHG	81.0; 0
1.064 nm, type I SHG	22.8; 90
1.064 nm, type II SHG	32.8; 0
Linear electro-optical coefficients ^g / pm V^{-1}	2.7 ± 0.4 ; ~ 0 ; 0.055
Hardness, Mohs	4.5
Elastic stiffnesses /GPa	
c_{11}	123.8
c_{12}	60.3
c_{13}	49.4
c_{14}	12.3
c_{33}	53.3
c_{44}	7.8
c_{66}	31.8
Young's modulus /GPa	39
Poisson's ratio	0.58
Thermal expansion coefficient, ⁱ $10^{-6} (\text{deg})^{-1}$	4; 36
Specific heat / J (g deg)^{-1}	0.49 ± 0.02
Thermal conductivity / W (m deg)^{-1}	
parallel to c axis	1.6
perpendicular to c axis	1.2
Resistivity / $\Omega \text{ cm}$	$> 10^{11}$
Relative static dielectric constants ^k	6.7; 8.1

^a The n_o and n_e values are respectively given. ^b e -Ray. ^c o -Ray. ^d The d_{22} value. ^e The d_{15} value. ^f Given are the θ and Φ values, respectively. ^g Listed are the r_{22} , r_{31} and r_6 values, respectively. ⁱ Given are the α_a and α_c values, respectively. ^k Given are the ϵ_{11}/ϵ_0 and ϵ_{33}/ϵ_0 values, respectively.

of transformations are of great importance. In this connection, investigations of the heat capacities of both modifications of BaB_2O_4 over a wide temperature range are also required.

Hübner's data^{62, 65} on the stability of compound $\text{Ba}_2\text{B}_2\text{O}_5$ and on the formation of BaB_2O_4 -based solid solutions strongly contradict the phase diagram of the $\text{BaO}-\text{B}_2\text{O}_3$ system proposed by Levin *et al.*^{12, 13} An indirect proof of variable composition of BBO is provided by small but, at the same time, noticeable variations of the lattice parameters of single crystals, determined by different authors. Both nonstoichiometry of BaB_2O_4 and the $\text{BaO}-\text{B}_2\text{O}_3-\text{Na}_2\text{O}$ system in the BaO -enriched region (in particular, in the $\text{Ba}_3\text{B}_2\text{O}_6-\text{NaBaBO}_3-\text{BaB}_2\text{O}_4$ concentration triangle) call for further investigation.

Studies of the phase equilibria in the BaO–B₂O₃–Na₂O ternary system showed that the BaB₂O₄–Na₂O section, which is most often used for growth of β -BaB₂O₄ single crystals from Na₂O, is unstable and that compound Na₂BaB₂O₅ does not exist. Compound NaBaBO₃ was identified and structurally characterised. The BaB₂O₄–Na₂O section passes nearly exactly through the eutectic in the BaB₂O₄–NaBaBO₃–NaBO₂ ternary system.

The BaB₂O₄–Na₂O melt used for growth of BaB₂O₄ crystals is multicomponent and unstable. Further search for optimum growth conditions and better solvents seems to be appropriate.

Improvement of methods of control of the heat and mass transfer during crystal growth including those involving variation of the heat field patterns is also topical.

This review has been performed as part of the Research Project 'Investigations of the Phase Diagrams, Search for Solvents and Growth of Nonlinear Optical Crystals in Heat Fields of Different Symmetry' carried out in the framework of the Integration Programme 'Novel Principles and Methods of Design and Targeted Synthesis of Chemical Compounds with Preset Properties' in accord with the Decision of the Presidium of the Siberian Branch of the Russian Academy of Sciences signed on 09.04.2002.

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Isothiazoles (1,2-thiazoles): synthesis, properties and applications

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Abstract. The most recent achievements in the chemistry of isothiazoles are generalised and systematised. The main applications of isothiazole derivatives are surveyed. The bibliography includes 293 references.

I. Introduction

Isothiazoles constitute a relatively novel class of heterocyclic compounds. Their ancestor, 1,2-thiazole, was first obtained in 1956.¹

Other 1,2-azoles had been rather well studied by that time, both theoretically and with respect to their practical applications. Further rapid progress in the chemistry of isothiazole and intense studies into the synthesis and chemical conversions of its derivatives carried out in the 1960–1990's were caused primarily by the extraordinarily broad range of useful properties manifested by various representatives of this class of compounds. Isothiazole-containing penicillins and cephalosporins competed successfully with ampicillin in their activities against gram-positive and gram-negative bacteria.^{2,3} In the last decade of the 20th century, some isothiazole derivatives were found to be efficient in the treatment of Alzheimer's disease,⁴ as antiinflammatory, antithrombotic and anticonvulsive drugs^{5,6} and serine protease inhibitors;^{7,8} physiologically active compounds interacting with glutamate receptors were synthesised.⁹ Auxin transport inhibitors based on isothiazoles^{10–14} are added to herbicides to enhance their activity. Isothiazole derivatives manifest synergistic effects when added to other biocidal preparations.^{15–19} Compositions containing isothiazole derivatives are used as protectors for polymers, dyes, detergents²⁰ and leather goods,²¹ for decontamination of pigments, latexes, foodstuffs²² and waste,²³ as antifouling agents,^{24,25} etc. Recently, isothiazoles have been patented for use in colour photography for stabilisation of photomaterials^{26,27} and as an inkbase for printers.^{28,29} Industrial production of some isothiazolones, which represent broad-spectrum biocides and are safe for human beings, animals and environment, has begun.³⁰

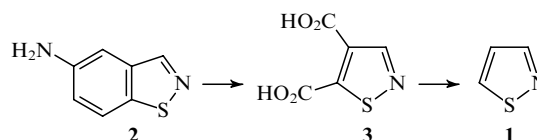
R V Kaberdin, V I Potkin Institute of Physical Organic Chemistry, National Academy of Sciences of Belarus, ul. Surganova 13, 220072 Minsk, Belarus. Fax (37-517) 284 16 79. Tel. (37-517) 284 16 00. E-mail: ifoch@ifoch.bas-net.by (R V Kaberdin) Tel. (37-517) 284 09 72. E-mail: potkin@ifoch.bas-net.by (V I Potkin)

The first data on the chemistry of isothiazoles were reviewed by Wooldridge *et al.*^{31,32} Further progress in the synthesis and conversions of isothiazoles is documented in the reviews^{33–39} some of which are inaccessible for Russian readers as well as in the monographs^{40–45} where isothiazoles are considered only in conjunction with other heterocyclic compounds. The fundamental monograph by Houben-Weyl,⁴⁶ which contains more than 500 references including some published in 1992, represents the most systematic and full generalisation of the experimental data on the chemistry of 1,2-thiazoles. The first review devoted to the physical and chemical properties of 1,2-azoles was published in Russian in 1979.⁴⁷ In addition, isothiazoles and their benzoannelated analogues are discussed in 'Comprehensive Organic Chemistry'.⁴⁸

The necessity for systematisation and generalisation of the newest data on isothiazoles stems from the appearance, in the past decade, of a great number of publications devoted to the synthesis, conversions and applications of this class of compounds. The material described here covers original papers and patent data published over the period 1993–2001 inclusive. In some cases, earlier sources concerned with the methods for isothiazole synthesis are cited for the sake of completeness.

II. Synthesis of isothiazoles

Isothiazole (**1**) was first prepared by the oxidation of 5-amino-1,2-benzisothiazole (**2**) with an alkaline solution of potassium permanganate with subsequent decarboxylation of isothiazole-4,5-dicarboxylic acid (**3**).^{1,49}



This synthetic procedure has a purely historical significance. Later, isothiazoles were synthesised from simpler and more accessible compounds.

1. Synthesis of isothiazoles based on cyclisation reactions

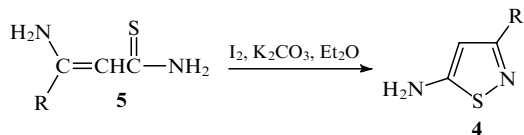
The main methods for the construction of the isothiazole ring are based on cyclisation of compounds containing N–C–C–C–S fragments and heterocyclisation of compounds containing nitrogen, sulfur and carbon atoms.

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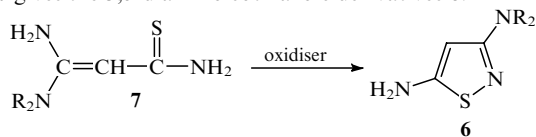
a. Synthesis of isothiazoles from compounds containing the N—C—C—C—S group

The construction of the isothiazole ring from compounds containing a preformed N—C—C—C—S fragment is the most attractive approach. Thus various 5-aminoisothiazole derivatives **4** can be prepared by the oxidation of 2-aminoalk-1-enethiocarboxamides **5**.⁵⁰



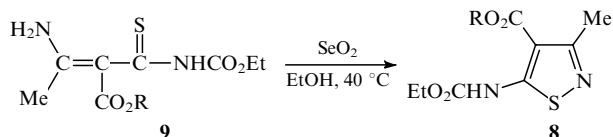
R = Et, Prⁱ, Buⁿ, Buⁱ, Bu^t, cyclo-C₆H₁₁.

Oxidation of 3-amino-3-(dialkylamino)thioacrylic acid amides **7** gives the 3,5-diaminoisothiazole derivatives **6**.⁵¹



R = Alk.

A procedure for the synthesis of alkyl 3-methyl-5-ethoxycarbonylaminoisothiazole-4-carboxylates (**8**) by the oxidation of substituted thioamides **9** with selenium dioxide has been developed recently.⁵²

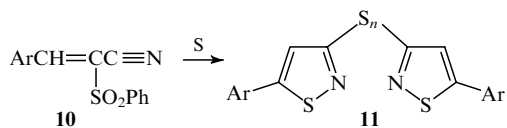


R = Me, Et.

b. Synthesis of isothiazoles from sulfur and compounds containing the C—C—C—N fragment

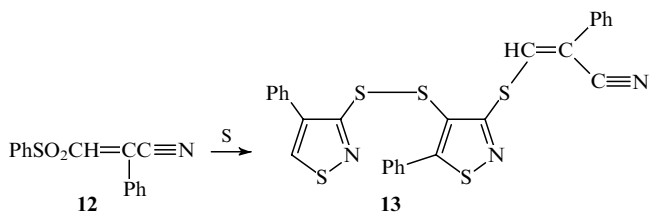
The construction of the isothiazole ring from sulfur and compounds containing the C—C—C—N fragment is relatively little studied. This approach makes use mainly of nitriles.⁴⁶

Thus the electrolysis of 3-aryl-2-phenylsulfonylacrylonitriles (**10**) in acetonitrile or DMF using a chemically active sulfur-graphite electrode affords bis(5-arylisothiazol-3-yl) di- or trisulfides (**11**).⁵³



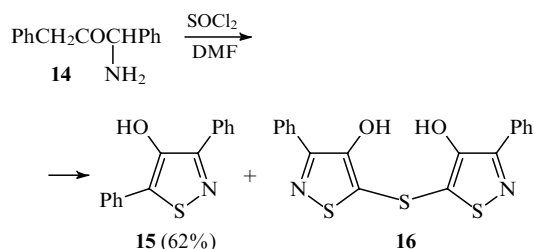
Ar = Ph, 4-MeC₆H₄, 4-PhC₆H₄; n = 2, 3.

In the case of 2-phenyl-3-phenylsulfonylacrylonitrile (**12**), di(isothiazolyl) disulfide **13** containing the (Z)-2-cyano-2-phenylvinylthio group in position 3 of one of the isothiazole rings was obtained.⁵³

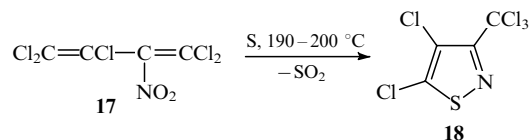


It is believed that electrochemical synthesis of sulfur-containing compounds consists in the elimination of the phenylsulfonyl group with concomitant addition of a polysulfide anion produced upon electroreduction of elemental sulfur.

According to the patent data,⁵⁴ substituted α -amino ketones react with thionyl chloride to give the corresponding 4-hydroxyisothiazoles. Thus the reaction of amino ketone **14** with SOCl₂ in DMF yields isothiazole **15**. When thionyl chloride was used in excess, the reaction products contained both isothiazole **15** and di(isothiazolyl) sulfide **16**.



The authors of the present review together with Yu A Oldekop have demonstrated^{55–57} that heating of 2-nitropentachlorobuta-1,3-diene (**17**) with sulfur resulted in its heterocyclisation and the formation of 4,5-dichloro-3-trichloromethylisothiazole (**18**).

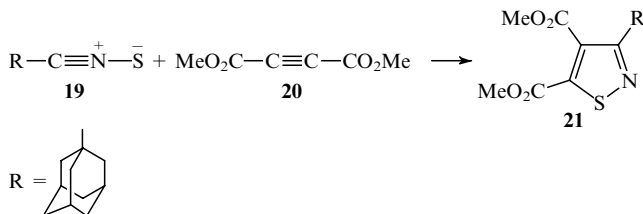


This reaction offers a new approach to the construction of the isothiazole ring. It is known that the reaction of halobutenes and -butadienes with sulfur is used for the synthesis of the corresponding halogenothiophenes.⁵⁸ In the case of nitrodiene **17**, the reaction follows a different route: the heterocyclisation involves the nitro group and is accompanied by the evolution of sulfur dioxide. The yield of isothiazole **18** reaches 52%. Tetrachlorothiophene (yield 4%) is the side product in this reaction. Apparently, the reaction has a radical character, since sulfur molecules exist in the form of reactive biradicals S_n at high temperature.⁵⁹

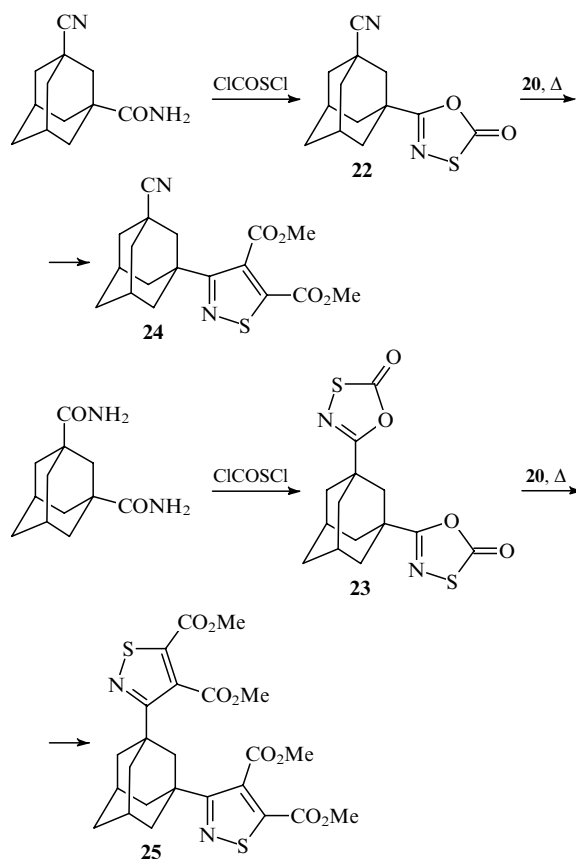
c. Synthesis of isothiazoles using cycloaddition and condensation reactions

The methods for the synthesis of isothiazoles using cycloaddition and condensation reactions of compounds containing a set of essential fragments are the most well-studied and attract, as before, the attention of investigators.

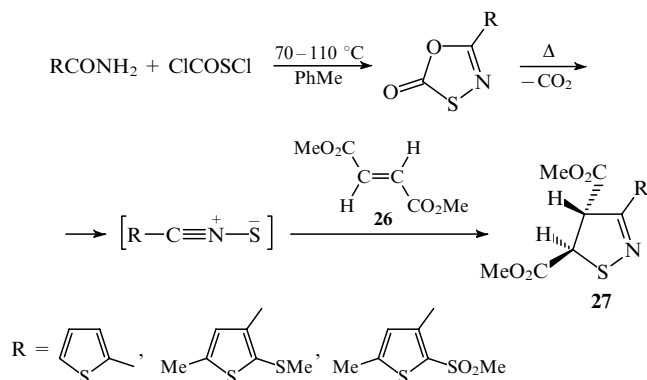
Thus the 1,3-dipolar cycloaddition of nitrile sulfide **19** to dimethyl acetylenedicarboxylate (**20**) yields the isothiazole derivative **21** the structure of which has been confirmed by X-ray diffraction analysis.⁶⁰



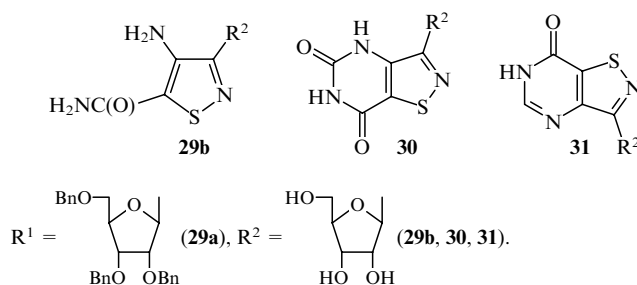
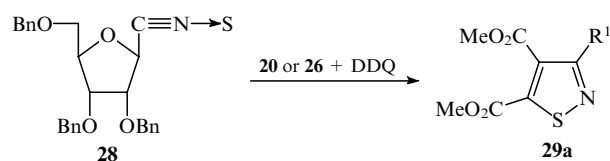
The reactions of 1-cyano-3-(2-oxo-1,3,4-oxathiazol-5-yl)adamantane (**22**) and 1,4-bis(2-oxo-1,3,4-oxathiazol-5-yl)adamantane (**23**) prepared from the corresponding adamantanecarboxamides and chlorosulfonylcarbonyl chloride with the alkyne **20** result in the decarboxylation of the oxathiazolone fragment. The reactions of the nitrile sulfides formed with the alkyne **20** proceed as 1,3-dipolar cycloadditions and yield 1-cyano-3-(4,5-dimethoxycarbonylisothiazol-3-yl)adamantane (**24**) and 1,3-bis(4,5-dimethoxycarbonylisothiazol-3-yl)adamantane (**25**), respectively.⁶¹



The reaction of nitrile sulfides of the thiophene series with dimethyl fumarate (**26**) gives substituted 4,5-dihydroisothiazoles **27**.⁶²

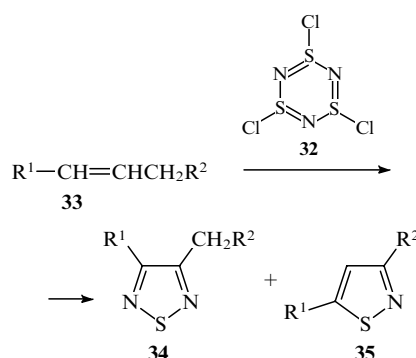


The cycloaddition of 3,4,6-tri-*O*-benzyl-2,5-anhydro-D-allo-nonitrile *N*-sulfide (**28**) to dimethyl acetylenedicarboxylate (**20**) or dimethyl fumarate (**26**) followed by the oxidation of the reaction products with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) results in *O*-benzyl-3-(β -D-ribofuranosyl)isothiazolidinecarboxylate **29a**, which was used for the preparation of the C-nucleoside **29b** and isothiazolo[4,5-*d*]pyrimidine analogues of the natural C-nucleosides pyrazofurin (**30**) and formycin (**31**).⁶³

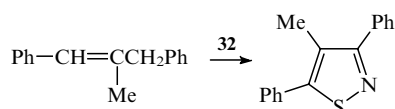


The use of 1,3,5-trichloro-1,3,5,2,4,6-trithiatiazine (**32**) seems to be very promising for the synthesis of isothiazoles.

It was found that ordinary allylic compounds of the type **33** react with the reagent **32** as two-carbon units to give 1,2,5-thiadiazoles **34** and as three-carbon units to give isothiazoles **35**. The ratio of compounds **34** and **35** depends on the reaction conditions and the nature of the substituents.⁶⁴

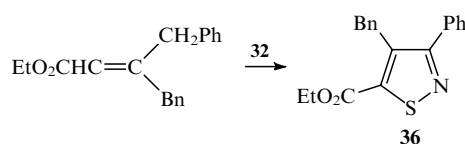


Thus 1,3-diphenylpropene (**33**, $\text{R}^1 = \text{R}^2 = \text{Ph}$) reacts with two equivalents of compound **32** in boiling CCl_4 to give 3,5-diphenylisothiazole **35** in 53% yield. The introduction of a substituent at the central carbon atom of the allylic system suppresses the formation of thiadiazoles. 4-Methyl-3,5-diphenylisothiazole was obtained from 2-methyl-1,3-diphenylpropene without any admixtures of the corresponding thiadiazole.



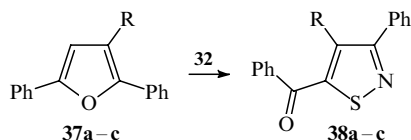
The presence of terminal electron-withdrawing groups in the allylic derivatives **33** increases their reactivities with respect to the reagent **32**.⁶⁴

In the case of non-symmetrical allylic compounds, the reaction proceeds regiospecifically and affords an isomer with the electron-withdrawing group adjacent to the sulfur atom of the ring. Thus the reaction of the trimer **32** with ethyl 3,3-dibenzylacrylate affords isothiazole **36** in 66% yield.⁶⁴



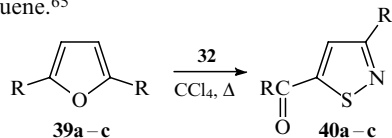
Trithiatiazine trichloride **32** can be used for the preparation of isothiazole derivatives from other heterocyclic compounds.

It was shown⁶⁵⁻⁶⁷ that treatment of di- and trisubstituted furans **37a-c** with trithiatiazine trichloride **32** in boiling CCl_4 results in their one-step conversion into 5-benzoylisothiazoles **38a-c** in high yields.



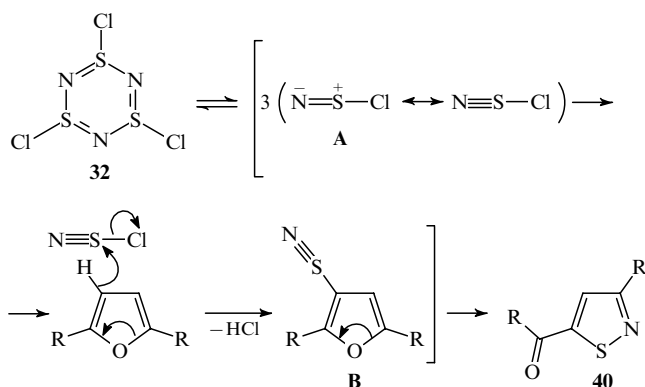
R = H (**a**), Ph (**b**), Br (**c**).

2,5-Disubstituted furans **39a–c** give similar products **40a–c** (yields 50%–60%) with compound **32** upon boiling in CCl₄ or toluene.⁶⁵



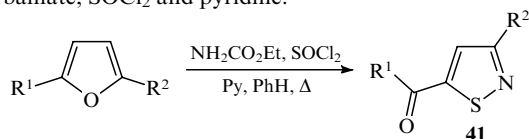
R = 4-MeC₆H₄ (**a**), 4-MeOC₆H₄ (**b**), Bu^t (**c**).

It is assumed that heating of 1,3,5-trichloro-1,3,5,2,4,6-trithiazine (**32**) results in its fragmentation and the formation of the reactive monomer **A** which attacks the furan molecule to give the intermediate **B**. Recyclisation of the latter affords isothiazoles.⁶⁵



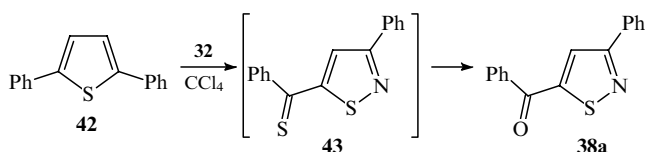
It has been shown⁶⁸ that fully substituted furans do not react with the reagent **32**, since the elimination of HCl requires the presence of a hydrogen atom in the β-position of the starting furan.

Yet another route to the synthesis of 5-acylthiazoles **41** is based on the reaction of 2,5-disubstituted furans with ethyl carbamate, SOCl₂ and pyridine.⁶⁸

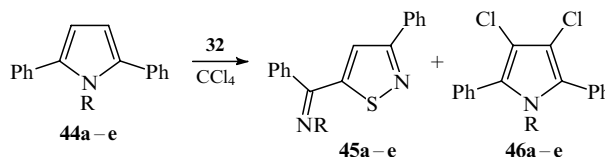


R¹ = R² = Ph, 4-MeC₆H₄, Bu^t; R¹ = 4-MeOC₆H₄, R² = 4-NO₂C₆H₄.

In contrast with 2,5-diphenylfuran (**37a**), the reaction of 2,5-diphenylthiophene (**42**) with the reagent **32** gives 5-benzoyl-3-phenylisothiazole (**38a**) in low yield. Presumably, the latter is formed upon oxidation of the intermediate 5-thiobenzoyl derivative **43**.⁶⁹



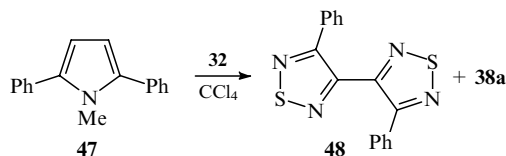
Reactions of *N*-substituted 2,5-diphenylpyrroles **44a–e** with compound **32** afford mixtures of thiazolyl-substituted imines **45a–e** and 3,4-dichloropyrrole derivatives **46a–e**. The ratio of the reaction products depends on the nature of the substituent R.⁶⁹



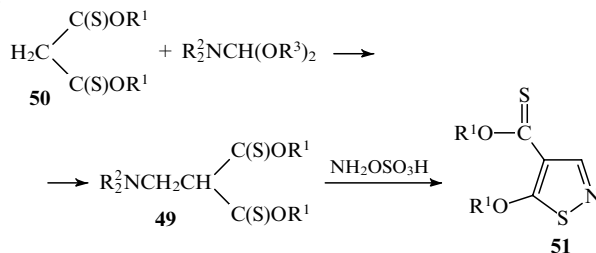
R = Ph (**a**), 4-MeOC₆H₄ (**b**), 4-O₂NC₆H₄ (**c**), MeOC(O) (**d**), Bu^tOC(O)H (**e**).

Compounds **45b,e** are formed as two geometrical isomers. Imine **45b** is easily hydrolysed to give ketone **38a**. The imine **45d** formed from *N*-methoxycarbonylpyrrole (**44d**) is completely hydrolysed even at room temperature to give ketone **38a**.

It is of note that the reaction of 1-methyl-2,5-diphenylpyrrole (**47**) with the reagent **32** follows a different route and results in the formation of bi(1,2,5-thiadiazol-3-yl) **48**; 5-benzoyl-3-phenylisothiazole (**38a**) is formed in only trace amounts.⁶⁹



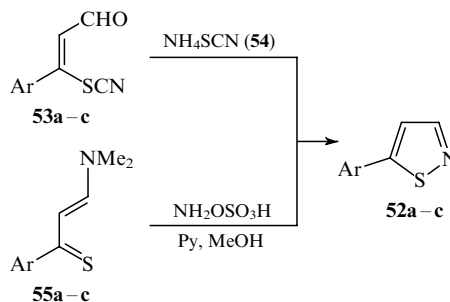
Condensation of 2-dialkylaminomethyldithiomalonates **49**, the reaction products of dithiomalonates **50** with formamide acetals, with hydroxylamine-*O*-sulfonic acid results in isothiazoles **51**.⁷⁰



R¹, R³ = Me, Et; R² = Me, Ph.

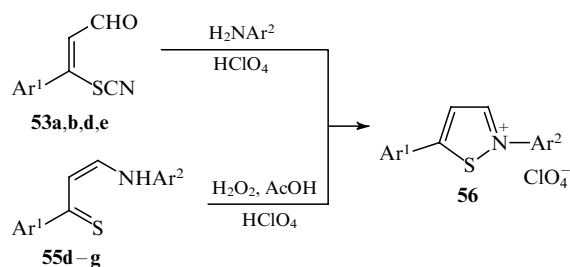
Schulze *et al.*⁷¹ have developed two procedures for the synthesis of isothiazoles **52a–c** containing fluoro-substituted aryl groups. The first of them is based on the reaction of β-thiocyanatocinnamaldehydes **53a,b** with ammonium thiocyanate (**54**). Isothiazoles **52a,b** were obtained in good yields (~60%). In this case, ammonium thiocyanate (**54**) acts as a source of ammonium required for ring closure. It is noteworthy that ammonium thiocyanate (**54**) was employed previously for the preparation of 4- and 5-alkylisothiazoles.⁷²

The second route is based on the use of enamino thiones **55a–c** as starting compounds; their reaction with hydroxylamine-*O*-sulfonic acid gives isothiazoles **52a–c**. In this case, the yields reach 98%.



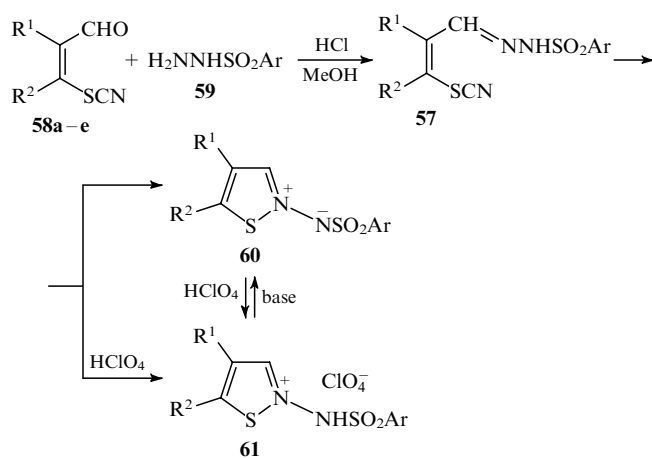
Ar = 4-CF₃C₆H₄ (**a**), 3-CF₃C₆H₄ (**b**), 3-FC₆H₄ (**c**).

Approaches to the synthesis of isothiazolium salts **56** were developed based on cinnamaldehydes **53a,b,d,e** and enamino thiones **55d–g**.⁷¹



$\text{Ar}^1 = 4\text{-CF}_3\text{C}_6\text{H}_4$ (**53a**, **55f**), $3\text{-CF}_3\text{C}_6\text{H}_4$ (**53b**, **55g**), $4\text{-FC}_6\text{H}_4$ (**53d**, **55d**), $4\text{-MeOC}_6\text{H}_4$ (**53e**, **55e**); $\text{Ar}^2 = \text{Ph}$, $4\text{-MeOC}_6\text{H}_4$.

4-Thiocyanato-1-aza-1,3-dienes **57** prepared from β -thiocyanato α,β -unsaturated aldehydes **58** and arenesulfonohydrazides **59** undergo cyclocondensation to yield *N*-arylsulfonylisothiazol-2-ylimines **60** and the corresponding *N*-arylsulfonyl-2-aminoisothiazolium salts **61**.⁷³



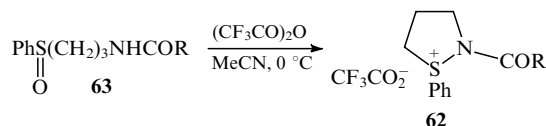
$\text{R}^1 = \text{R}^2 = \text{Me}$ (**a**); $\text{R}^1 = \text{Ph}$, $\text{R}^2 = \text{Me}$ (**b**);

$\text{R}^1\text{--R}^2 = (\text{CH}_2)_n$, $n = 3$ (**c**), 4 (**d**), 5 (**e**);

$\text{Ar} = \text{Ph}$, $4\text{-MeC}_6\text{H}_4$, $4\text{-BrC}_6\text{H}_4$, $2,4,6\text{-Me}_3\text{C}_6\text{H}_2$, $2,4,6\text{-Pr}_3\text{C}_6\text{H}_2$.

Thus, depending on the nature of the substituents R^1 , R^2 and Ar , the reactions of unsaturated thiocyanato aldehydes with arenesulfono hydrazides afford different products. Isothiazoles are formed directly from compounds **58a,b**, whereas alicyclic thiocyanato aldehydes **58c–e** yield stable hydrazones **57**. Treatment of the latter with perchloric acid yields isothiazolium salts **61c–e**.

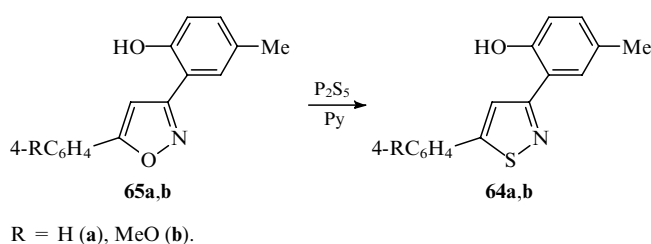
A convenient procedure for the synthesis of *N*-acylisothiazolidinium trifluoroacetates **62**, which includes treatment of *N*-acylamino sulfoxides **63** with trifluoroacetic anhydride, has been developed.⁷⁴



$\text{R} = \text{Bu}^t$, Ph .

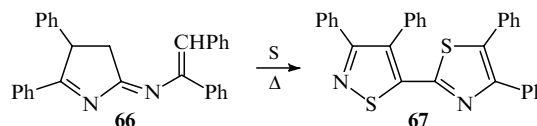
2. Synthesis of isothiazoles from other heterocyclic compounds

Methods of synthesis of substituted isothiazoles from other heterocyclic compounds find wide application despite the fact that they belong to the most ancient ones. Thus 3,5-disubstituted isothiazoles **64a,b** were prepared from isoxazoles **65a,b** by the reaction with phosphorus pentasulfide in pyridine.⁷⁵

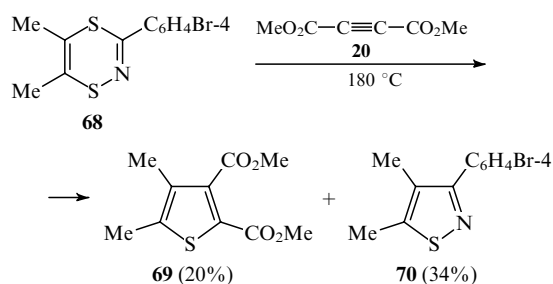


$\text{R} = \text{H}$ (**a**), MeO (**b**).

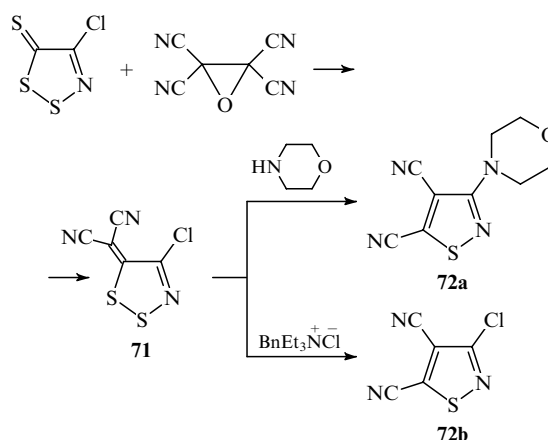
The reaction of 2-imino-3,4-dihydro-2*H*-pyrrole **66** with sulfur on heating is accompanied by dehydrogenation and incorporation of the sulfur atom into the pyrrole ring resulting in the previously unknown thiazolylisothiazoles **67**.⁷⁶



The thermal fragmentation of 1,4,2-dithiazines in the presence of dienophiles aimed at the synthesis of 1,4-dithyines has been studied.⁷⁴ It was found that 1,4,2-dithiazine derivatives **68** react with dimethyl acetylenedicarboxylate (**20**) on heating in *o*-dichlorobenzene to give a mixture of dimethyl 4,5-dimethylthiophene-2,3-dicarboxylate (**69**) and 3-(4-bromophenyl)-4,5-dimethylisothiazole (**70**). The latter is formed upon thermolysis of dithiazine **68** and is accompanied by a loss of the sulfur atom from position 4.⁷⁷

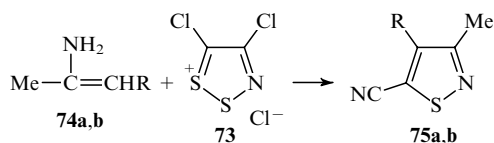


A new method for the synthesis of the isothiazole ring from 4-chloro-5-dicyanomethylidene-5*H*-1,2,3-dithiazole (**71**) prepared by the condensation of 4-chloro-1,2,3-dithiazole-5-thione with tetracyanoethylene oxide has been proposed recently. Treatment of the nitrile **71** with morpholine or benzyltriethylammonium chloride gives 3-morpholino- (**72a**) and 3-chloroisothiazole-4,5-dicarbonitriles (**72b**), respectively.⁷⁸



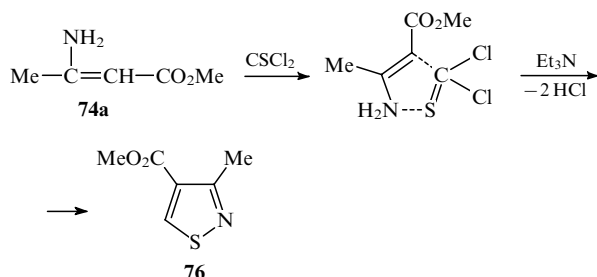
A new simple procedure for the synthesis of isothiazoles from primary enamines and 4,5-dichloro-1,2,3-dithiazolium chloride (**73**) has been developed. Thus the reaction of methyl 3-aminocrotonate (**74a**) and 3-aminocrotononitrile (**74b**) with the salt **73** under mild conditions ($20\text{ }^\circ\text{C}$, dichloroethane) afforded

4-methoxycarbonyl-5-cyano-3-methylisothiazole (**75a**) and 4,5-dicyano-3-methylisothiazole (**75b**).⁷⁹



R = CO₂Me (**a**), CN (**b**).

Presumably, the conversion of enamine **74a** into isothiazole **75a** upon treatment with the salt **73** proceeds similarly to its conversion into isothiazole **76** under the action of thiophosgene used by Woodward *et al.* in the synthesis of colchicine back in 1965.⁸⁰

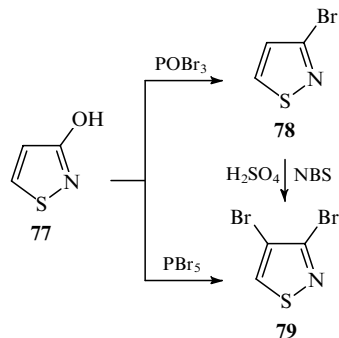


3. Synthesis of isothiazole derivatives by modification of compounds containing the isothiazole ring

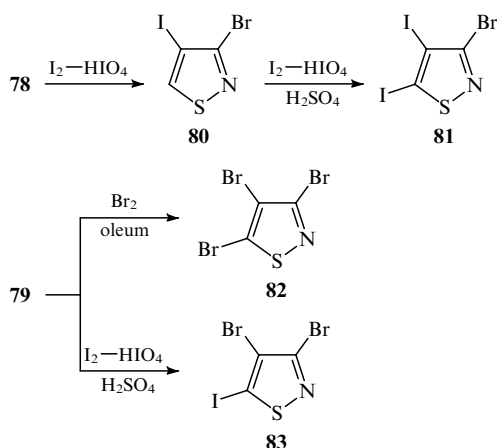
The syntheses of functionalised isothiazoles by exchange of substituents in the isothiazole ring or by transformation of the side chain of accessible derivatives are well documented.⁴⁶

a. Substitution reactions

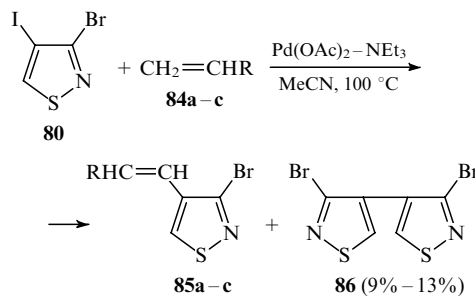
Recently, Russian chemists have developed novel procedures for the synthesis of halogenated isothiazoles.^{81–83} Thus bromo- and iodoisothiazoles **78–83** have been synthesised from the readily available 3-hydroxyisothiazole (**77**).⁸¹



NBS, *N*-bromosuccinimide.

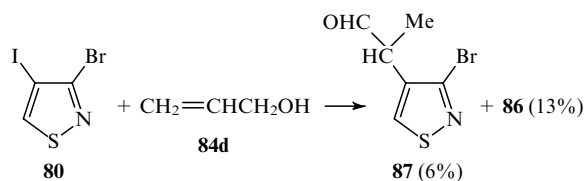


The possibility of synthesis of alkenylhaloisothiazoles by palladium-catalysed cross-coupling of the halogen derivatives **80** and **83** with the terminal alkenes **84a–d** (the Heck reaction) has been studied.⁸² It was found that 3,4-dibromo-5-iodoisothiazole (**83**) does not react with alkenes under the reaction conditions. 3-Bromo-4-iodoisothiazole **80** enters into the Heck reaction with the alkenes **84a–c** in the presence of the catalytic system Pd(OAc)₂–NEt₃ to give 4-alkenyl-3-bromoisothiazoles **85a–c**. 4,4'-Bi(3-bromoisothiazole) (**86**) is the side product in this reaction; it is also formed in the absence of the alkene.

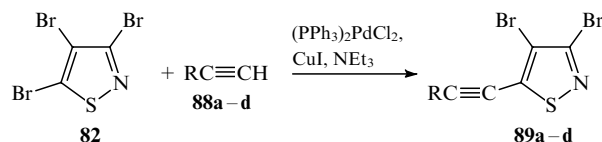


R = Ph (**a**, 60%), CO₂Me (**b**, 29%), CN (**c**, 33%).

3-Bromo-4-(1-oxopropan-2-yl)isothiazole (**87**) and biisothiazolyl **86** were isolated from a complex mixture of reaction products of isothiazole **80** with allyl alcohol (**84d**).



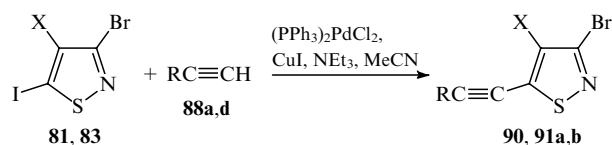
Under conditions of metal-complex catalysis, bromo- and iodoisothiazoles react with terminal alkynes.⁸³ Thus tribromoisothiazole (**82**) reacts with phenylacetylene (**88a**), oct-1-yne (**88b**), propargyl alcohol (**88c**) and methoxymethylacetylene (**88d**) in the presence of (PPh₃)₂PdCl₂ even at 20 °C to give the cross-coupling products (**89a–d**).



R = Ph (**a**), n-C₆H₁₃ (**b**), CH₂OH (**c**), CH₂OMe (**d**).

The highest yields (20%–56%) were obtained with 4 mol.% of (PPh₃)₂PdCl₂. 1,4-Diphenylbuta-1,3-diyne was isolated as a side product in the reaction of isothiazole **82** with phenylacetylene **88a**.

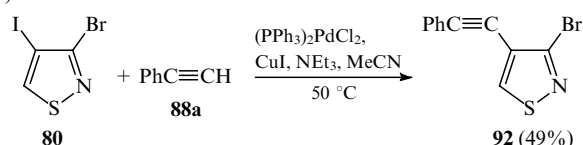
It should be noted that unsubstituted acetylene does not enter into the cross-coupling reaction with isothiazole **82** even at 80 °C; the reaction mixture contained only 3,4-dibromoisothiazole (**79**), the partial reduction product of the tribromide **82**. Compound **79** did not react with phenylacetylene, *i.e.*, only the bromine atoms in position 5 were active in the cross-coupling reaction. 5-Iodoisothiazoles were found to be the most reactive compounds. The reactions of 3,4-dibromo-5-iodoisothiazole (**83**) and 3-bromo-4,5-diiodoisothiazole (**81**) with terminal alkynes **88a,d** occur in the presence of 2 mol.% of (PPh₃)₂PdCl₂ and result in the corresponding 3,4-dibromo-5-alkynyl- (**90**) and 3-bromo-4-iodo-5-alkynylisothiazoles (**91a,b**).



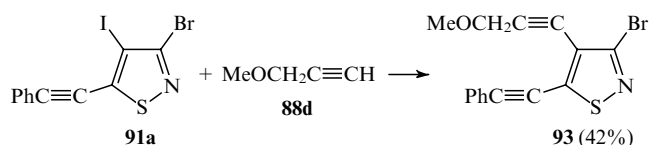
Compounds	X	R
90	Br	Ph
91a	I	Ph
91b	I	CH_2OMe

The side reaction products of terminal alkynes with 3,4-dibromo-5-iodo-1,2-thiazole (**83**) and 3-bromo-4,5-diiodo-1,2-thiazole (**81**), viz., the dibromide **79** and 3-bromo-4-iodo-1,2-thiazole (**80**), represent the reduction products of iodine in position 5.

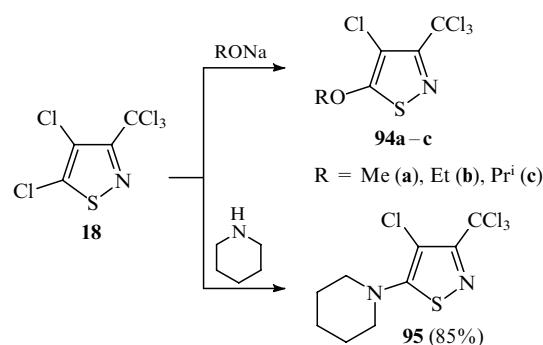
3-Bromo-4-iodo-1,2-thiazole (**80**) enter into cross-coupling reactions with phenylacetylene (**88a**) under conditions of metal-complex catalysis to give 3-bromo-4-(phenylethynyl)-1,2-thiazole (**92**).⁸³



3-Bromo-4-(3-methoxyprop-1-ynyl)-5-(phenylethynyl)-1,2-thiazole (**93**), the first representative of isothiazoles with two alkynyl substituents, was synthesised by the reaction of 3-bromo-4-iodo-5-(phenylethynyl)-1,2-thiazole (**91a**) with methoxymethylacetylene (**88d**) under similar conditions.⁸³

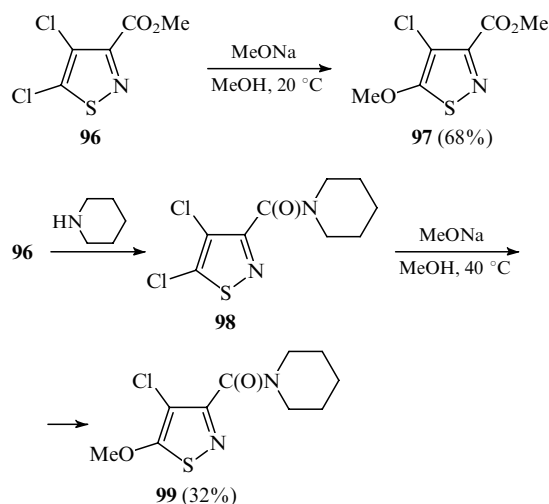


4,5-Dichloro-3-trichloromethylisothiazole (**18**) reacts smoothly with various nucleophilic reagents resulting in the substitution of the chlorine atom in position 5 of the isothiazole ring. Thus its reactions with sodium methoxide, ethoxide and isopropoxide afford the corresponding 5-alkoxy-4-chloro-3-trichloromethylisothiazoles (**94a–c**) in 73%–78% yields. The reaction of isothiazole **18** with piperidine results in 4-chloro-5-piperidino-3-trichloromethylisothiazole (**95**).⁵⁶

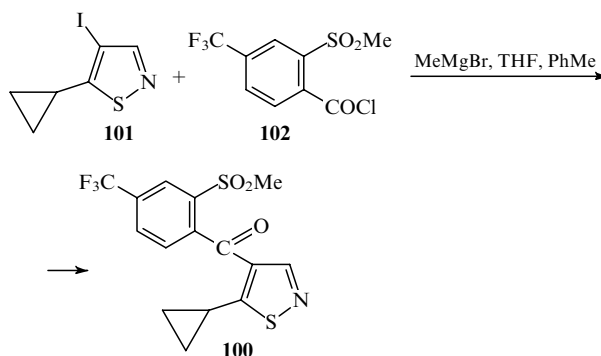


The reaction of methyl 4,5-dichloroisothiazole-3-carboxylate (**96**) with sodium methoxide in methanol at $20^\circ C$ proceeds in a similar way and yields methyl 5-methoxy-4-chloroisothiazole-3-carboxylate (**97**).⁸⁴ At a higher temperature, the saponification of the ester **96** occurs. The reaction of sodium methoxide with 4,5-dichloroisothiazole-3-carboxylic acid piperidide (**98**) prepared by treatment of the ester **96** with piperidine yields compound **99**,

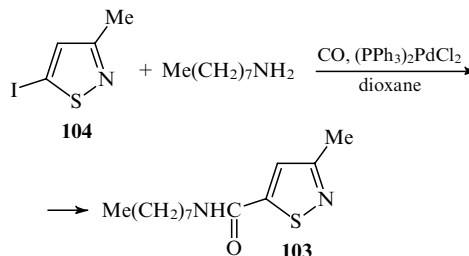
the substitution product of the methoxy group for the chlorine atom in position 5.⁸⁴



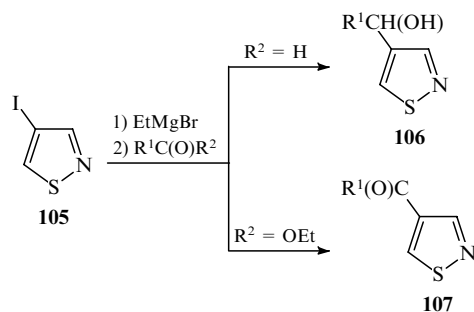
A vast variety of 4-aryl- and 4-heteroaryl isothiazoles were prepared from substituted 4-iodoisothiazoles.^{85–88} This is exemplified in the synthesis of 5-cyclopropyl-4-(2-methylsulfonyl-4-(trifluoromethyl)benzoyl)isothiazole (**100**) from 5-cyclopropyl-4-iodoisothiazole (**101**) by treatment with methylmagnesium bromide and 2-methylsulfonyl-4-(trifluoromethyl)benzoyl chloride (**102**).



N-Alkylisothiazolecarboxamides are synthesised from iodoisothiazoles by treatment with CO and amines in the presence of palladium catalysts.⁸⁹ Thus *N*-octyl-3-methylisothiazole-5-carboxamide (**103**) was prepared by heating a 5-iodo-3-methylisothiazole (**104**)–octylamine–triphenylphosphine mixture in an atmosphere of CO (10 atm) in the presence of $(PPh_3)_2PdCl_2$ ($100^\circ C$, 6 h).



A convenient regiospecific method for the synthesis of isothiazole derivatives of the type **106** and **107** based on the reactions of thiazol-4-ylmagnesium bromide (prepared from 4-iodoisothiazole (**105**) and ethylmagnesium bromide) with carbonyl compounds has been developed.⁹⁰



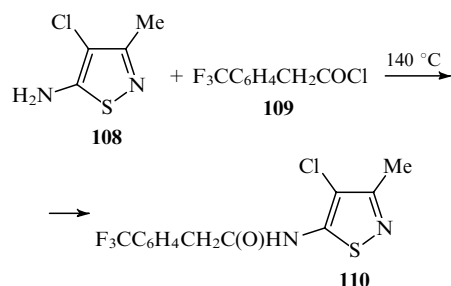
R¹ = Ph, 4-ClC₆H₄, 2,4-Cl₂C₆H₃, Ph; R² = H, OEt.

For the first time, isothiazolyl gold(I) complexes were prepared by the reaction of isothiazol-5-yl lithium with gold(I) chloride or tetrahydrothiophene(pentafluorophenyl)gold; their protonation or alkylation gave the corresponding isothiazolinyldiene complexes.⁹¹

b. Modification of amino, hydroxy, carboxy and other groups and functionalisation of the side chain in isothiazole derivatives

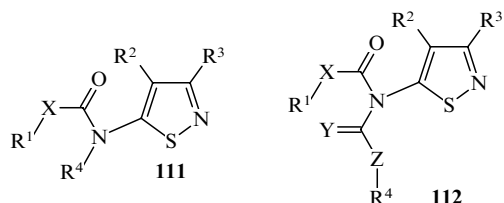
In-depth studies into biological properties of functionalised isothiazoles carried out in the past decade were aimed at the development of methods for the synthesis of such compounds based on the known amino- and hydroxyisothiazoles, isothiazolecarboxylic acids and their chlorides, *etc.*, and by functionalisation of the side chain.⁴⁶

Heating of a 5-amino-4-chloro-3-methylisothiazole (**108**) – (4-trifluoromethylphenyl)acetyl chloride (**109**) mixture in xylene gave *N*-isothiazol-5-ylamide **110**.⁹²



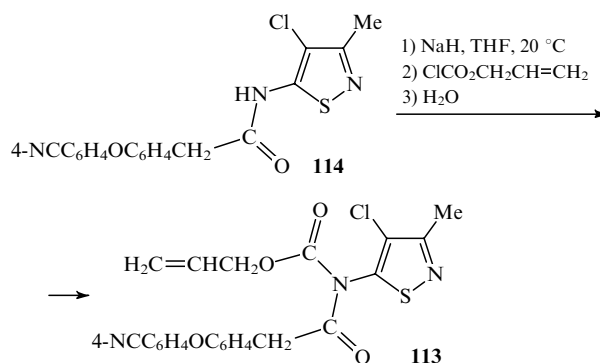
A vast variety of novel useful *N*-isothiazol-5-ylamides have been prepared starting from structurally more complex acid chlorides and aminoisothiazoles containing various substituents in positions 3 and 4.^{92, 93}

The methods for the synthesis of acylated 5-aminoisothiazoles of the type **111** and **112** have been developed.^{94–96}

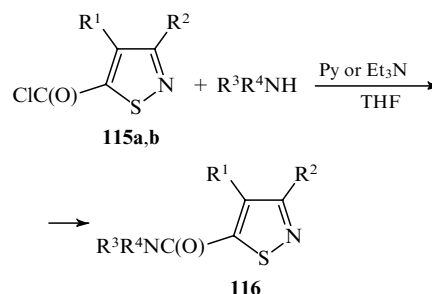


R¹, R², R³, R⁴ = H, CN, NO₂, CHO, alkyl, halogenoalkyl, alkoxyalkyl, alkoxy, alkylthio;
X = alkylene, alkyleneoxy; Y, Z = O, S.

For example, acylated 5-aminoisothiazole **113** was prepared from 4-chloro-5-[4-(4-cyanophenoxy)phenyl]acetyl amino-3-methylisothiazole (**114**) by treatment with NaH in tetrahydrofuran and then with a twofold excess of allyloxycarbonyl chloride.⁹⁵



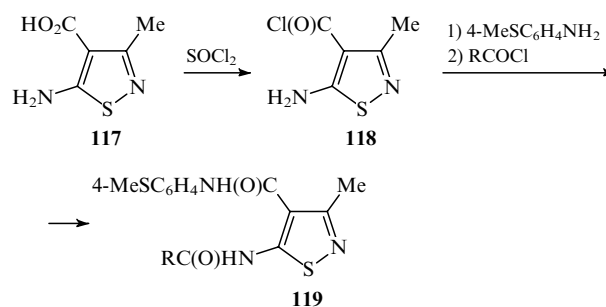
Carboxylic acids and acid chlorides of the isothiazole series are convenient starting compounds in the synthesis of isothiazolecarboxamides. Thus a series of biologically active amides **116** have been synthesised from 3-methylisothiazole-5-carbonyl chloride (**115a**) and 3,4-dichloroisothiazole-5-carbonyl chloride (**115b**) and various amines in the presence of triethylamine or pyridine.^{97–101}



R¹ = H, R² = Me (**115a**); R¹ = R² = Cl (**115b**);
R³ = Ph, C₆H₅SO₂, 4-ClC₆H₄, 1,2,4-triazolyl, pyrazolyl, piperazinyl;
R⁴ = H, Et.

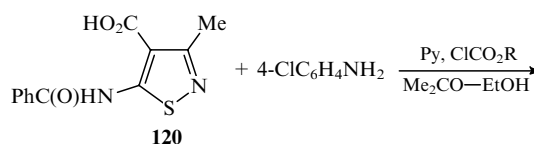
Amides **116** (R³ = Het, R⁴ = H) can be prepared by the reaction of 3,4-dichloroisothiazole-5-carboxamide with derivatives of the corresponding heterocyclic compounds.¹⁰¹

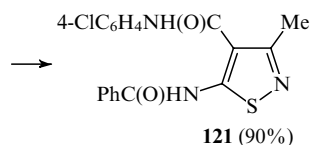
5-Amino-3-methylisothiazole-4-carboxylic acid (**117**) is the starting compound in the synthesis of structurally more complex amides. Thus the reaction of the chloride **118** with 4-methylthioaniline and subsequent acylation with acid chlorides yields 5-acylaminoisothiazole-4-carboxamides **119**.¹⁰²



R = Me, Et, Ph.

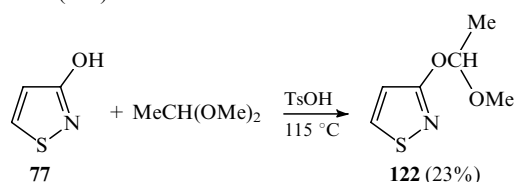
The reaction of 5-benzoylamino-3-methylisothiazole-4-carboxylic acid (**120**) with *p*-chloroaniline in the presence of pyridine as the catalyst and alkoxycarbonyl chloride as the activating reagent gave 5-benzoylamino-3-methylisothiazole-4-carboxylic acid (**121**) *p*-chloroanilide.¹⁰³



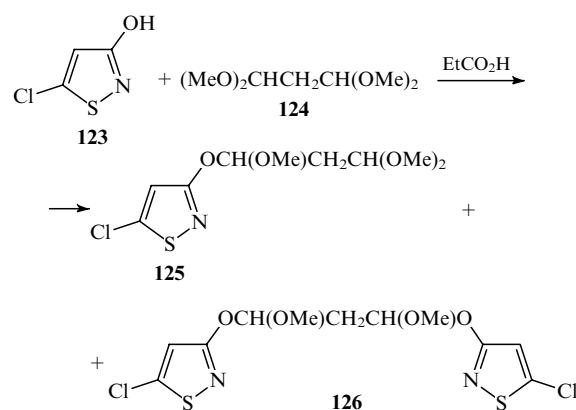


R = Me, Et, Prⁿ.

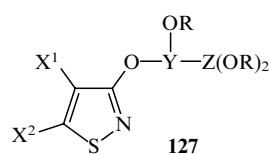
3-Hydroxyisothiazole and its 4-halogeno derivatives react with acetals in the presence of toluene-*p*-sulfonic acid to give mixed acetals. For example, the reaction of isothiazole **77** with acetaldehyde dimethyl acetal results in 3-(1-methoxyethyloxy)isothiazole (**122**).¹⁰⁴



The reaction of 5-chloro-3-hydroxyisothiazole (**123**) with malonic dialdehyde bis(dimethylacetal) (**124**) in propionic acid yields a mixture of 5-chloro-3-(1,3,3-trimethoxypropyl)oxyisothiazole (**125**) and 1,3-bis(5-chloroisothiazol-3-yloxy)-1,3-dimethoxypropane (**126**).¹⁰⁵

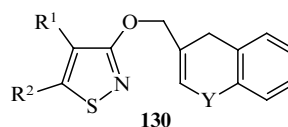
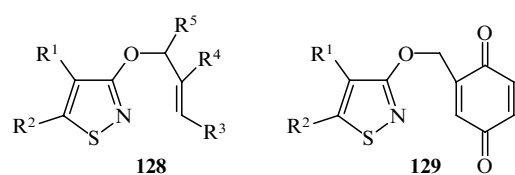


A great number of isothiazole derivatives of the general formula **127** have been prepared using a similar approach.



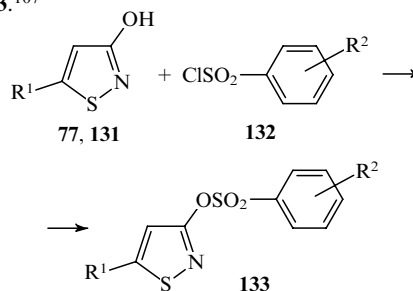
R = Alk(C₁–C₁₈); X¹ = H, Br, Cl, Me; X² = H, Br, Cl;
Y–Z = HC(CH₂)_nCH.

4,5-Disubstituted 3-hydroxyisothiazoles react with various allylic bromides to give alkenyl ethers of 3-hydroxyisothiazoles **128–130**.¹⁰⁶



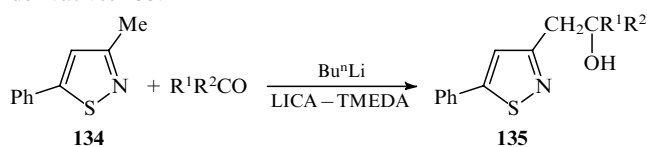
R¹, R² = H, Cl, alkyl(C₁–C₄); R³ = H, alkyl, alkenyl, alkynyl, Ph, *etc.*;
R⁴, various electron-withdrawing groups;
R⁵ = H, alkyl; Y = O, S, SO₂.

The condensation of isothiazole **77** and its 5-methylthio derivative **131** with arenesulfonyl chlorides **132** in the presence of a base yields the corresponding 3-arylsulfonyloxyisothiazoles **133**.¹⁰⁷



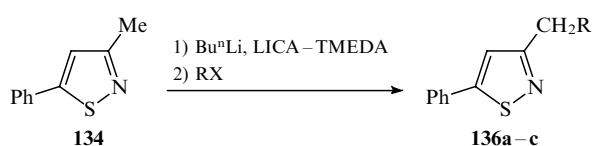
R¹ = H (**77**), SMe (**131**); R² = H, 4-Me, 2-NO₂, 4-NO₂, 4-Br, 2-CO₂Et.

Aldehydes and ketones can be used for the functionalisation of isothiazoles. The reaction of the lithium derivative prepared by the metallation of 3-methyl-5-phenylisothiazole (**134**) with *n*-butyllithium in the presence of a lithium isopropylcyclohexylamide–*N,N,N',N'*-tetramethylenediamine system (LICA–TMEDA) with carbonyl compounds leads to hydroxy derivatives **135**.¹⁰⁸



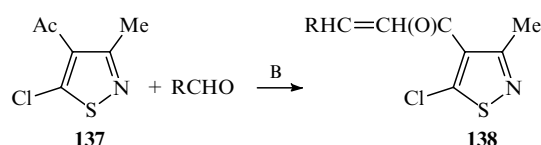
R¹ = H, R² = Et, CH=CH₂, Ph, CH=CHPh;
R¹–R² = (CH₂)_n, n = 4, 5; R¹ = Ph; R² = Me, CH=CH₂,
Ph, CH=CHPh.

The alkylation of a lithium derivative of isothiazole **134** with alkyl iodides or bromides gives compounds **136a–c** in up to 83% yields.¹⁰⁹



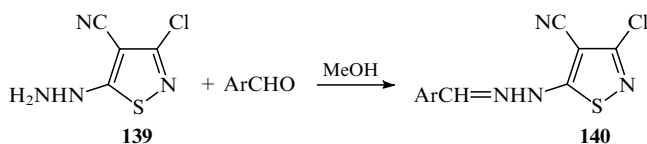
R = Me, X = I (**a**); R = Bn, X = Br (**b**); R = Bu, X = Br (**c**).

The condensation of 4-acetyl-5-chloro-3-methylisothiazole (**137**) with some aromatic and heterocyclic aldehydes involves the methyl group of the acetyl group rather than the methyl group in position 3 of the isothiazole ring to give α,β-unsaturated carbonyl compounds **138**.¹¹⁰



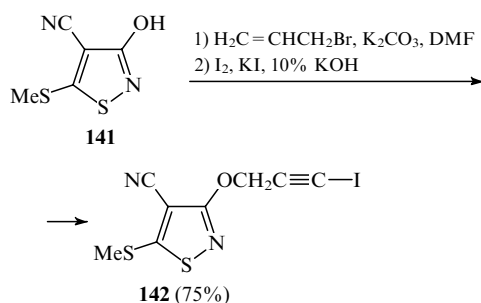
R = 2-ClC₆H₄, 4-ClC₆H₄, 4-Me₂NC₆H₄, 2-furyl.

(3-Chloro-4-cyanoisothiazol-5-yl)hydrazine (**139**) reacts with aromatic aldehydes to give the corresponding (3-chloro-4-cyanoisothiazol-5-yl)hydrazones **140**.¹¹¹

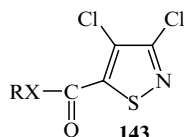


Ar = Ph, 4-O₂NC₆H₄, 4-MeOC₆H₄, 4-ClC₆H₄, 2,4-Cl₂C₆H₃, 3-O₂NC₆H₄, 2,4-(O₂N)₂C₆H₃, 4-HOC₆H₄, 2-HOC₆H₄, 3-MeOC₆H₄, 2-MeOC₆H₄.

Treatment of 4-cyano-3-hydroxy-5-methylthioisothiazole (**141**) with allyl bromide in the presence of potassium carbonate in DMF and subsequent treatment with iodine, potassium iodide and KOH yield the iodopropargyloxy derivative **142**.¹¹² Other cyanoisothiazole derivatives containing various alkyl, alkenyl and alkynylthio groups in positions 3 and 5 were synthesised using a similar approach.¹¹²



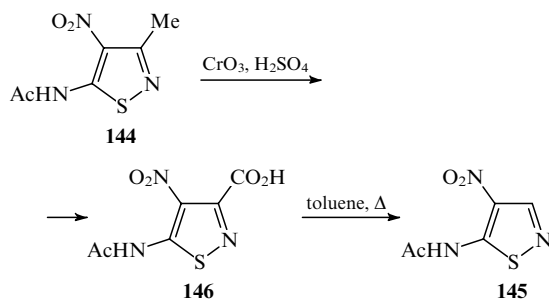
3,4-Dichloroisothiazole-5-carboxylic acid derivatives **143** (X = O, S; R is substituted alkyl, aryl and heterocyclic residues containing halogen, CN, NO₂, carbonyl, halogenalkylthio and other groups) have been synthesised recently from the acid chloride **115b**.¹¹³



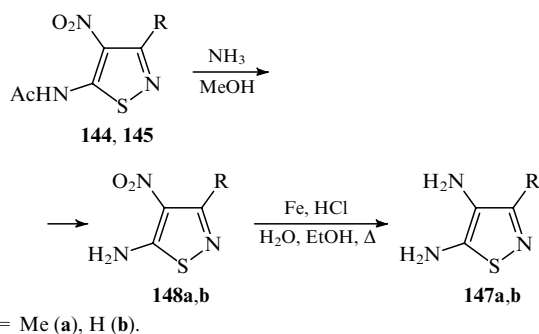
4. Miscellaneous reactions for the synthesis of isothiazole

The preparation of 3-substituted 4,5-diaminoisothiazoles used in the synthesis of novel heterocyclic systems (see Section III) is based on the conversions of 5-acetylamino-3-methyl-4-nitroisothiazole (**144**) which is readily obtainable from the commercially available 5-amino-3-methylisothiazole hydrochloride.¹¹⁴

Isothiazole **145** non-substituted in position 3 is formed upon oxidation of isothiazole **144** to carboxylic acid **146** and subsequent decarboxylation.

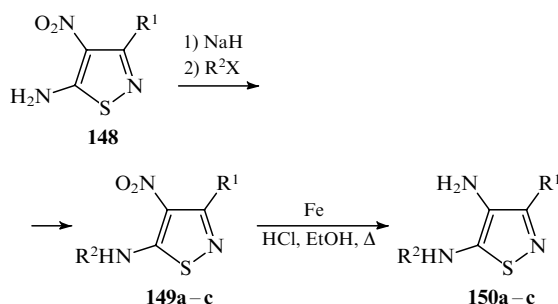


4,5-Diaminoisothiazoles **147a,b** are obtained from compounds **144** and **145** by deacetylation and reduction of the nitro group in the derivatives **148a,b**.¹¹⁴



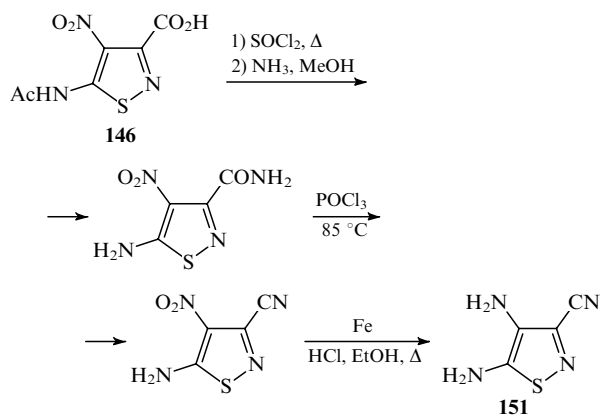
R = Me (a), H (b).

5-(*N*-Alkylamino)-4-nitroisothiazoles **149a–c** were synthesised in high yields by the alkylation of sodium salts of 5-amino-4-nitroisothiazoles **148**. The reduction of the nitro group in compounds **149a–c** gives 5-(*N*-alkylamino)-4-aminoisothiazoles **150a–c**.¹¹⁵

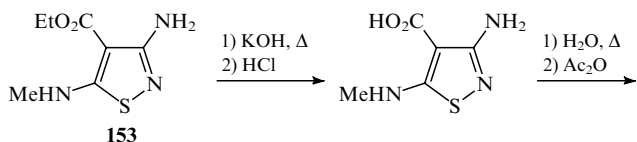


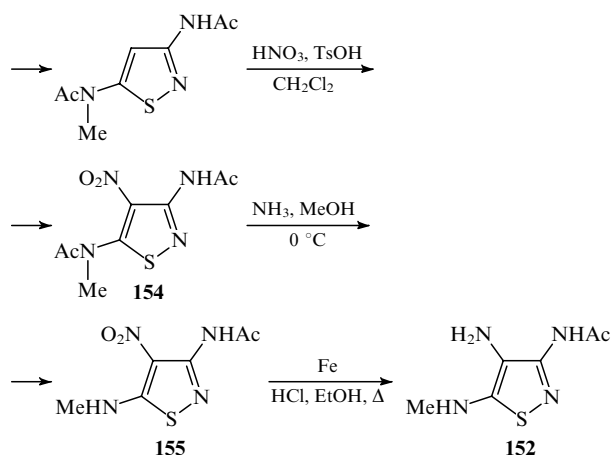
R¹ = R² = Me (a); R¹ = H, R² = Me (b); R¹ = Me, R² = Buⁿ (c).

4,5-Diamino-3-cyanoisothiazole (**151**) was obtained from 5-acetylamino-4-nitroisothiazole-3-carboxylic acid (**146**) in four steps which included the conversion of the carboxy group into the nitrile group and the reduction of the nitro derivative to diamine **151**.¹¹⁵

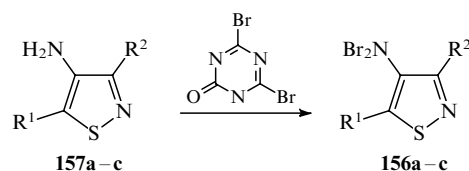


3-Acetamido-4-amino-5-(*N*-methylamino)isothiazole (**152**) is the starting compound in the synthesis of novel annelated heterocycles. This is prepared from ethyl 3-amino-5-(*N*-methylamino)-isothiazole-4-carboxylate (**153**) which is converted into the nitro derivative **154** in several steps. Selective removal of the acetyl protective group from the amino group in position 5 by treatment with methanolic ammonia and subsequent reduction of the 3-acetamido-5-(*N*-methylamino)-4-nitroisothiazole (**155**) formed completes the synthetic scheme.^{115, 116}





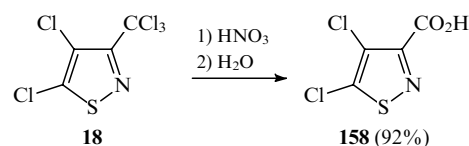
4-Dibromoaminoisothiazoles **156a–c** used in the synthesis of the bisisothiazolopyrazine system are prepared by the reaction of 4-aminoisothiazoles **157a–c** with dibromoisocyanuric acid.^{117–119}



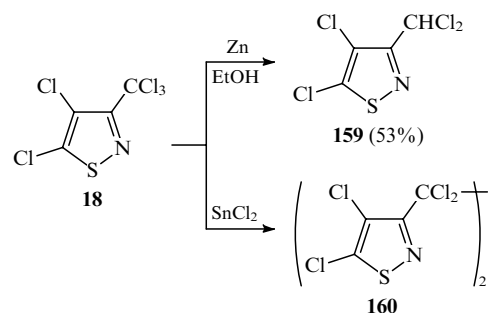
$R^1 = \text{Br}; R^2 = \text{Me}$ (a), Ph (b); $R^1 = R^2 = \text{Cl}$ (c).

A procedure for the synthesis of 3,4-dichloro-5-cyanoisothiazole by the chlorination of the reaction product of carbon disulfide with NaCN in DMF¹²⁰ has been improved.¹²¹ 3,4-Dichloro-5-cyanoisothiazole synthesised (yield ~ 88%) was converted into 3,4-dichloroisothiazole-5-carboxylic acid, which is employed in the synthesis of efficient plant growth regulators. Analogously, 3,5-dichloroisothiazole-4-carboxylic acid was prepared from 3,5-dichloro-4-cyanoisothiazole.¹²²

4,5-Dichloroisothiazole-3-carboxylic acid (**158**) was prepared by hydrolysis of the trichloromethyl group of 4,5-dichloro-3-trichloromethylisothiazole (**18**) with fuming nitric acid and subsequent treatment of the reaction mixture with water.⁵⁶

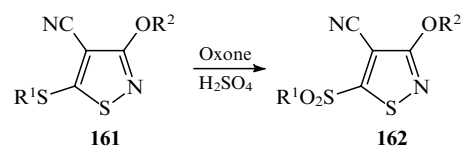


The direction of reduction of the isothiazole **18** depends on the nature of the reducing agent. Boiling with zinc powder in ethanol results in the partial reduction of the trichloromethyl group and the formation of 4,5-dichloro-3-dichloromethylisothiazole (**159**). When tin dichloride is used, isothiazole **18** undergoes dechlorodimerisation resulting in 1,2-bis(4,5-dichloroisothiazol-3-yl)tetrachloroethane (**160**) in high yield.⁵⁶



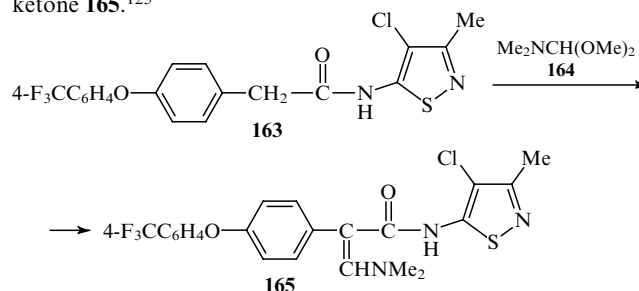
The oxidation of 3-alkoxy-5-alkyl-4-cyanothioisothiazoles **161** under the action of Oxone ($2\text{KHSO}_3 \cdot \text{KHSO}_4 \cdot \text{K}_2\text{SO}_4$)

involves selectively the exocyclic sulfur atom and affords the corresponding 5-alkylsulfonylisothiazoles **162** in high yields.^{123, 124}

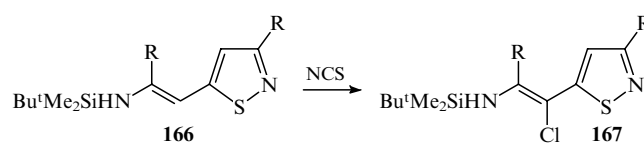


$R^1, R^2 = \text{H}, \text{C}_1\text{--C}_{12}\text{-alkyl}, \text{C}_2\text{--C}_7\text{-alkenyl}, \text{C}_3\text{--C}_7\text{-alkynyl}, \text{C}_3\text{--C}_7\text{-cycloalkyl}, \text{Ph}, \text{PhO}$.

The oxidation of the methylene group in substituted acetamide **163** by dimethylformamide dimethylacetal (**164**), which can be regarded as a variant of the condensation reaction associated with the elimination of two MeOH molecules, gives enamino ketone **165**.¹²⁵



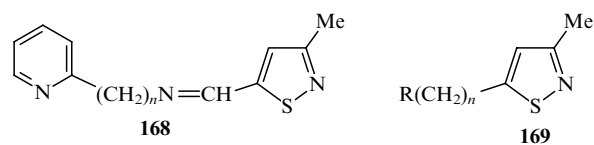
The chlorination of 5-[2-(*N-tert*-butyldimethylsilylamino)vinyl]isothiazoles **166** with *N*-chlorosuccinimide (NCS) proceeds selectively at the vinyl group resulting in the *Z*-isomers of isothiazole **167**.¹²⁶



$R = 4\text{-ClC}_6\text{H}_4, \text{Ph}$.

The monochlorination of related compounds with *N*-chlorosuccinimide also proceeds in a selective manner.

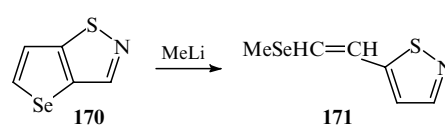
Isothiazoles **168** and **169** react with AgO_3SCF_3 to give dimeric silver(I) complexes the isothiazole fragment in which is linked to the metal centre through the nitrogen atom.¹²⁷



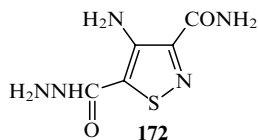
$n = 1, 2$.

$R = [\text{Et}_2\text{N}(\text{CH}_2)_2]_2\text{N}, n = 1;$
 $R = \text{MeS}, n = 2$.

Treatment of selenolo[2,3-*d*]isothiazole (**170**) with methyl-lithium yields a mixture of compounds including isothiazole **171**.¹²⁸

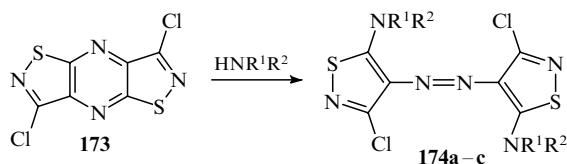


Treatment of 5-substituted 4,5-dihydro-3-ethoxycarbonylisothiazolo[4,3-*d*]pyrimidin-7(6*H*)-ones with hydrazine is accompanied by the opening of the dihydropyrimidinone ring and the formation of 4-amino-3-carbamoyl-5-hydrazinocarbonylisothiazole (**172**).¹²⁹



It is of note that the ring opening reactions in bicyclic isothiazole derivatives described above present purely theoretical interest.

The reactions of 3,7-dichlorodiiisothiazolo[4,5-*b*:4'5'-*e*]pyrazine (**173**) with benzylamine, aniline and morpholine are accompanied by the opening of the pyrazine ring to give *N,N'*-bis-(5-amino-3-chloroisothiazol-4-yl)diazenes (**174a–c**). The reaction of compound **173** with benzylamine gives 3,7-bis(benzylamino)bisisothiazolo[4,5-*b*:4'5'-*e*]pyrazine (yield 5%) as a side product.¹³⁰

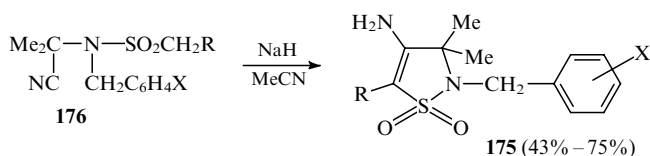


$\text{R}^1 = \text{H}, \text{R}^2 = \text{Bn}$ (**a**, 25%); $\text{R}^1 = \text{H}, \text{R}^2 = \text{Ph}$ (**b**, 25%);
 $\text{R}^1 - \text{R}^2 = (\text{CH}_2)_2\text{O}(\text{CH}_2)_2$ (**c**, 28%).

A mechanistic scheme for the synthesis of compounds **174a–c** has been proposed. Its first step consists in the addition of the amine at the $\text{C}=\text{N}$ bond of the pyrazine ring. Interestingly, the reaction of compound **173** with MeONa in MeOH results in 5,6-dimethoxy-3-chloroisothiazolo[4,5-*b*]pyrazine, *i.e.*, in the opening of one of the isothiazole rings. The difference in the behaviour of compound **173** in the reaction with the alkoxide anion and amines is explained by the difference in their basicities as well as by the presence of a mobile hydrogen atom in the amines which ensures their addition at the multiple bonds of the pyrazine ring.¹³⁰

5. Synthesis of isothiazole 1,1-dioxides

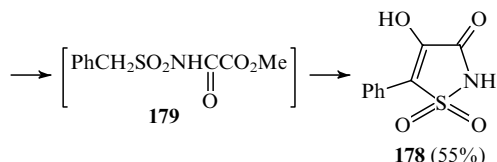
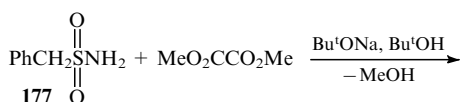
Methods for the synthesis, reactions and biological properties of isothiazole 1,1-dioxides were reviewed in 1997.¹³¹ Here we consider only the most recent publications. Thus a novel procedure for the synthesis of 4-amino-3,3-dimethyl-2,3-dihydroisothiazole 1,1-dioxide derivatives **175** based on substituted *N*-benzyl-*N*-sulfonylaminonitriles **176** has been developed recently. The cyclisation was performed by treatment with sodium hydride in acetonitrile.¹³²



$\text{R} = \text{H}, \text{Me}, \text{Ph}; \text{X} = \text{H}, 4\text{-Cl}, 3\text{-Cl}.$

Other 4-amino-2,3-dihydroisothiazole 1,1-dioxide derivatives,¹³³ particularly compounds containing a cyano group in position 5, were prepared using analogous methods.^{134–136}

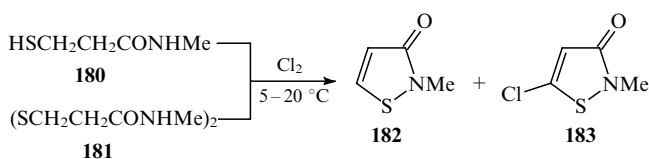
In the presence of bases, phenylmethanesulfonamide (**177**) reacts with dimethyl oxalate to give 4-hydroxy-5-phenylisothiazol-3(2*H*)-one 1,1-dioxide (**178**). It is assumed that the linear methyl *N*-(benzylsulfonyl)oxalamidate **179**, which is formed first, undergoes further cyclisation. A complex of dioxide **178** with DMF has been prepared.¹³⁷



6. Synthesis of dihydroisothiazolones

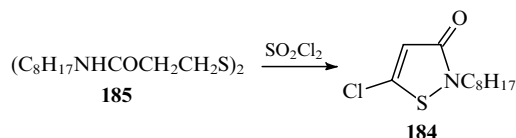
Among representatives of this group, dihydroisothiazol-3-ones possessing high biological activities hold the greatest interest. The data on these compounds are summarised in the review.¹³⁸

Some novel data on the synthesis of dihydroisothiazolones have been published recently. Thus the chlorination of 2-(*N*-methylcarbamoyl)ethanethiol (**180**) or bis[2-(*N*-methylcarbamoyl)ethyl] disulfide (**181**) gave a mixture of 2,3-dihydro-2-methylisothiazol-3-one (**182**) and 5-chloro-2,3-dihydro-2-methylisothiazol-3-one (**183**).¹³⁹



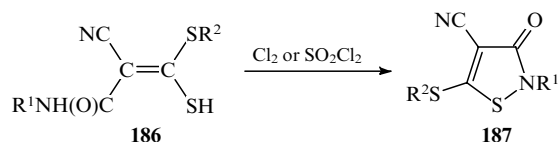
Isothiazol-3-ones **182** and **183** can also be prepared by treatment of compounds **180** and **181** with thionyl chloride.^{140, 141}

5-Chloro-2,3-dihydro-2-octylisothiazol-3-one (**184**) was synthesised by treatment of disulfide **185** with SO_2Cl_2 .¹⁴²



The clathrate of compound **184** containing four molecules of 4,4'-dihydroxydiphenylmethane manifests increased solubility in water.

A procedure for the synthesis of isothiazol-3-one derivatives **187** from 3-alkylthio-2-cyano-3-mercaptoacrylamides **186** has been developed.¹⁴³



$\text{R}^1, \text{R}^2 = \text{H}, \text{lower alkyl}, \text{alkenyl}, \text{alkynyl}, \text{aryl}, \text{aralkyl}, \text{hetarylalkyl}.$

The synthesis of isothiazol-3-ones devoid of highly toxic and carcinogenic nitrosoamines has been described in a patent.¹⁴⁴

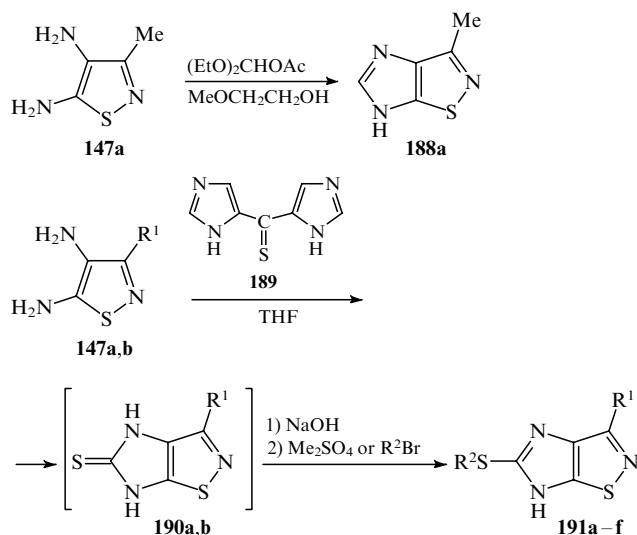
III. Chemical transformations of isothiazoles

Isothiazoles manifest aromatic properties and enter into the same reactions as other heteroaromatic compounds. Ring opening and transformations of the isothiazole ring, which give either functionalised alkenes or other heterocyclic compounds, deserve special attention. Addition reactions of isothiazoles leading to novel bisheterocyclic structures containing an isothiazole fragment are especially attractive. Oxidation reactions of the sulfur atom of the isothiazole ring yield reactive dioxides and present significant interest.⁶⁴

1. Condensation reactions

In recent years, isothiazole derivatives were used as starting compounds for the synthesis of several novel bicyclic compounds. Thus the reaction of 4,5-diamino-3-methylisothiazole (**147a**) with diethoxymethyl acetate affords 3-methylimidazo[4,5-*d*]-isothiazole (**188a**) in low yield. Unsubstituted imidazo[4,5-*d*]iso-

thiazole could not be prepared from compound **147b**.¹¹⁴ Isothiazoles **147a,b** easily undergo cyclisation with thiocarbonyldiimidazole (**189**) to give unstable thiones **190a,b** which are methylated *in situ* in alkaline media under the action of Me_2SO_4 to give 5-methylthioimidazo[4,5-*d*]isothiazoles (**191a,b**) in good yields. Sodium salts of thiones **190a,b** are also alkylated by benzyl and allyl bromides to give the corresponding imidazo[4,5-*d*]isothiazoles **191c–f** in preparative yields.^{114, 115}

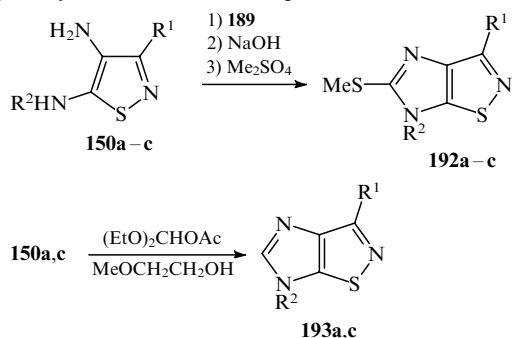


$\text{R}^1 = \text{R}^2 = \text{Me}$ (**191a**); $\text{R}^1 = \text{H}$, $\text{R}^2 = \text{Me}$ (**191b**);

$\text{R}^1 = \text{Me}$, $\text{R}^2 = \text{Bn}$ (**191c**); $\text{R}^1 = \text{Me}$, $\text{R}^2 = \text{All}$ (**191d**);

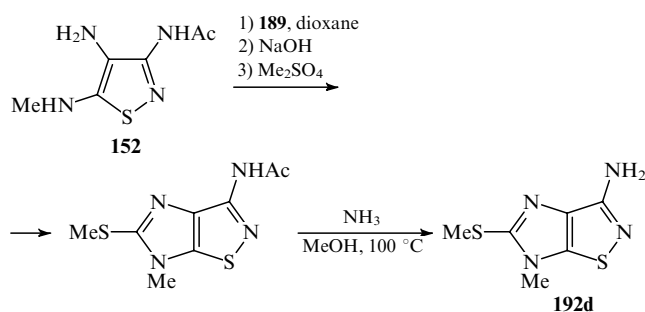
$\text{R}^1 = \text{H}$, $\text{R}^2 = \text{Bn}$ (**191e**); $\text{R}^1 = \text{H}$, $\text{R}^2 = \text{All}$ (**191f**).

6-Alkyl-5-methylthioimidazo[4,5-*d*]isothiazoles **192a–c** were prepared by treatment of 5-(*N*-alkylamino)-4-aminoisothiazoles **150a–c** with thiocarbonyldiimidazole (**189**) and subsequent methylation. The reactions of isothiazoles **150a,c** with diethoxymethyl acetate result in compounds **193a,c**.¹¹⁵



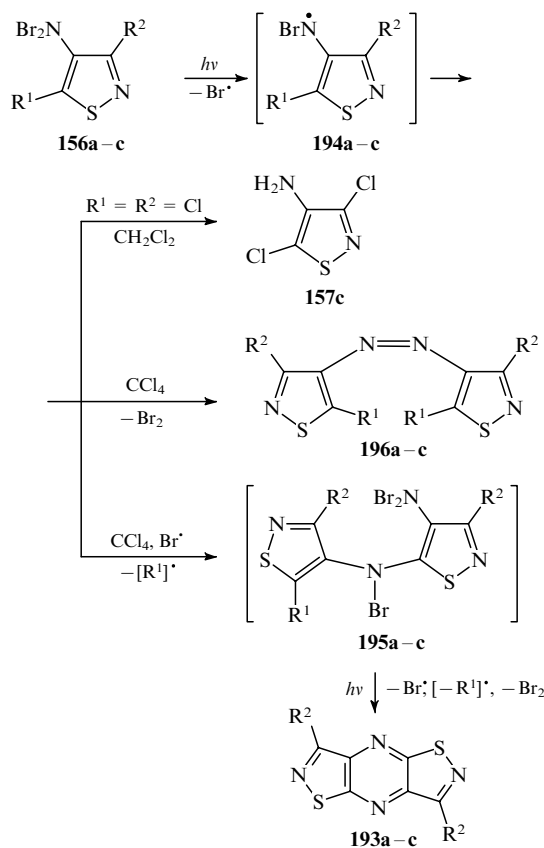
$\text{R}^1 = \text{R}^2 = \text{Me}$ (**a**); $\text{R}^1 = \text{H}$, $\text{R}^2 = \text{Me}$ (**b**); $\text{R}^1 = \text{Me}$, $\text{R}^2 = \text{Bu}^n$ (**c**).

3-Amino-6-methyl-5-methylthioimidazo[4,5-*d*]isothiazole (**192d**) was obtained in good yield by successive treatment of 3-acetamido-4-amino-5-(*N*-methylamino)isothiazole (**152**) with thiocarbonyldiimidazole (**189**) and dimethyl sulfate.¹¹⁵



It should be noted, however, that not all 4,5-diamino-3-*R*-isothiazoles yield annelated products. Thus isothiazole **151** containing a cyano group in position 3 does not react with either diethoxymethyl acetate or thiocarbonyldiimidazole.¹¹⁵

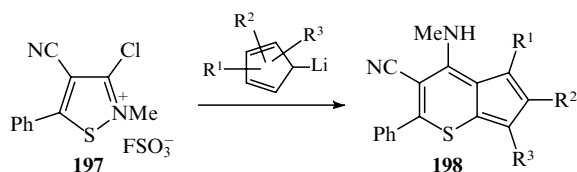
Two approaches to the synthesis of 3,7-disubstituted bisisothiazolo[4,5-*b*:4',5'-*e*]pyrazines **193a–c**, the first compounds containing a novel heterocyclic system, have been proposed.^{117–119} It was found that the reaction of 3,5-dichloro-4-dibromoaminoisothiazole (**156c**) with a $\text{Cu}(0)$ –collidine system affords 3,7-dichlorodisothiazolo[4,5-*b*:4',5'-*e*]pyrazine (**193c**) in 67% yield.¹¹⁷ Zlotin *et al.*¹¹⁸ suggested that this reaction has a radical character and studied the effect of UV light on isothiazoles **156a–c**. Irradiation of compounds **156a,c** with a mercury lamp results in the cleavage of the $\text{N}–\text{Br}$ bond and the formation of radicals **194a,c**; their further transformations depend on the nature of the solvent used. Thus in dichloromethane, isothiazole **156c** is converted into 4-amino-3,5-dichloroisothiazole virtually completely (**157c**). In CCl_4 , 3,7-disubstituted diisothiazolo[4,5-*b*:4',5'-*e*]pyrazines **193a,c** (yields 58% and 76%, respectively) are the main reaction products of compounds **156a,c**; their formation seems to proceed *via* the intermediate compounds **195a,c**. *N,N'*-Di(isothiazol-4-yl)diazenes **196a,c** (yields 37% and 13%, respectively) were identified as the side products.¹¹⁸



$\text{R}^1 = \text{Br}$, $\text{R}^2 = \text{Me}$ (**a**), Ph (**b**); $\text{R}^1 = \text{R}^2 = \text{Cl}$ (**c**).

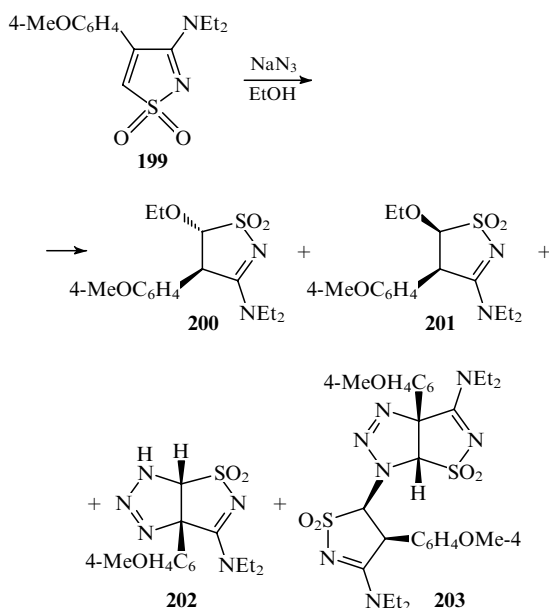
5-Bromo-4-dibromoamino-3-phenylisothiazole (**156b**) manifests a similar behaviour upon irradiation with UV light; 3,7-diphenyldisothiazolo[4,5-*b*:4',5'-*e*]pyrazine (**193b**) and *N,N'*-bis(5-bromo-3-phenylisothiazol-4-yl)diazene (**196b**) are the main reaction products.¹¹⁹

The isothiazolium salt **197** is condensed with cyclopentadienyl-, *tert*-butylcyclopentadienyl- and di-*tert*-butylcyclopentadienyllithium to give thialenes **198**.¹⁴⁵

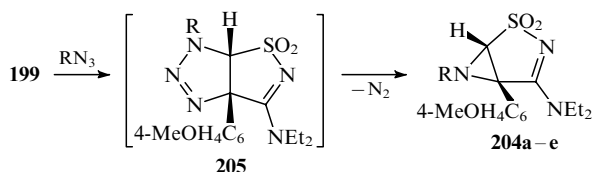


$R^1 = R^2 = R^3 = H$; $R^1 = Bu^t$, $R^2 = R^3 = H$;
 $R^1 = R^3 = H$, $R^2 = Bu^t$; $R^1 = R^3 = Bu^t$, $R^2 = H$.

Reactivities of certain isothiazole 1,1-dioxide derivatives have been studied.¹⁴⁶ It was found that 3-diethylamino-4-(4-methoxyphenyl)isothiazole 1,1-dioxide (**199**) reacts with sodium azide in ethanol to give a mixture of dihydroisothiazole oxides **200** and **201** and isothiazolotriazoles **202** and **203** in a ratio 72 : 12 : 9 : 7.¹⁴⁶



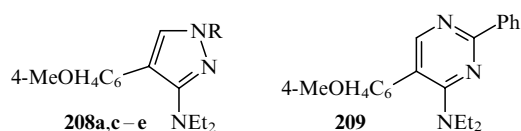
Cycloaddition of the dioxide **199** to arylalkyl and aryl azides results in *N*-arylalkyl- or *N*-arylthiadiazabicyclo[3.1.0]hexene **204**. The unstable cycloadducts **205**, which are formed first (in some cases, they were isolated from the reaction mixture), easily eliminate the nitrogen molecule.



$R = Ph$ (**a**), Bn (**b**), $PhCH_2CH_2$ (**c**), $4-MeOC_6H_4$ (**d**), $4-O_2NC_6H_4$ (**e**).

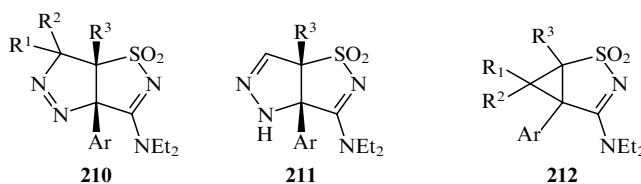
Thermal rearrangement of *N*-aryl- and *N*-phenyl-substituted bicyclic compounds **204a,c-e** affords 1,2-thiazete 1,1-dioxides **206a,c-e**, 1,2,6-thiadiazine 1,1-dioxides **207a,c-e** and pyrazole derivatives **208a,c-e**. Under optimum conditions, compound **207a** was isolated in 51% yield.

If the aziridine nitrogen atom has a benzyl substituent (compound **204b**), the reaction follows a different route to afford the thiadiazine derivative **207b** and pyrimidine **209**.¹⁴⁷



$R = Ph$ (**a**), Bn (**b**), $PhCH_2CH_2$ (**c**), $4-MeOC_6H_4$ (**d**), $4-O_2NC_6H_4$ (**e**).

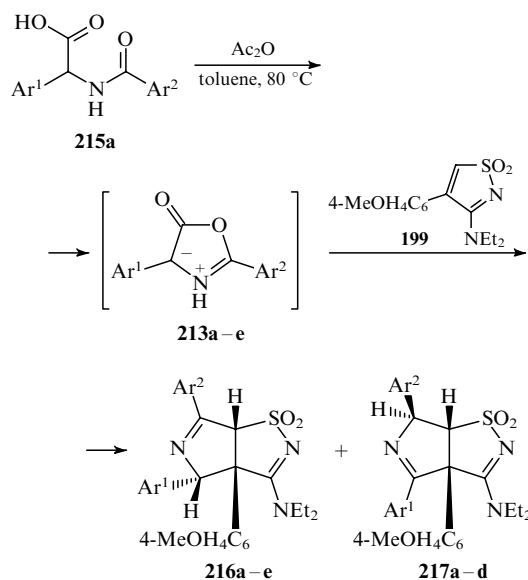
4-Aryl-3-diethylamino-5-*R*-isothiazole 1,1-dioxides enter into cycloaddition reactions with diazoalkanes to give bicyclic compounds **210** with high regio- and stereoselectivity. The reaction with diazomethane yields a mixture of tautomeric pyrazolines **210** ($R^1 = R^2 = H$) and **211**. Thermolysis of compounds **210** and **211** follows two routes. The loss of the nitrogen molecule leads to 2-thia-3-azabicyclo[3.1.0]hex-3-ene 2,2-dioxides **212**. Elimination of SO_2 and diethylcyanamide from the cycloaddition products results in the corresponding pyrazoles.¹⁴⁸



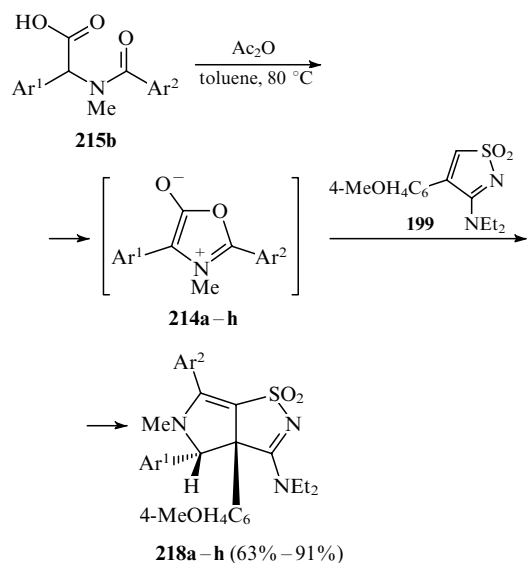
$R^1 = R^2 = H, Me$; $R^1 = H$, $R^2 = CO_2Et$; $R^3 = H, Me, Ph$;
 $Ar = Ph, 4-MeC_6H_4, 4-MeOC_6H_4$.

The readily available dioxide **199** enters into cyclocondensation reactions with oxazolones **213a-e** and munchnones **214a-h**, which are prepared by cyclisation of (*N*-aroylamino)arylacetic acids **215a,b**.¹⁴⁹

The reactions with compounds **215a** afford 4,6-diaryl-3-diethylamino-3a,4-dihydro-3a-(4-methoxyphenyl)-6a*H*-pyrrolo[3,4-*d*]-isothiazole 1,1-dioxides (**216a-e**) (yields 60%–74%) and their isomers **217a-d** (yields 5%–13%). 4,6-Diaryl-3-diethylamino-3a-(4-methoxyphenyl)-5-methyl-3a,4-dihydropyrrolo[3,4-*d*]isothiazole 1,1-dioxides **218a-h** are the main products in the reaction with munchnones **214a-h**.¹⁴⁹

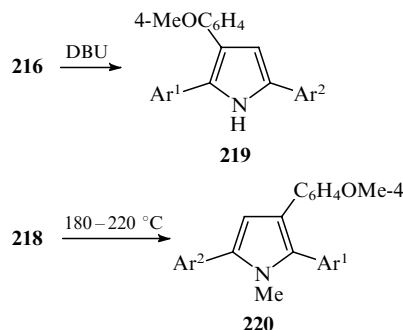


Compounds 216, 217	Ar^1	Ar^2
a	Ph	Ph
b	$4-ClC_6H_4$	Ph
c	Ph	$4-ClC_6H_4$
d	$4-MeC_6H_4$	Ph
e	Ph	$4-MeC_6H_4$



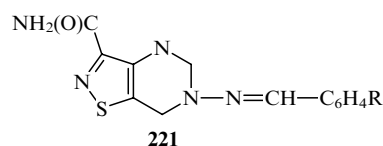
Compound 218	Ar ¹	Ar ²	Compound 218	Ar ¹	Ar ²
a	Ph	Ph	e	4-MeOC ₆ H ₄	Ph
b	Ph	4-MeC ₆ H ₄	f	Ph	4-FC ₆ H ₄
c	4-MeC ₆ H ₄	Ph	g	Ph	4-BrC ₆ H ₄
d	Ph	4-MeOC ₆ H ₄	h	Ph	4-NO ₂ C ₆ H ₄

The cycloadducts **216** and **218** are decomposed at elevated temperatures or in alkaline media with the elimination of SO₂ and diethylcyanamide to give 2,3,5-triarylpyrroles **219** and 1-methyl-2,3,5-triarylpyrroles **220**, respectively.¹⁴⁹



DBU, diazabicycloundecene.

4-Amino-3-carbamoyl-5-(ethoxycarbonyl)isothiazole is used in the synthesis of the isothiazolo[4,5-*d*]pyrimidine derivatives **221**.¹⁵⁰

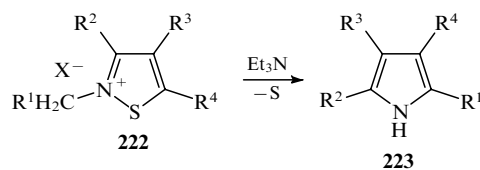


R = 2-OMe, 2-Cl, 3-Br, 3-NO₂.

2. Ring transformation reactions

In recent years, some readily available isothiazolium salts have been used in the synthesis of other heterocyclic compounds, pyrrole derivatives, in particular. Thus the reactions of *N*-alkoxycarbonylmethyl- and *N*-cyanomethylisothiazolium **222** salts with

triethylamine result in the elimination of sulfur and recyclisation resulting in pyrrole-2-carboxylic acid derivatives **223**.¹⁵¹

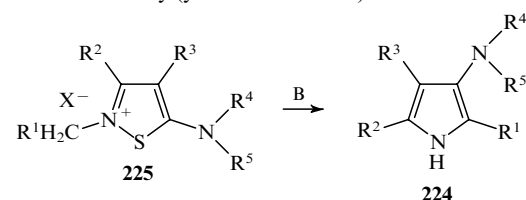


R¹ = CO₂Me, CO₂Et, CN; R² = H, Me, Ph;

R³ = H, Ph, 2-MeC₆H₄, 4-FC₆H₄, CO₂Et;

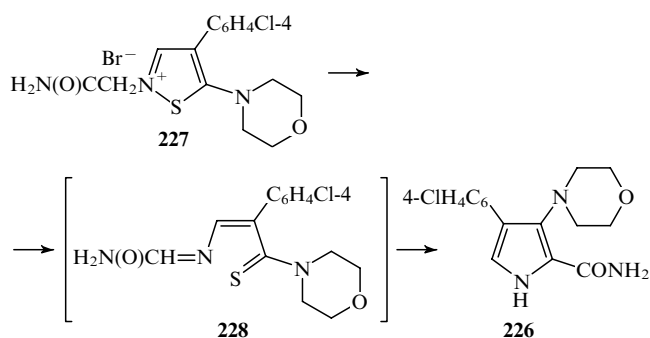
R⁴ = Ph, , NHPh, SMe, 4-ClC₆H₄, ; X = Cl, Br.

Aminopyrroles **224** were obtained from isothiazolium salts **225** in a similar way (yields 70%–90%).¹⁵²

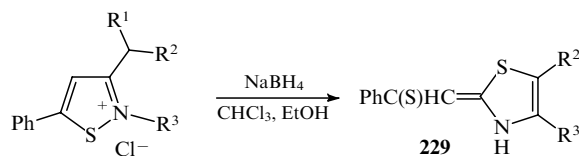


R¹ = H, alkenyl, aryl, NO₂; R², R³ = H, substituted or unsubstituted alkyl, Ar, HetAr; R⁴, R⁵ = H, heterosubstituted aryl or alkyl; X = Hal, ClO₄⁻, BF₄⁻, HSO₄⁻, SO₄²⁻, OH⁻, CF₃SO₃⁻.

The mechanism of formation of 3-aminopyrrole derivatives in the desulfurisation of isothiazolium salts has been studied.¹⁵³ It was found that pyrrole **226** is formed from the salt **227** by a cascade of reactions *via* thioamide **228**.¹⁵³

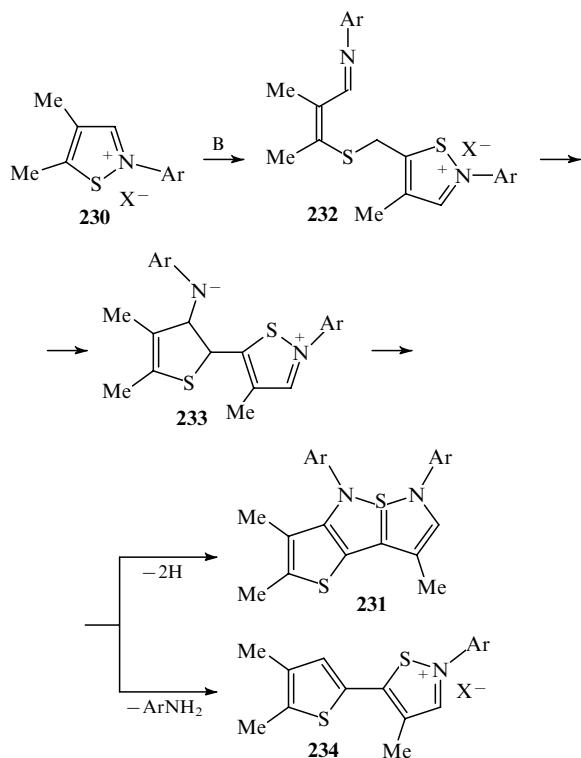


A convenient procedure for the synthesis of 2-phenylthiocarbonylmethylidenedihydrothiazole derivatives **229** from isothiazolium chlorides has been developed.¹⁵⁴



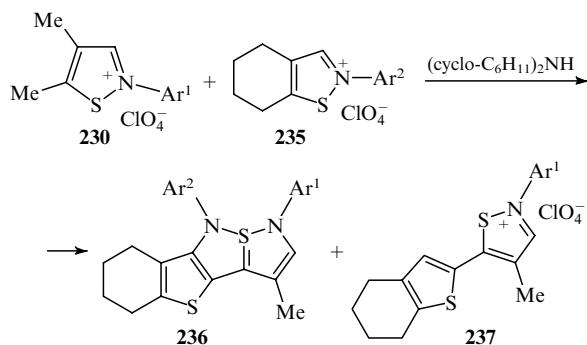
R¹ = Ac, EtCO; R² = CO₂Et, CO₂Me; R³ = Me, Et.

N-Arylisothiazolium salts **230** containing an activated methyl group in position 5 dimerise into thiadiazapentalenes **231** upon treatment with a base. The sulfur atom of one molecule of the salt is attacked by an activated methyl group of another molecule to give the intermediates **232**. Subsequent oxidative closure of the ring *via* zwitterionic intermediates **233** results in thienothiadiaza-pentalenes **231**. A competing reaction gives 5-(2-thienyl)isothiazolium salts **234** with elimination of aniline.¹⁵⁵



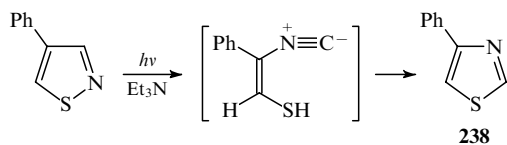
Ar = Ph, 4-MeC₆H₄; X = Cl⁻, ClO₄⁻; B = (cyclo-C₆H₁₁)₂NH.

The reaction between the salts **230** and **235** catalysed by dicyclohexylamine in methanol or DMSO yields 'mixed' thiadiazapentalenes **236** upon oxidative cyclisation and salts **237** upon elimination of aniline.^{156, 157}



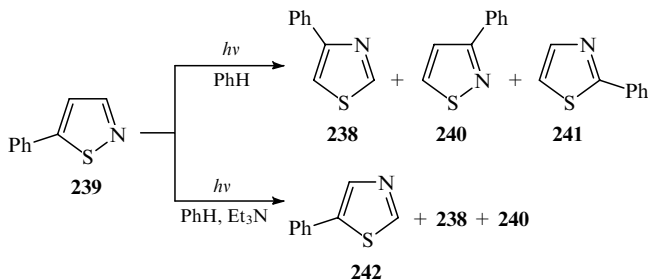
Ar¹ = Ph, 4-MeC₆H₄; Ar² = Ph, 4-MeC₆H₄, 4-MeOC₆H₄.

Photochemical reactions of several isothiazoles have been studied. Irradiation of 4-phenylisothiazole yielded small amounts of 4-phenylthiazole (**238**). When the photolysis was carried out in the presence of triethylamine, this rearrangement becomes predominant.¹⁵⁸



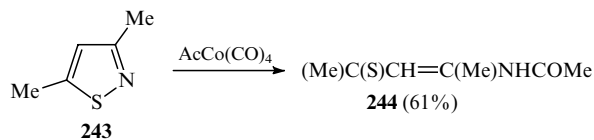
The effect of triethylamine and the solvent polarity on the photochemical reaction of 5-phenylisothiazole (**239**) has been studied.¹⁵⁹ It was found that irradiation in the absence of triethylamine gives 4-phenylthiazole (**238**) as the main product (yield 15%). Other reaction products are represented by 3-phenylthiazole (**240**) and 2-phenylthiazole (**241**). In the presence of Et₃N, 5-phenylthiazole (**242**) is the main product (yield 14%).

Irradiation of 5-phenylisothiazole (**239**) in polar solvents makes this rearrangement more regioselective. The photolysis in methanol in the presence of Et₃N gives exclusively compounds **238** and **242** (yields 9% and 34%, respectively). In a more polar solvent (*e.g.*, 2,2,2-trifluoroethanol), only thiazole **241** was identified in the reaction mixture; in the presence and in the absence of Et₃N, its yield was 42% and 32%, respectively.¹⁵⁹



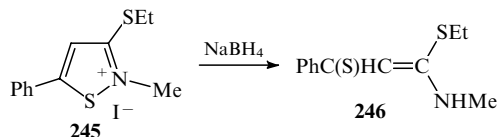
3. Ring opening reactions

Under conditions of phase-transfer catalysis [PhH, H₂O, tris(2,6-dioxaheptyl)amine], the reaction of 3,5-dimethylisothiazole (**243**) with acetylcobalttetracarbonyl generated *in situ* from Co₂(CO)₈, CO and MeI is accompanied by ring opening and *N*-acylation, resulting in thione (**244**) (the ratio of the *E*- and *Z*-isomers is equal to 1 : 10).¹⁶⁰

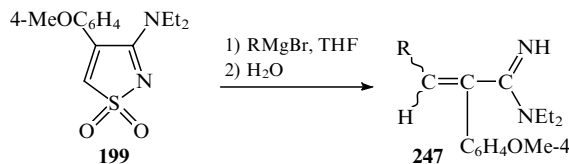


Other *N*-acylated unsaturated thiones are synthesised from isothiazoles in a similar way.

A convenient procedure has been developed for the synthesis of phenylthiocarbonylketene *S,N*-acetals (**246**) based on the reaction of 2-alkyl-3-alkylthio-5-phenylisothiazolium salts (*e.g.*, the salts **245**) with sodium borohydride.¹⁶¹



The reaction of 3-diethylamino-4-(4-methoxyphenyl)isothiazole 1,1-dioxide (**199**) with organomagnesium compounds in THF occurs *via* ring opening leading to a mixture of *E*- and *Z*-isomers of 3-substituted 2-arylpropeneamides **247**.¹⁶²



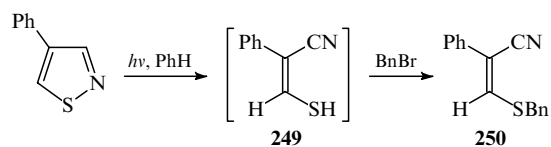
R = Me, Et, Ph, HC≡C, MeC≡C, PhC≡C.

The chemistry of the 4-nitroisothiazole-5(2*H*)-imine derivatives **248**, particularly, their isomerisation and desulfurisation, has been discussed in the papers^{163, 164} and a recent review.¹⁶⁵



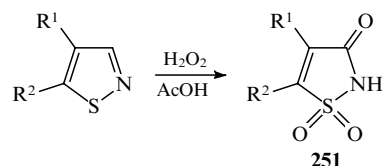
It has already been noted (Section III.2) that the photolysis of 4-phenylisothiazole in benzene gives small amounts of 4-phenylthiazole (**238**) as a result of a rearrangement; cyanothiol **249**,

which was trapped as benzyl sulfide **250**, is the main photolysis product in the absence of a base.¹⁵⁸



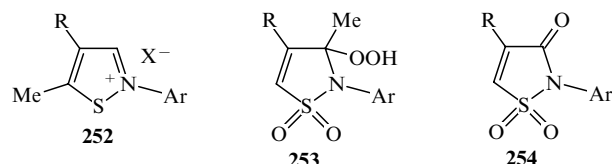
4. Miscellaneous reactions of isothiazole derivatives

The oxidation of 4,5-disubstituted isothiazoles with hydrogen peroxide results in the corresponding isothiazol-3(2*H*)-one 1,1-dioxides **251**.¹⁶⁶



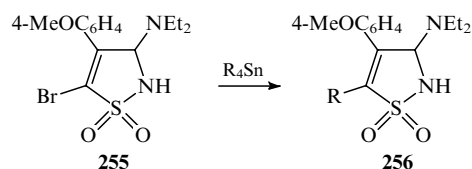
$\text{R}^1 = \text{Me, Ph, H; R}^2 = \text{Me, Ph, 4-BrC}_6\text{H}_4, 4\text{-MeOC}_6\text{H}_4$.

Dioxides **253**, **254** are the oxidation products of the isothiazolium salts **252**.¹⁶⁷



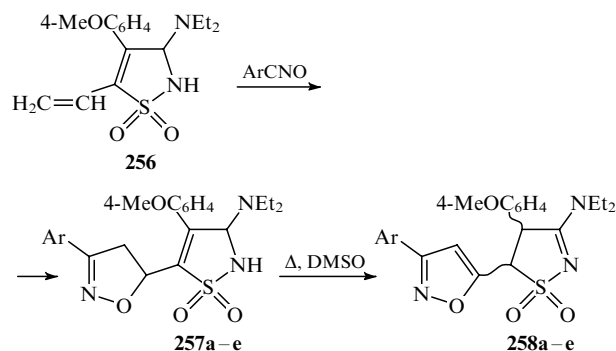
$\text{R} = \text{Alk, Ph}$.

5-Bromo-3-diethylamino-4-(4-methoxyphenyl)-2,3-dihydroisothiazole 1,1-dioxide (**255**) reacts smoothly with various organotin compounds in the presence of palladium catalysts to yield the corresponding 5-substituted derivatives **256**.¹⁶⁸



$\text{R} = \text{CH}_2=\text{CH, Ph, HetAr, Ar}$.

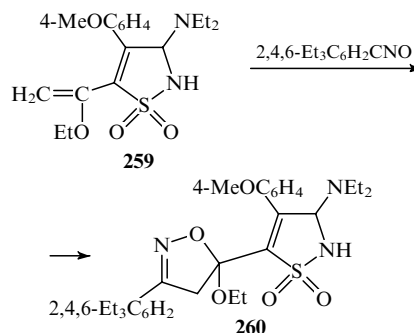
The reaction of the vinyl derivative **256** with nitrile oxides yields the cycloadducts **257a–e**, which are rearranged into 4,5-dihydro-5-(isoxazol-5-yl)isothiazole 1,1-dioxides **258a–e** (an equimolar mixture of *cis*- and *trans*-isomers) upon heating in DMSO.¹⁶⁹



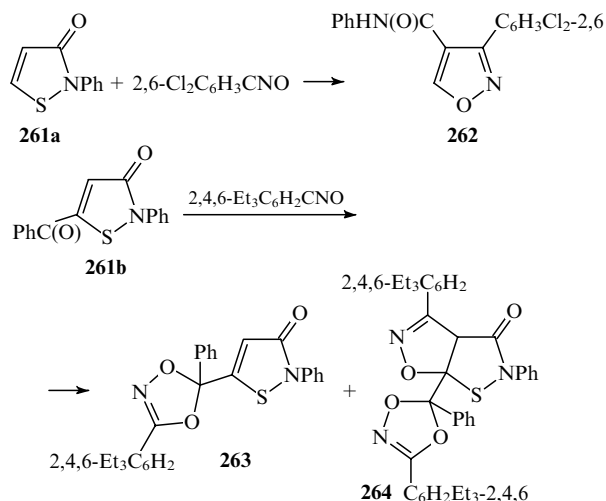
$\text{Ar} = 3,5\text{-Cl}_2\text{-2,4,6-Et}_3\text{C}_6$ (**a**), $2,6\text{-Cl}_2\text{C}_6\text{H}_3$ (**b**), $4\text{-ClC}_6\text{H}_4$ (**c**), $2,4,6\text{-Et}_3\text{C}_6\text{H}_2$ (**d**), $4\text{-NO}_2\text{C}_6\text{H}_4$ (**e**).

3-Diethylamino-2,3-dihydro-5-(1-ethoxyvinyl)-4-(4-methoxyphenyl)isothiazole 1,1-dioxide (**259**) enters into the cycloaddition

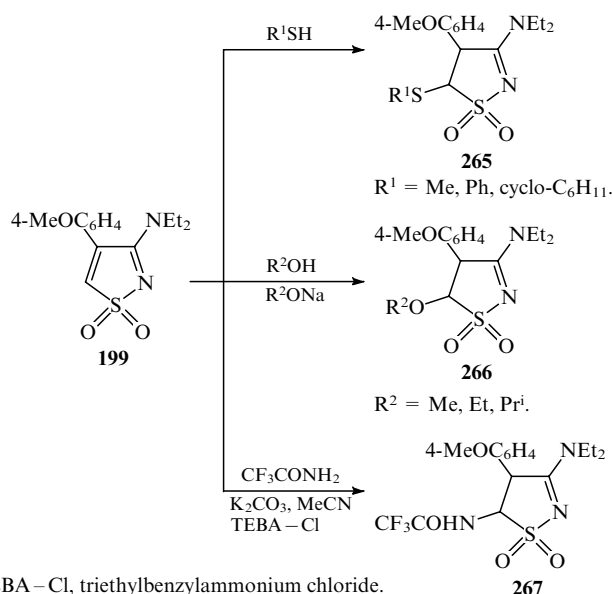
reaction with 2,4,6-triethylbenzonitrile oxide to give the dihydroisoxazole derivative **260**.¹⁶⁹



2,6-Dichlorobenzonitrile oxide reacts with isothiazolone (**261a**) at the double bond to give isoxazolecarboxanilide (**262**) as a result of transformation of the primary cycloadducts formed. Contrary to expectations, 2,4,6-triethylbenzonitrile oxide adds to the exocyclic carbonyl group of isothiazolone **261b** to give the monoadduct **263** and the bisadduct **264**.¹⁷⁰



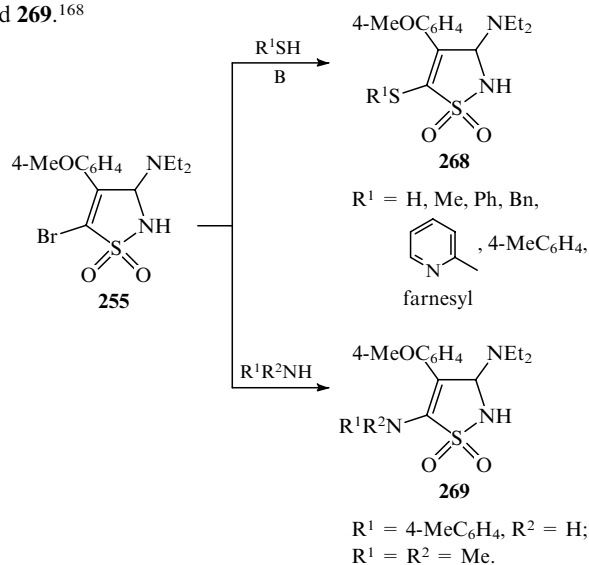
An efficient approach based on the Michaelis reaction is used in the synthesis of 5-substituted 3-amino-4-arylisothiazole 1,1-dioxides and their 4,5-dihydro derivatives. The addition of thiols, alcohols and trifluoroacetamide to 3-diethylamino-4-(4-methoxyphenyl)isothiazole 1,1-dioxide (**199**) in the presence of bases



TEBA – Cl, triethylbenzylammonium chloride.

occurs regioselectively and yields a mixture of (4*S*,5*S*)- and (4*R*,5*S*)-diastereomers of 5-substituted 4,5-dihydroisothiazole 1,1-dioxides **265**–**267**.¹⁷¹

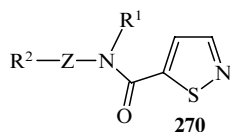
The reaction of the 5-bromo-derivative **255** with thiols or amines gives the substituted products of the bromine atom **268** and **269**.¹⁶⁸



IV. Areas of application of isothiazoles

As noted above, isothiazole derivatives manifest a broad spectrum of useful properties. Back in 1967, isothiazoles were used as starting compounds in the synthesis of highly efficient penicillins and cephalosporins,^{2,3} which gave a strong impetus to systematic studies of the biological properties of isothiazole derivatives. In 1988, Mel'nikov who studied the production and application of pesticides and plant growth regulators drew attention to the broad potentialities of isothiazole derivatives.¹⁷² Recent years have been marked by numerous publications (including patents and patent applications) devoted to various applications of isothiazoles as efficient agrochemical and medicinal agents.

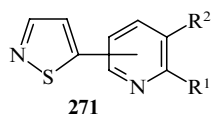
It was found that 4-benzoyl- and 4-(hetaroyl)isothiazole derivatives manifest herbicidal activities.^{85–88,173} There is evidence of the use of substituted isothiazole-5-carboxamides **270**,¹⁷⁴ isothiazolylpyridines **271**¹⁷⁵ and dihydroisothiazolone derivatives as herbicides.¹⁷⁶



$R^1 = H, (\text{un})\text{substituted alkyl}, (\text{un})\text{substituted acyl};$

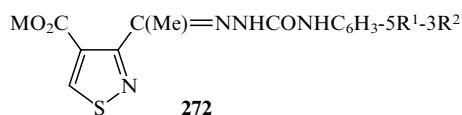
$R^2 = (\text{un})\text{substituted aryl}, \text{hetaryl};$

$Z = (\text{un})\text{substituted } C_1-C_4\text{-alkylene}.$



$R^1 = Hal, MeO, FCH_2O, F_3CO;$
 $R^2 = CN, CO_2H, CHO.$

When used as herbicides, isothiazole derivatives manifest synergistic effects and are included in various compositions. Thus compounds **272** are auxin transport inhibitors and are used together with other herbicides in order to enhance their action.^{10–14}

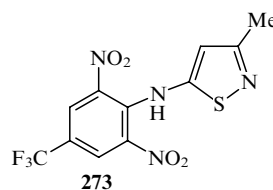


$R^1, R^2 = H, F, Cl; M = H, Na.$

The role of herbicides in these compositions is played by different compounds, *e.g.*, dicamba, glifosat, 2,4-D¹⁰ and herbicides based on phenoxypropionic¹¹ and phenoxybutyric acids.¹⁴

Some isothiazoles manifest high insecticidal activities. These include 4,5-dihydro-1*H*-pyrazole derivatives containing various isothiazole substituents in position 4,^{177,178} 1,2,3-triazole derivatives containing isothiazole substituents in position 3,¹⁷⁹ *etc.* The cyanoisothiazole derivatives **161** manifest high insecticidal activities against termites.¹⁸⁰

Many isothiazole derivatives, particularly acylated 5-aminoisothiazoles,^{94,95} isothiazolecarboxamides,^{96–98} 4-cyanoisothiazoles,^{112,123,124} 3,4-dichloroisothiazole-5-carboxylic acid and its derivatives,¹²¹ *etc.*, manifest fungicidal activities. (3-Methylisothiazol-5-yl)(2,6-dinitro-4-trifluoromethylphenyl)amine (**273**) is used as an agrochemical.¹⁸¹



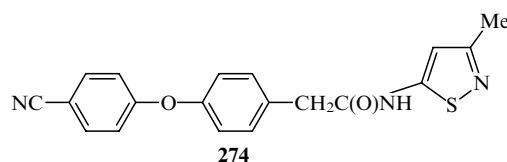
Many heterocyclic and aromatic compounds containing various isothiazole residues^{182,183} and 3-isothiazolone derivatives^{184–189} in their side chains manifest high fungicidal activities. Isothiazolones are broad-spectrum biocides; they are included in various compositions including commercial ones. They hold great promise for the technology and agriculture being non-harmful to humans, animals and the environment.^{20,23,30,190–197}

Isothiazole and isothiazolone derivatives are used in photography,^{198–212} cosmetics,^{213–215} and as dyes;^{216–218} besides, they are components of synergistic bactericidal preparations^{219–225} and are used in the chemiluminescent analysis^{226,227} of radiographic visualisation.²²⁸ Many of them are antifouling agents.^{229–235}

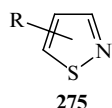
A great number of isothiazole derivatives manifest high antimicrobial activities and are widely used for the protection of natural and technical materials, plants and other objects from harmful microorganisms. These include 3-alkoxyisothiazoles (particularly, compound **122**),¹⁰⁴ allylic ethers **128–130**,¹⁰⁶ 5-aminoisothiazoles,²³⁶ 3,5-diaminoisothiazole derivatives **6**,⁵¹ isothiazolecarboxamides¹⁰¹ and the derivatives **125** and **126**.¹⁰⁵

The overwhelming majority of compounds endowed with antimicrobial activities were found among isothiazolone derivatives.^{237–265} It was found that the addition of even the simplest isothiazolones to various compositions, *e.g.*, 2-methyl- or 5-chloro-2-methyl-2,3-dihydroisothiazol-3-one, increase markedly their activities.^{266–271}

Some isothiazole derivatives manifest different types of biological activities. Thus acylated aminoisothiazoles (compounds **165**^{125,272} and **274**²⁷³) are used as insecticides and acaricides.



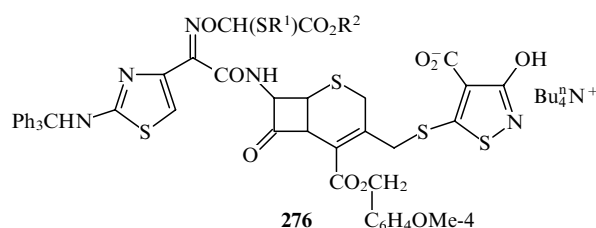
Compositions possessing bactericidal and fungicidal properties were prepared from some dihydroisothiazolones.²⁷⁴ Cyanoisothiazoles¹¹² are used as fungicides and bactericides. Compositions comprising aminoacrylamides and trisubstituted isothiazoles possess insecticidal, fungicidal and herbicidal activities.²⁷⁵ Compounds **275** have been patented as nematocides, insecticides and acaricides.²⁷⁶



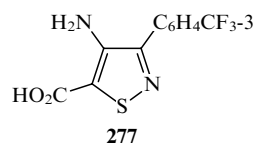
$R = CF_2=CHCH_2CH_2SO_n, n = 0-2$.

N-Isothiazol-5-ylamides (e.g., compound **110**⁹²) manifest an even broader range of pesticidal activities and possess nematocidal, insecticidal, miticidal and fungicidal properties.

An intense search for therapeutic agents among isothiazole derivatives has been carried out over the past decade. Cephalosporins containing a (4-carboxy-3-hydroxyisothiazol-5-yl)thiomethyl group in position 3 (**276**) are used as medicinal drugs possessing a broad spectrum of antibacterial activities, particularly with respect to gram-negative bacteria.²⁷⁷

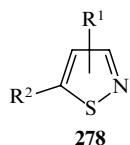


Isothiazolyl aminoalkyl ketones were patented as myorelaxants.²⁷⁸ 5-Carboxy-3-phenylisothiazoles, particularly 4-amino-3-(3-trifluoromethylphenyl)isothiazole-5-carboxylic acid (**277**), were recommended for use as antiinflammatory agents.²⁷⁹⁻²⁸¹



Dihydroisothiazol-3-one 1,1-dioxide derivatives inhibit serine proteases. They have been recommended for the treatment of various inflammatory diseases and as antimetastatic agents.^{7,8} Some aromatic and heterocyclic compounds containing isothiazole residues inhibit phosphodiesterase and are widely used in the clinical practice as antiasthmatic drugs and in the treatment of diabetes, hypertension, allergic rhinites, nephritis and other diseases.^{282, 283}

Compounds **278** and their salts have been patented as effective agents for the treatment of Alzheimer's disease.⁴



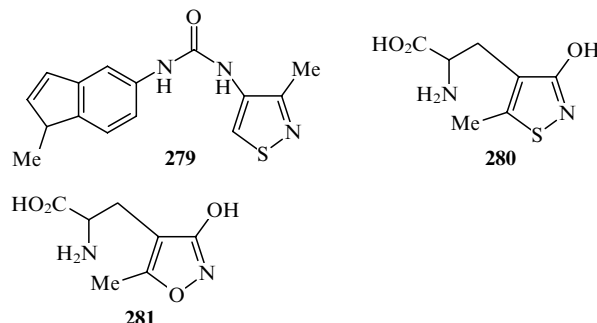
$R^1 = H, \text{ alkyl, cycloalkyl, (un)substituted phenyl};$
 $R^2 = \text{substituted pyrrolidinyl}.$

Trisubstituted isothiazole derivatives containing an amino acid or cyclobutene fragment in position 3 were recommended for the treatment of brain ischemia, Huntington's and Parkinson's diseases, epilepsy, Alzheimer's disease, schizophrenia, stress, anxiety and various memory disorders.²⁸⁴

5-Hydrazinoisothiazole derivatives act as immunodepressants,²⁸⁵ whereas 3-isothiazolone derivatives are included in the composition of weight reduction drugs.²⁸⁶ They are also used for modification of the interleukin-5 receptor.²⁸⁷

The isothiazole ring is the constituent of various physiologically active compounds. Thus heterocyclic derivatives of urea containing an isothiazole substituent act as antagonists of 5-HT_{2C} and 5-HT_{2B} receptors and are used in the preparation of antidepressant drugs and in the treatment of Alzheimer's disease, schizophrenia, etc.²⁸⁸ Compound **279** is a highly efficient antag-

onist of 5-HT_{2B} receptors, although its activity is not too high.²⁸⁹⁻²⁹¹ 2-Amino-3-(3-hydroxy-5-methylisothiazol-4-yl)propionic acid (**280**), the isothiazole analogue of 2-amino-3-(3-hydroxy-5-methylisoxazol-4-yl)propionic acid (**281**, AMPA), blocks the activation of glutamate receptors which are crucial for brain ischemia, Alzheimer's disease, hypoglycemia, etc.^{292, 293}



V. Conclusion

As can be seen from the material presented above, new original methods for the synthesis of many isothiazole derivatives have been developed in recent years. These include some previously unknown heterocyclisation reactions (e.g., the syntheses based on α -amino ketones and 2-nitropentachloro-1,3-butadiene), the syntheses of isothiazoles from other, more accessible heterocyclic compounds (particularly, the syntheses based on trithiatiazine trichloride) as well as the syntheses of previously unknown fluoro-substituted isothiazoles. Studies aimed at the functionalisation of isothiazoles, e.g., cross-coupling reactions which made possible the synthesis of previously unavailable derivatives (e.g., isothiazoles containing two acetylene groups) have received further development. The syntheses of biologically active amides, isothiazolones and highly reactive 1,1-dioxides have been carried out. Isothiazoles were used as starting materials for the synthesis of novel, previously unavailable biheterocyclic structures, such as imidazoisothiazoles, diisothiazolopyrazines, isothiazolotriazines, substituted pyrroloisothiazole 1,1-dioxides and other compounds.

Methods for the synthesis of various heterocyclic compounds (pyrazoles, thiadiazapentalenes and other hardly accessible compounds) from readily available isothiazole derivatives have been developed.

High biological activities of isothiazoles is the main impetus for conducting in-depth studies in the field of isothiazole chemistry. More than 50% of work cited in this review are patents devoted to the synthesis and applications of isothiazoles as efficient agrochemical and medicinal preparations.

Obviously, the exceptionally broad spectrum of useful properties of isothiazoles determines the expediency of further studies into their chemistry. We hope that the present review will help attract more attention to this field of chemistry.

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The use of molecular-statistical methods for the calculation of thermodynamic characteristics of adsorption for identification of organic compounds by gas chromatography – mass spectrometry

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Abstract. The current state of research on the theoretical description of adsorption in the Henry region by semiempirical molecular-statistical procedures, as applied to identification of organic compounds in complex mixtures, is considered. Various approaches to correcting the atom–atom potential parameters used to determine thermodynamic characteristics of adsorption are compared. Examples of calculations involved in the chromatographic and chromatography–mass spectrometric identification of model and real organic compounds including isomers are given. The bibliography includes 89 references.

I. Introduction

Identification of organic compounds in mixtures is one of the most complicated problems of physical organic chemistry. The main difficulty arising in the work with mixtures is that simultaneous solution of two problems is required: the mixture should be separated into components and the components should be identified. At present, the most informative and reliable method for identification of organic compounds is the chromatography–mass spectrometry (GC-MS) technique.¹ Modern instruments make it possible to analyse volatile compounds in the gas chromatography–mass spectrometry mode (GC-MS) and non-volatile compounds, in the liquid chromatography–mass spectrometry mode (LC-MS).² The use of different ionisation techniques allows one to produce stable molecular ions, to vary fragmentation and to detect both positive and negative ions.^{2,3} In recent years, the range of masses that can be determined has markedly extended due to application of new ionisation techniques.⁴ A significant advantage of mass spectrometry is the possibility to determine the masses of molecular and fragment ions in the high-resolution mode with an accuracy of millionths of atomic mass units. Thus, it is possible to determine almost unambiguously the elemental compositions of molecules.⁵ The only limitation that holds up extensive use of high-resolution mass spectrometers for identification of substances is their high cost, which is 5–10 times as high as the cost of instruments for routine analysis.⁶ Chromatography–IR spectroscopy or chromatography–NMR spectroscopy could be possible alternatives to the

GC-MS;⁷ however, the development of these techniques is held up by relatively low sensitivity of IR spectroscopy and insufficient speed of operation of NMR spectrometers.

Even a highly potent method such as high-resolution mass spectrometry does not allow reliable identification of isomers in complex mixtures. This is due to the fact that differences in the fragmentation can hardly be attributed unambiguously to the structure of a particular isomer. Therefore, the use of chromatographic data for identification of substances becomes very important.⁸ The procedures for chromatographic identification of compounds based on the use of reference compounds, specific detectors, preliminary chemical reactions,⁹ chromatographic spectra¹⁰ and dependences of retention indices on various molecular characteristics¹¹ have been developed fairly comprehensively and we do not consider them here. However, all these methods are much inferior to the GC-MS technique in labouriousness, information content and reliability.

When discussing the GC-MS identification, one should note that the methods of structure determination based on mass spectrometry data can be classified into three groups.

(1) Library search which consists in comparing the spectrum of an unknown compound with the spectra deposited in databases or libraries and selecting those spectra that fit best the spectrum of the compound under study.¹²

(2) Methods for representing the compound structure on the basis of fragmentation rules.¹³

(3) Methods for substance identification consisting in determination of structural features by statistical analysis.¹⁴

Successful utilisation of mass spectrometry and determination of the structures of organic compounds requires the use of empirical rules and regularities elucidated in the studies of large numbers of compounds belonging to different structural classes,^{13,15} the presence of vast libraries of standard mass spectra (up to 300 thousand) of compounds, the use of high-end software for image recognition which resort to data of other spectroscopic methods¹⁶ (not only experimental but also obtained by calculations¹⁷) for structure determination and advanced computing machinery. The use of GC-MS provides not only mass-spectroscopic but also chromatographic information, namely, the retention indices for various stationary phases. These values are sufficiently accurate because a mass spectrometer is a highly selective detector and chromatographic peaks are usually much better resolved in ionic mass chromatograms than in chromatograms recorded with other detectors.

Combination of chromatographic identification techniques with GC-MS to identify isomers in complex mixtures is usually resorted to in investigations carried out along two lines, namely, identification based on semiempirical molecular-statistical calcu-

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lations of retention values¹⁸ and identification using retention indices calculated theoretically.¹⁹

Retention index is a qualitative characteristic of a molecule correlated with physicochemical parameters, for example, with the molecule polarisability or with the melting or boiling point of the substance.^{8, 11, 19} Numerous equations have now been found to relate retention parameters (calculated as retention indices) to various physicochemical properties of molecules, in particular, isomer molecules.²⁰ Commonly, these equations make use of so-called increments which characterise separate fragments of a molecule that can be joined to form a new molecule. The main drawback of this approach is that assembling the increments gives an approximate geometrical structure rather than the real molecule. Therefore, fine intramolecular effects, especially those characteristic of isomers, can be taken into account only by introducing special corrections, which are rather arbitrary.²¹ Generally, this situation resembles the situation faced by an attempt to obtain precise values for molecular polarisability in terms of additive schemes — one too many corrections are needed to reach high accuracy. One more drawback of this method is the necessity of experimental determination of increments on the basis of a broad range of reference molecules.²² Extensive databases of experimental retention indices have now been composed; they can be efficiently used to identify separate classes of organic molecules.^{23, 24} Such bases are also supplemented by theoretically calculated indices; however, these have not yet found wide use.

Using the semiempirical molecular-statistical theory of adsorption, one can calculate the thermodynamic characteristics of adsorption (TCA) including the retention values for organic molecules of various classes. The theory is based on the use of atom–atom potentials (AAPs) for the interaction between the sorbent and sorbate atoms. An important advantage of this theory is the fact that the calculations of retention indices are based on the real structures of molecules, determined from electron diffraction data or constructed with allowance for the regularities of variation of bond angles and bond lengths. In the case of isomers, the TCA calculations alone based on real data on the molecular structure permit reliable identification of compounds.

II. Semiempirical molecular-statistical theory of adsorption

1. Scope of molecular-statistical calculations

To date, molecular-statistical calculations of TCA have been carried out for a broad range of adsorbents and adsorbates. The calculations of TCA for inert gases, simple polar molecules and hydrocarbons on zeolites of various types²⁵ and on porous crystalline silica (silicalite) have been reported.^{26–28} The molecular-statistical calculations have been developed most thoroughly for systems comprising graphitised thermal carbon black (GTCB) and hydrocarbons or their derivatives.²⁹ Graphitised thermal carbon black is a good model sorbent because it has a homogeneous planar surface the geometry and the chemical properties of which have been studied in sufficient detail. Vast experimental information on the adsorption of organic compounds of various classes on the GTCB surface has been accumulated.^{29, 30} The main reason why the molecular-statistical calculations for the adsorption on GTCB surface are being developed and improved is the fact that this process is exceptionally sensitive to the structure of adsorbed molecules. This creates conditions for the separation of geometric isomers.^{30–32} In most cases, a combination of the molecular-statistical calculations and GC-MS data provides unambiguous identification of individual isomers in complex mixtures.^{18, 32}

2. The procedure of molecular-statistical calculations

Kiselev and Poshkus^{29, 30} developed a semiempirical molecular-statistical method for the calculation of thermodynamic characteristics of the physical adsorption of gases on GTCB at very low surface coverages. Within the framework of this method, the

Henry constant (K_1) for the adsorption of quasi-rigid molecules is calculated using the equation

$$K_1 = \frac{1}{4\pi} \int \left(\frac{2\pi kT}{\Phi_z''} \right)^{1/2} \exp\left(-\frac{\Phi_0}{kT}\right) \sin \Theta d\Theta d\psi, \quad (1)$$

where Φ_0 and Φ_z'' are the potential function Φ values for the interaction between the adsorbate and adsorbent molecules in a potential minimum and its second derivative with respect to the distance z from the center of gravity of the molecule to the adsorbent surface; Θ and ψ are Euler angles, which define the orientation of the molecule relative to the adsorbent surface. The Φ_z'' and Φ_0 values and the equilibrium distance z_0 depend on Θ and ψ . The potential function Φ is presented as the sum of the AAPs for the interaction of each atom of the adsorbed molecule (A) with each carbon atom of GTCB (C_{GTCB}).

$$\Phi = \sum_A \sum_{C_{\text{GTCB}}} \varphi_{A...C_{\text{GTCB}}}. \quad (2)$$

The $\varphi_{A...C_{\text{GTCB}}}$ potential is written in the Buckingham–Corner form (6, 8, exp)

$$\varphi_{A...C_{\text{GTS}}} = -C_6 r^{-6} - C_8 r^{-8} + B \exp(-qr), \quad (3)$$

where C_6 , C_8 are the parameters of the dipole–dipole and dipole–quadrupole dispersion interaction potentials; r is the interatomic distance; B and q are parameters of the repulsion potential. The C_8 and C_6 values are estimated using approximate quantum-mechanical formulae. The parameter C_6 is found using the Kirkwood–Müller relation

$$C_6 = -6m_e c^2 \frac{\alpha_a \alpha_b}{(\alpha_a/\chi_a) + (\alpha_b/\chi_b)}, \quad (4)$$

where m_e is the mass of an electron; c is the velocity of light; α_a , α_b are polarisabilities of atoms a and b ; χ_a and χ_b are diamagnetic susceptibilities of atoms a and b .

The parameter C_8 is estimated using the formula

$$C_8 = \frac{45h^2}{32\pi^2 m_e} \alpha_a \alpha_b \left[\frac{1}{2} \left(\frac{\alpha_b/\chi_b}{\alpha_a/\chi_a} + 1 \right)^{-1} + \frac{1}{2} \left(\frac{\alpha_a/\chi_a}{\alpha_b/\chi_b} + 1 \right)^{-1} \right], \quad (5)$$

where h is Planck's constant. The repulsion parameter B is expressed in terms of the equilibrium interatomic distance r_0 and other AAP parameters using the equilibrium condition for all the attraction and repulsion forces for $r = r_0$

$$\left(\frac{d\varphi}{dr} \right)_{r=r_0} = 0, \quad (6)$$

$$B = \frac{6C_6 \exp(qr_0)}{qr_0^7} \left(1 + \frac{4C_8}{3C_6 r_0^2} \right). \quad (7)$$

The parameter q is taken to be 35.7 nm^{-1} . The equilibrium distance r_0 is normally estimated using crystal parameters or data on the interaction of atoms of the adsorbate molecule with GTCB. In particular, the value $r_0 = 0.382 \text{ nm}$ was accepted for $C...C_{\text{GTCB}}$ (this value was obtained from data on the graphite lattice properties) and $r_0 = 0.341 \text{ nm}$ was taken for $H...C_{\text{GTCB}}$. The summation of φ over the GTCB carbon atoms above the graphite basis plane is done using the Crowell approximation.³⁰ The potential function Φ_i for the interaction of an i -th atom of the molecule with the graphite basis plane is calculated from the equation

$$\begin{aligned} \Phi_i = & -C_{6,i} \frac{\pi^9}{2d^4} \zeta \left[\frac{z_i}{d}, 4 \right] - C_{8,i} \frac{\pi^9}{3d^6} \zeta \left[\frac{z_i}{d}, 6 \right] + \\ & + \frac{2B_i \pi^9}{q^2} (qz_i + 1) e^{-qz}, \end{aligned} \quad (8)$$

where $\vartheta = 0.382 \times 10^{-3} \text{ nm}^{-2}$ is the number of carbon atoms per unit area of the graphite basis plane; d is the interplanar spacing in graphite equal to 0.356 nm; ξ is the Riemann zeta function; z_i is the distance from the i -th atom to the plane passing through the centres of atoms of the outermost atomic layer of graphite. Relation (8) takes into account the contribution of only the outermost atomic layer of graphite to the repulsion energy.

The differential molar changes of the intrinsic energy ΔU_1 and entropy ΔS_1 upon adsorption are calculated using the relations

$$\Delta U_1 = RT^2 \frac{d \ln K_1}{dT}, \quad (9)$$

$$\frac{\Delta S_1}{R} = \ln K_1 + T \frac{d \ln K_1}{dT} - 1. \quad (10)$$

A special program is used to calculate the TCA.³³ The parameter C_6 is first estimated from Eqn (4). However, the K_1 and ΔU_1 values found using the C_6 value determined in this way differ markedly from the corresponding experimental data.²⁹ Therefore, the AAPs for the interaction of atoms in the adsorbate molecule with GTCB ($\varphi_{H...C_{GTCB}}$ and $\varphi_{C...C_{GTCB}}$ for each atom of the molecule in different valence states) are further corrected using relations (4)–(11) and the experimental K_1 values for one or two simple representatives of the class of hydrocarbons under consideration. The $\varphi_{H...C_{GTCB}}$ and $\varphi_{C(sp^3)...C_{GTCB}}$ values are corrected assuming that the parameters C_8/C_6 , r_0 and q , estimated in terms of the properties of the adsorbate and the adsorbent taken separately, differ only slightly from the exact values and that the following equality holds:

$$\frac{C_{6,C...C}}{C_{6,C...H}} = \frac{C_{6,C...C}^{KM}}{C_{6,C...H}^{KM}}, \quad (11)$$

where $C_{6,C...C}$ and $C_{6,C...H}$ are the values of parameters that satisfy experimental data; $C_{6,C...C}^{KM}$ and $C_{6,C...H}^{KM}$ are the C_6 values estimated using the Kirkwood–Müller formula. If these assumptions are valid, the corrected potential functions φ are related to the rough functions φ^* in the following way:

$$\varphi = \beta \varphi^*, \quad (12)$$

$$\Phi = \sum_A \sum_{C_{GTCB}} \varphi = \beta \sum_A \sum_{C_{GTCB}} \varphi^* = \beta \Phi^*, \quad (13)$$

where

$$\beta = \frac{C_{6,C...C}}{C_{6,C...C}^{KM}} = \frac{C_{6,C...H}}{C_{6,C...H}^{KM}}. \quad (14)$$

The β coefficient is usually determined by comparing the K_1 values calculated on the basis of Φ^* with those found experimentally. The equations for the interaction potentials of atoms in alkanes with GTCB corrected in this way (kJ mol^{-1}) have the form

$$\varphi_{C(sp^3)...C_{GTCB}} = -1.386 \times 10^{-3} r^{-6} - 2.148 \times 10^{-5} r^{-8} + 1.89 \times 10^5 \exp(-35.7r), \quad (15)$$

$$\varphi_{H...C_{GTCB}} = -0.498 \times 10^{-3} r^{-6} - 0.950 \times 10^{-5} r^{-8} + 3.60 \times 10^4 \exp(-35.7r). \quad (16)$$

The K_1 and ΔU_1 values calculated using these potentials for alkanes with known molecular structures are close to experimental results. Assuming that the $\varphi_{H...C_{GTCB}}$ potential of the hydrogen atom in a hydrocarbon molecule does not depend on the valence state of the carbon atom and that the r_0 and q parameters are identical for carbon in any valence state, it was found that

$$\varphi_{C(sp^2)...C_{GTCB}} = \delta \varphi_{C(sp^3)...C_{GTCB}}, \quad (17)$$

where δ is the parameter depending on the valence state of the carbon atom.

Using the experimental K_1 values, it was found for ethylene that

$$\varphi_{C(sp^2)...C_{GTCB}} = -1.48 \times 10^{-3} r^{-6} - 2.30 \times 10^{-5} r^{-8} + 2.026 \times 10^5 \exp(-35.7r). \quad (18)$$

Relying on the K_1 values determined experimentally for acetylene adsorption, the potential $\varphi_{C(sp)...C_{GTCB}}$ can also be calculated. These potentials were used to calculate the TCA for a large number of hydrocarbons: alkanes,³⁴ cycloalkanes,^{29, 35} alkenes, alkynes³⁶ and aromatic hydrocarbons³⁷ on the GTCB surface. In the case of hydrocarbons with known molecular structures, the TCA values found in this way coincide with the corresponding experimental values to within the error of determination.

The above-described procedure was used to determine the AAPs for the interaction of the carbon atoms in graphite with oxygen in two valence states (in ethers and ketones)³⁸ and to calculate the TCA for a number of oxygen-containing organic compounds on the GTCB surface.³⁹

Guiochon and coworkers^{40, 41} also used the molecular-statistical method for calculation of the TCA for various hydrocarbons and their chlorinated derivatives; however, these calculations were performed using uncorrected AAPs, therefore, the calculated and experimental TCA markedly differ. When calculating Φ for complex conjugated molecules, researchers attempted to take into account the anisotropy of graphite polarisability.⁴² For chloro-derivatives of aromatic hydrocarbons, it was found that the order of elution of isomers out of the column is better described by a model that does not take into account the electrostatic interaction of the adsorbate molecule with the adsorbent surface.⁴¹

Apart from the organic compounds mentioned above, adsorption of noble gases^{29, 30} and nitrogen,⁴³ sulfur- and selenium-containing⁴⁴ compounds on the GTCB surface has also been studied. Some of the AAP parameters known to date are listed in Table 1. Satisfactory agreement of the experimental results with the theoretical results obtained using these parameters is attained in those cases where the mutual influence of atoms in the adsorbed molecule is insignificant. When the mutual influence of atoms is substantial, corrections should be applied to the AAPs. In some

Table 1. Parameters of the AAPs for the interaction of various atoms with the GTCB carbon atom.

Element	AAP parameter ^a			β
	C_6	C_8	B	
Hydrogen	−0.5672	−0.06403	1618.0	—
Fluorine	−0.9775	−0.07000	2903.800	0.85
Carbon				
sp^3	−1.5750	−0.14530	8491.0	—
sp^2	−1.6853	−0.15547	9085.370	—
Chlorine				
see ^b	−4.2180	−0.38000	31189.489	0.95
ortho	−4.0848	−0.36800	30204.558	0.92
ortho-ortho	−3.9516	−0.35600	29219.626	0.89
Oxygen				
ketone	−1.1194	−0.11005	3250.015	—
ether	−1.7519	−0.17223	5086.273	1.565
Sulfur	−3.8672	−0.45069	26759.806	—
Bromine				
see ^b	−5.0740	−0.45060	37501.136	0.76
ortho	−4.9404	−0.43878	36514.270	0.74
Nitrogen	−1.6318	−0.26445	6194.358	—

^a C_6 is expressed in $\text{kJ m}^6 \text{mol}^{-1}$, C_8 is in $\text{kJ m}^8 \text{mol}^{-1}$, and B is in kJ mol^{-1} . ^b An atom not interacting with the neighbouring atoms in the molecule.

cases, the calculations are hampered by the absence of precise structural parameters for sorbate molecules.⁴⁵

Thus, fairly good agreement between the calculated and experimental TCA values for compounds with known molecular structures is attained if corrected AAP values are used to calculate the potential function of intermolecular interactions.

However, for some molecules, TCA cannot be predicted with a satisfactory accuracy. For example, during identification of isomers in mixtures, the sequence of isomer emergence from the column with GTCB predicted by calculations does not coincide in some cases with the experimental one. This is due to the difference between the AAP parameters for atoms incorporated in the molecule in question and the parameters corrected using the reference molecules. The difference is caused by the change in the nearest environment or valence state of the atom, manifested as a change in polarisability. Therefore, to identify separate isomers in complex mixtures and to determine reliable TCA (especially, the Henry constants), one must find the precise values for the AAP parameters.

3. Correction methods for the parameters of the atom – atom potentials

Several methods for correcting the AAP parameters have been developed to date.

a. Traditional method

The approach proposed by the developers of the semiempirical molecular-statistical theory of adsorption²⁹ can be considered to be the first of the known methods for correcting the AAP parameters. This approach is based on determination of individual AAPs (using reference molecules) for atoms forming the molecule under study, including chemically identical atoms in different valence states. In terms of the semiempirical molecular-statistical theory,²⁹ the AAP parameters are determined from approximate quantum-mechanical formulae (see above) using some characteristics of adsorbate and adsorbent atoms, *e.g.*, polarisability, diamagnetic susceptibility and equilibrium distances. The atom – atom potentials determined for the interaction of atoms of the adsorbate molecule with the adsorbent (GTCB) carbon atoms are corrected using the comparison of the theoretical and experimental Henry constants K_1 for the adsorption of a representative of the class of compound studied. The correction is carried out using so-called reference molecules, whose adsorption has been studied most comprehensively. The obtained AAPs are assumed to be transferable, *i.e.*, they allow correct prediction of the TCA for any molecule that contains the corresponding atoms. This procedure was used to determine and correct the AAP parameters for the adsorption of alkanes, alkenes, alkynes and aromatic hydrocarbons on GTCB; methane and ethane, ethylene, acetylene, and benzene, respectively, served as the reference molecules. In these calculations, three AAPs for carbon atoms corresponding to the sp^3 , sp^2 and sp^1 hybridisation states were found; they differ only by the correction factors, which are equal to 1.00, 1.07, and 1.27, respectively. Two AAPs for the oxygen atoms in ethers and ketones were found in the same way; they differ by the correction factors, which are 0.72 and 0.92, respectively.³⁸ The AAPs for sulfur, selenium,⁴⁴ fluorine,⁴⁶ chlorine,⁴⁷ and bromine⁴⁸ were determined. The corresponding correction factors are equal to 0.87, 0.89, 0.85, 0.95 and 0.76, respectively. Actually, this approach is similar to the calculation of polarisabilities, diamagnetic susceptibilities, and the dipole moments of molecules in terms of additive schemes.⁴⁹ The AAPs determined in this way were used to predict the TCA for a number of hydrocarbons and their derivatives, which are in good agreement with experimental data.^{36,38,46} However, for many molecules [both relatively simple ones such as *ortho*-halobenzenes,⁵⁰ perhydroanthracenes, perhydrophenanthrenes,⁵¹ heterocyclic nitrogen-containing compounds,^{52,53} and fairly complex molecules such as molecules with abnormal geometric parameters (strained mole-

cules), with bulky substituents, with several heteroatoms, and their unusual combinations], the TCA could not be correctly predicted.

The main drawbacks of the above method are as follows. For each valence state (and, in the general case, for each type of the atom nearest environment), one must know a separate AAP, which has to be corrected on the basis of experimental data for reference molecules. However, the number of these AAPs may become too large (especially for carbon, oxygen and nitrogen atoms), which would complicate the calculation. In addition, this procedure does not take into account the changes in the AAPs caused by the influence of atoms not bound by valence bonds.

b. Taking into account the dependence of the atom – atom potentials on the bond angles

The method proposed by Arkhipova⁵⁴ takes into account the effect of the change in the geometric parameters of a molecule on the carbon atom hybridisation and, correspondingly, on the AAP parameters. A pattern of dependence of AAP parameters on the deviation of the bond angles formed by carbon atoms from the ideal values corresponding to the sp^3 , sp^2 and sp^1 hybridisation states has been proposed. Using this dependence, one can determine more precisely the AAP values for atoms that form non-ideal bond angles. The results obtained by this method for a series of strained molecules (for example, cyclopropane derivatives and some bicyclic compounds) are in good agreement with experimental data. An example illustrating the efficiency of this method is the correct (experimentally confirmed) prediction of the order of elution of C_8H_{12} isomers, cyclobutadiene and bicyclo[3,3,0]oct-1,5-ene, from a column with GTCB, which could not be determined without applying corrections.

However, this method also suffers from serious drawbacks: first, it is applicable only to molecules with a known geometry because corrections are based on structure differences; second, determining a correction requires the knowledge of, at least, two boundary potentials, because the correction provides some intermediate value of the AAP parameters; third, this method cannot be used to correct the AAP parameters that change under the influence of non-bonded atoms, which does not distort the geometric structure of the molecules. Other 'AAP parameter – atom property' relationships have also been constructed; the atom properties used in these relationships are, in particular, the polarisability, the effective charge, the shielding constant, and the hybridisation state. The methods based on these dependences suffer from the above drawbacks.⁵⁵

c. Variation of the parameters of atom – atom potentials

The variation of the AAP parameters is done in order to minimise the discrepancy between the experimental and calculated data for all molecules of the group chosen for the investigation; this can be done, for example, by the regularisation technique.⁵⁶ A single parameter can also be varied. For example, in the calculation of AAP for a series of bromobenzene molecules, the role of this parameter was played by the equilibrium distance between the GTCB carbon atom and the bromine atom.⁴⁸

However, this method allows one to attain the optimal agreement between the experimental and theoretical results only for the considered group of molecules. The transfer of parameters corrected for a given group of molecules to other (even 'related') molecules usually results in a deviation between the experimental and calculated values for new molecules. For example, the AAP values corrected by varying the GTCB carbon – halogen equilibrium distance are in good agreement with experimental data only for the molecules of halobenzenes containing no halogen atoms in *ortho*-positions.⁴⁸ Otherwise, to describe experimental data with a satisfactory accuracy, additional corrections taking into account the mutual influence of atoms (corrections for *ortho*-effects) should be applied when calculating the AAPs.

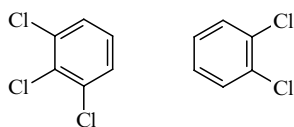
d. The use of corrected initial data for the calculation of atom – atom potentials

It is known⁵⁷ that the mutual influence of atoms can change their polarisabilities. In calculations of the TCA, these changes are taken into account either by applying additional corrections to the equations for AAP⁴⁸ or by using corrected polarisabilities. In our opinion, the use of corrected polarisabilities is most efficient for calculating the TCA of perhalogenated compounds, first of all, freons, for which isostructural fragments can hardly be chosen (or there are too many of them). The adsorption heats⁵⁸ of such compounds are described satisfactorily, within the experimental error, without introducing any corrections; however, for predicting the Henry constants, the correction of the AAPs is necessary. The method in which corrected initial data (first of all, polarisabilities and diamagnetic susceptibilities) are used in the calculation of the AAP parameters is of undisputed interest also due to the fact that a vast experimental base has now been accumulated and detailed additive schemes for polarisability calculations for molecules of diverse compounds,⁵⁹ especially perhalogenated ones, have now been developed.

A shortcoming of this method is the need to measure the polarisabilities, which requires a substantial amount of the material. In addition, one should borne in mind the relatively low accuracy of the polarisability values calculated according to additive schemes,^{60,61} which can lead to greater errors in the calculations of the TCA.

e. The introduction of corrections for *ortho*-effects

Changes in the AAP parameters are due to the mutual influence of atoms, in particular, when they occupy *ortho*-positions.⁶¹ By varying these parameters, one can attain the correspondence between experimental and theoretical data for an *ortho*-substituted molecule with known experimental TCA. The corrected AAPs can be used for the calculation of TCA for other molecules with atoms in *ortho*-positions. The applicability of this approach (the introduction of corrections for the *ortho*-effect) was demonstrated in relation to halobenzenes.⁴⁸ Actually, this method for correcting the AAPs is similar to the method using reference molecules (and, correspondingly, the drawbacks are also the same) but applies to a more limited group of molecules. In some cases, additional corrections are required to bring the theoretical results in correspondence with the experiment, for example, *ortho* – *ortho*-effect corrections.⁶² As an example, one can consider 1,2-dichlorobenzene and 1,2,3-trichlorobenzene molecules in which corrections for the *ortho*- and *ortho* – *ortho*-effects are required.



Probably, it is expedient to apply such corrections to molecules that possess specific properties, for example, to adamantane in which 1-substituents are subject to the 'cage effect', which is also involved in adsorption.

The term 'cage effect' implies the overlap of the electronic orbitals of the carbon atoms at the 1-positions which are not bound by valence bonds. This overlap brings about a substantial difference between the properties of 1- and 2-substituted isomers, which is manifested, in particular, in the chromatographic separation on phases having different polarity. The allowance made for the cage effect for chloro-⁶³ and amino-substituted adamantane isomers⁶⁴ permitted the prediction of the correct order of isomer elution from a column packed with GTCB, whereas traditional calculations⁶⁵ did not provide a correct prediction. The overlap of the orbitals of the bridgehead carbon atoms and their influence on the substituent (amino group) polarisability is illustrated by Fig. 1.

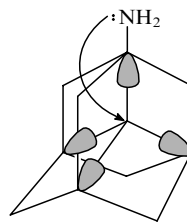


Figure 1. Cage effect in the 1-aminoadamantane molecule.

f. The method of isostructural fragments

The method of isostructural fragments⁶⁶ (IF) is based on the use of AAPs corrected for some single molecule or its fragment in the calculations made for other molecules containing the same fragment. For a molecule containing the isostructural fragment, the AAPs are corrected by processing the theoretical and experimental values by the least-squares calculations, their agreement being attained by varying the correction factor. In doing this, the AAPs for atoms of one sort are changed, in order to decrease the total number of AAPs used in calculations. The IF is chosen on the basis of comparison of the geometrical structures of molecules of the group under interest; in particular, the specially obtained electron diffraction data, the known regularities of the change in the bond angles and bond lengths in groups of related molecules, or the results of quantum-chemical calculations can be compared. Usually, molecules with a geometrical structure (or its fragment) common to the given class of molecules are chosen as the IF. For example, in the case of cyclopropane derivatives, this is the cyclopropane molecule, and for *ortho*-substituted chlorobenzenes and naphthalenes, this is the 1,2-dichlorobenzene molecule.

In fact, the IF method allows one to overcome the limitations of the atom – atom approximation and takes into account the mutual influence of atoms and groups of atoms including the change in the polarisabilities and geometric parameters of the interacting fragments.

g. The method of variation of the molecular geometry

An important benefit of the semiempirical molecular-statistical theory of adsorption is the use of structural parameters of molecules in the TCA calculations. However, this benefit is simultaneously a drawback, because exact parameters of the molecular structure have been determined for a limited range of substances and, normally, they are lacking for most of isomers. An alternative to all the methods of AAP correction considered above is the method of variation of the geometric parameters of the molecule. This procedure has been used to predict the retention values for perhydroanthracenes and perhydrophenanthrenes.⁵¹ By using this variation, the researchers predicted the order of isomer elution from a GTCB column that coincided with the experimental results. However, the geometry variation, especially for molecules with an unknown structure, is legitimate only in the case of quantitative comparison of theoretical and experimental data, and, naturally, it is impossible to estimate the variation of the AAP parameters in terms of this method.

4. Comparison of various methods for the correction of the atom – atom potential parameters

Among the methods for correcting the AAP parameters considered above, the following are most important: the method based on the use of corrected initial data (first of all, polarisability); the introduction of *ortho*-effect corrections and the IF method. The Henry constants calculated using the AAP parameters corrected by these methods for a number of molecules have been compared.^{66,67} The results of comparative analysis confirm the good prospects of the IF method.

For a number of chlorobenzenes with different degrees of substitution, the Henry constants were calculated using the AAP values corrected by various methods and the results were com-

pared. The chlorobenzene molecules were chosen as the model series because they represent groups of isomers, and the sequence of elution of isomers from a GTCB column is an important criterion of the reliability of calculations. In addition, both experimental and calculated TCA determined by various methods are available for molecules of this series (Table 2).^{41, 47, 48, 68} Of all possible TCA that can be calculated using the semiempirical molecular-statistical adsorption theory, the Henry constants were chosen as the characteristics most sensitive to variations of the AAP parameters and the geometrical structures of molecules. It was shown^{48, 50} that even for molecules containing no strained fragments or *ortho*-arranged atoms, the experimental and theoretical values of the Henry constants can be brought in correspondence by correcting the AAP only in terms of the procedure of reference molecules. Therefore, corrections were applied to the already corrected potential, which was 5% smaller than the initial one.

In the calculations in terms of the IF method, known AAPs tested in the calculations of TCA for chlorobenzenes were used as the basic parameters. The IF chosen were 1,2-di- and 1,2,3-trichlorobenzenes. Relying on the experimental data for these molecules (the Henry constants and their differences for isomers

Table 2. Values $\ln K_1$ ($\text{cm}^3 \text{m}^{-2}$) for the adsorption of chlorobenzenes on GTCB at 473 K obtained experimentally and calculated using the AAPs corrected by various methods.⁵⁰

Molecule	Experiment	Calculations				
		1	2	3	4	5
Chlorobenzene	−0.44	−0.44	−0.44	−0.44	−0.44	−0.44
1,3-Dichlorobenzene	0.93	0.98	0.98	0.98	0.98	0.98
1,2-Dichlorobenzene	1.01	1.15	1.10	1.01	1.01	1.08
1,4-Dichlorobenzene	1.06	1.06	1.06	1.06	1.06	1.06
1,3,5-Trichlorobenzene	2.23	2.25	2.25	2.25	2.25	2.25
1,2,4-Trichlorobenzene	2.41	2.59	2.54	2.44	2.44	2.50
1,2,3-Trichlorobenzene	2.42	2.82	2.74	2.52	2.52	2.60
1,2,3,5-Tetrachlorobenzene	3.86	4.19	4.11	3.86	3.88	3.40
1,2,4,5-Tetrachlorobenzene	3.89	4.23	4.12	3.92	3.92	4.02
1,2,3,4-Tetrachlorobenzene	4.24	4.47	4.37	4.03	4.06	3.58

Notes. The correction of the AAPs by method 1 was carried out using the reference 1,4-dichlorobenzene molecule;⁴⁸ the correction by method 2 was based on the experimental polarisability value determined in Ref. 60 for the chlorine atoms in 1,2-dichlorobenzene (in the calculations of $\ln K_1$ for other chlorobenzenes, these corrected AAP values were used only for *ortho*-arranged chlorine atoms); in method 3, the corrections for the *ortho*- and *ortho-ortho*-effects were taken from Refs 48, 50; in the case of method 4, 1,2-di- and 1,2,3-trichlorobenzenes were chosen as the isostructural fragments; the corrections for the AAPs based on the experimental Henry constants or the differences between the retention of neighbouring isomers is 0.92 for the fragment containing two chlorine atoms in *ortho*-positions and 0.91 for the fragment containing three atoms of this type; in the correction by method 5, the molecular geometry was varied assuming that *ortho*-chlorine atoms cause a deflection of the carbon–chlorine bond from the benzene ring plane; for the first five chlorobenzene molecules, the angles of deflection of the carbon–chlorine bonds from the benzene ring plane were taken from Ref. 48, while for other isomers, the transferability of the angles was assumed, in particular, in calculations of the Henry constant for 1,2,3-trichlorobenzene, a value of 78 was taken, as for 1,2,4-trichlorobenzene, while in the case of 1,2,3,4- and 1,2,3,5-tetrachlorobenzenes, this value was 128, as for the 1,2,4,5-substituted isomer.

closest in retention values), researchers obtained corrections for the AAPs to describe the interaction between the chlorine atom and the graphite carbon atom. In any case, the molecular-statistical calculations were carried out as described above (see Section II.2). The geometric parameters of molecules were found either from electron diffraction data or by combining the known parameters for other molecules of the given group.

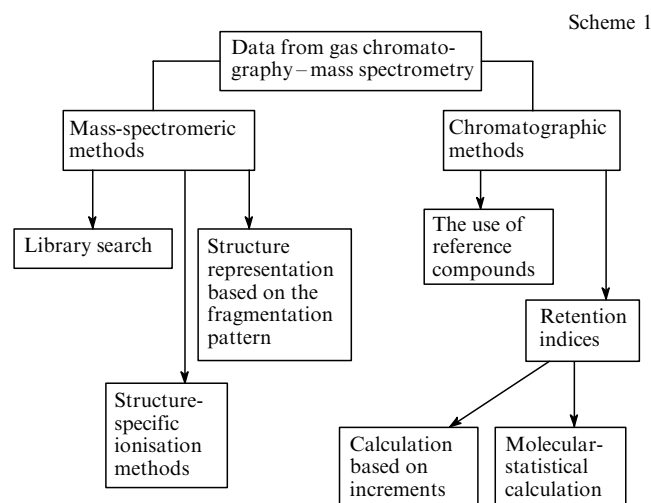
However, the introduction of corrections by some procedures does not always provide the best correspondence between the experimental and calculated data. For example, the use of the method of reference molecules, the method of correcting the polarisability values and the geometry variation give rise to inconsistency between the experimental and calculated orders of isomer elution out of a GTCB column, and for some isomers, the experimental and theoretical $\ln K_1$ values differ appreciably (see Table 2). The best results are provided by the IF method and by applying the *ortho*-effect corrections.

The IF method appears to be more versatile and reliable because its application rules out the uncertainty related to the geometrical structures of molecules. Naturally, it is suitable for refining the parameters of AAPs not only for the molecules considered above. In our opinion, this method is especially advantageous for calculating the TCA of complex (in particular, isomeric) molecules containing heteroatoms and strained fragments.

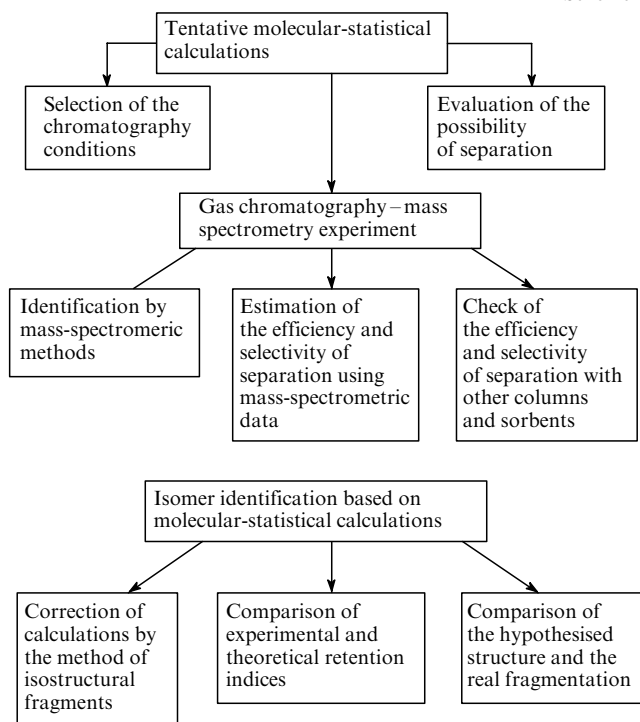
5. Combination of the gas chromatography – mass-spectrometry data with semiempirical molecular-statistical calculations

When calculating retention indices, in particular, Kovac indices, an approximate rather than real structure of the molecule is actually used.^{8, 10} Therefore, in those cases where corrections for definite effects have not been applied, identical values are usually obtained for isomers. The corrections are not transferable: usually, they are applicable only to the group of molecules for which they have been determined. When the retention indices are calculated within the framework of the semiempirical molecular-statistical adsorption theory, the real structure of the molecule is used.^{18, 30} To increase the efficiency of GC-MS identification, one should take into account the retention indices calculated in terms of this theory. Scheme 1 represents the pattern of usual GC-MS identification,^{1, 5} while Scheme 2 shows the identification procedure based on the molecular-statistical calculations.⁶⁷

The first stage consists in molecular-statistical calculations performed to estimate tentatively the possible efficiency of the chromatographic column. The tentative calculations help to answer the key question of whether the isomers under consideration can be separated by chromatography using a GTCB column. Adsorption of a broad range of substances on this sorbent has now been studied, but their number, of course, is not



Scheme 2



commensurate with the number of known organic compounds; therefore, the tentative calculation of the TCA is a necessary item in the research. In addition, these calculations permit one to optimise the conditions of the chromatographic experiment planned, to choose the temperature, the carrier gas velocity, the adsorbent weight and the column length.

The next stage is the GC-MS study in which individual isomers are to be separated and identified on the basis of differences in the mass spectra or, if the spectra are identical, it is necessary to confirm that the substances being analysed belong to the group of isomers in question. The efficiency and selectivity of the chromatographic separation is evaluated on the basis of the observed overlapping mass spectra. The modern instrumentation and computer software for data processing allow this to be done in the mass chromatography and mass fragmentography modes. To verify the completeness of separation attained on a micropacked column with GTCB, it is expedient to record the chromatogram on a highly efficient capillary column most appropriate regarding the selectivity (in order to compare the results obtained with different columns).

The next stage is conduction of molecular-statistical calculations for isomers using corrections for the possible variations of the AAP parameters. In the simplest case, identification can be performed by comparing the sequence of isomer elution from a GTCB column observed experimentally with the calculated one. The experimental retention indices and those determined by molecular-statistical calculations can also be compared, which is generally preferred. In addition, the data on the molecular structure used in the calculations can be verified by examining fragmentation of the molecule, induced, for example, by an electron impact.

Comparison of Schemes 1 and 2 shows that the identification procedure resorting to molecular-statistical calculations provides more reliable results. It is evident that combination of the results obtained in terms of the molecular-statistical theory with the results of a mass-spectrometric experiment would allow one to increase the efficiency, reliability and the information contents of the method and, hence, to solve the problem of isomer identification at a new level.

Correlation equations that relate the Henry constant,⁶⁹ the second virial coefficient of the intermolecular interaction,⁷⁰ or the

heat of adsorption⁷¹ to some characteristics of the molecule are usually considered as alternatives to the molecular-statistical calculations. The critical temperature and pressure or both,⁷¹ the molecular refraction,⁷² the dipole moments and the boiling points⁷³ are used most often. An advantage of such calculations is the possibility of changing the sorbent^{71,73} or specifying the degree of its inhomogeneity,⁷⁴ which helps to elucidate the applicability of a sorbent to the separation and analysis of a particular group of substances. Good correlation coefficients are usually obtained for series of related molecules;⁶⁹ however, the relationship between the molecular structure and the physico-chemical characteristics of adsorption remains obscure. Therefore, these methods are suitable only as auxiliary ones in the identification of isomers.

An *ab initio* molecular-statistical method for calculation of the Henry constant has been developed.^{75–80} The method makes use of the relationship between the structural characteristics of molecules and the energetic, geometric and topological^{81–84} properties involved in the adsorption. Unlike the traditional semiempirical molecular-statistical theory, the main idea of this approach has been the refusal of the additivity principle for AAP. Instead, the view of generalised charge of the molecule was introduced and a law for summing these charges was postulated. This theory was used to calculate the TCA for various types of hydrocarbons on GTCB and to determine the Kovac indices on a nonpolar stationary liquid phase (squalane). The calculated values are in good agreement with experimental data. This calculation method appears rather promising; however, it belongs to quantum chemistry and requires a separate review to be described.

III. The use of theoretical methods for identification of compounds

Mixtures of isomers can be separated into groups in conformity with the known numbers of isomers present. The simplest situation arises when the mixture is known to contain all the possible isomers or when this can be determined from the results of a GC-MS experiment. When analysing mixtures of isomers with a 'rigid' structure on a GTCB column, one should merely calculate the order of elution and thus identify the isomers. Such procedure has been carried out for the components of a mixture of *endo*- and *exo*-tetrahydrobicyclopentadienes. The *endo*-isomer has lower TCA and, correspondingly, it is the first to come out of the GTCB column. In this case, the fact that the mass spectra of the isomers are identical does not hamper the analysis.⁶⁷

The isomers of 1-methyl-1,2-dicyclopentylcyclopropane³² are more complex objects for identification, as their molecules are capable of internal rotation. The internal rotation angles are unknown; therefore, these isomers can be identified only on the basis of calculations performed for all the possible values of these angles; the differences between the Henry constants were calculated and compared with the difference found in the experiment. Upon this comparison, it was found that the *cis*-isomer is the first to come out of the GTCB column. In this case, the molecular-statistical calculations represent the only possible method for identification because the mass spectra of the isomers are identical.

The isomer mixtures for which the composition can be suggested from a known chemical reaction pattern can reasonably be regarded as another group. The catalytic oxidative dimerisation of methyl-, fluoro- and chlorobenzenes normally furnishes mixtures of six isomers containing one substituent in each benzene ring. Using molecular-statistical calculations, all the isomers of dimethyl-⁸⁵ and dichlorobiphenyls⁸⁶ were identified based only on the order of their elution from a GTCB column. The molecular-ion mass chromatograms are presented in Fig. 2. The following calculated values of $\ln K_1$ ($\text{cm}^3 \text{m}^{-2}$) were obtained for dichlorobiphenyls at 475 K and dimethylbiphenyls at 450 K:

Substituent position	2,2'	2,3'	2,4'	3,3'	3,4'	4,4'
Methyl	3.02	3.42	4.24	5.42	6.24	7.12
Chlorine	2.39	4.25	4.78	5.75	6.24	7.20

Despite the fact that only traces of 2,2'-substituted isomers were present, they were identified on the basis of mass spectra.⁸⁷

In the case of difluorobiphenyls, the chromatogram exhibits only five peaks. To identify the isomers in conformity with Scheme 2, the Henry constants and the numbers of theoretical plates needed for the complete (n_1) and partial (n_2) resolution of each isomer pair were calculated. This gave the following results:

Isomer pair	2,2' and 2,3'	2,3' and 2,4'	2,4' and 3,3'	3,3' and 3,4'	3,4' and 4,4'
n_1	22	1500	22	5100	3500
n_2	5	380	5	1300	900

For some isomers, only partial resolution is possible and this is confirmed by the chromatogram presented in Fig. 3 *a*. It can be seen that the mixture contains 2,2'-difluorobiphenyl, which is the first to be eluted. To verify this, a chromatogram on a capillary column was obtained; however, in this case, too, the isomers could not be completely resolved (Fig. 3 *b*). The isomers cannot be identified using a mass spectrometry because they exhibit identical mass spectra. Therefore, comparison of the calculated and experimental retention values is the only way to confirm the presence of all isomers in the mixture. The results of calculations confirming that a mixture of difluorobiphenyls also contains all six isomers have been reported.⁸⁷

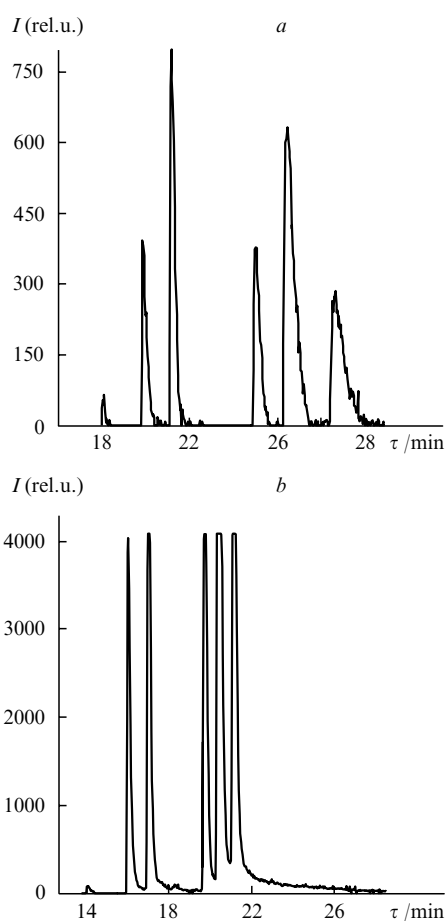


Figure 2. Molecular ion mass chromatograms of dimethylbiphenyl (*a*) and dichlorobiphenyl (*b*), $m/z = 182$ and $222(224)$, respectively.^{85,86}

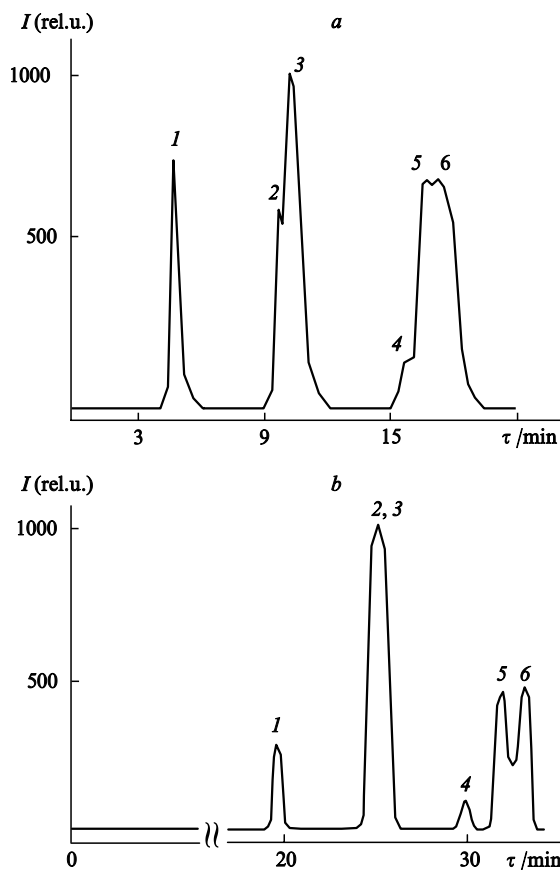


Figure 3. Chromatograms of a difluorobiphenyl isomer mixture obtained on a micropacked column with GTCB (*a*) and a capillary column (*b*).⁸⁷ Isomer (position of the substituent): (1) 2,2'; (2) 2,3'; (3) 2,4'; (4) 3,3'; (5) 3,4'; (6) 4,4'.

The advantages of calculations using the AAPs corrected by the IF method can be demonstrated in relation to the identification of trace impurities formed upon the catalytic oxidative dimerisation of chlorobenzene.^{66,88} The isostructural fragments used are presented in Fig. 4. The results of identification of the major components, dichlorobiphenyls, are presented above. The formation of trichlorobiphenyls can easily be confirmed on the basis of mass-spectrometry data; however, it is impossible to identify individual isomers, as their mass spectra are identical. Figure 5 shows the mass chromatograms of the molecular ions of tri- and dichlorobiphenyls with $m/z = 256$ and 226 , respectively. It can be seen that the trichlorobiphenyls come out of the column with GTCB between two groups of dichlorobiphenyls.

All the dichlorobiphenyls have been identified (see above), and their Henry constants can be used as the reference values in the identification of trichlorobiphenyl isomers. The results of calculations of the Henry constants for *ortho*-substituted tri- and dichlorobiphenyls are listed in Table 3. In this case, there is no need to carry out calculations for all the isomeric trichlorobiphenyls, because only *ortho*-substituted isomers have retention times

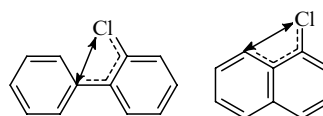


Figure 4. Isostructural fragments (marked by dashed lines) in molecules used for correction of the AAP parameters in calculations of the Henry constants of chlorobiphenyls.

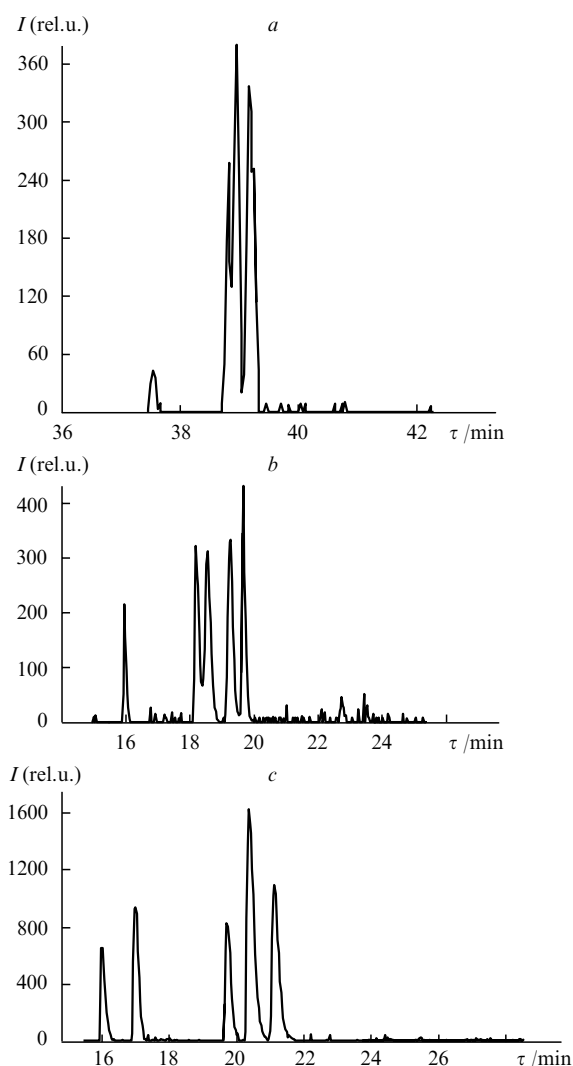


Figure 5. Characteristic-ion mass chromatograms of di- and trichlorobiphenyls obtained from the chromatograms for total ion currents in the separation of a chlorobiphenyl mixture on a capillary (a) and micropacked (b, c) columns.⁶⁶ The characteristic ion has $m/z = 256$ (a, b), 226 (c).

comparable with the retention times of dichlorobiphenyls. It can be seen from Table 3 that the elution of 3,3'-dichlorobiphenyl from the GTCB column is preceded by the elution of 2,4,6-, 2,6,4'- and 2,3,6-trichlorobiphenyls. The isomer whose retention time is close to that of 2,3'-dichlorobiphenyl is 2,3,2'-trichlorobiphenyl, while the compound with a retention time similar to that of 3,3'-dichlorobiphenyl is 2,5,4'-trichlorobiphenyl. It is noteworthy that the efficiency of separation of these isomers achieved on a microcolumn packed with GTCB is higher than that on a capillary column with a slightly polar liquid stationary phase. This outcome is attributable to the high 'sensitivity' of the GTCB surface to the structural differences between the adsorbed molecules. In view of the large difference between the Henry constants for tri- and dichlorobiphenyls (see Table 3), one can state that in this case, complete separation of the mixture has been attained and each chromatographic peak really corresponds to a single isomer.

In the case of nonsymmetrical molecules, for example, 2,3,2'-trichlorobiphenyl, two conformers can exist differing by the internal rotation angles. Since the structure of the adsorbed molecule is unknown, the calculations were carried out for the two possible conformations, *syn* and *anti*.

The catalytic oxidative dimerisation of toluene⁸⁵ was found to give, in addition to dimethylbiphenyls, impurities with a molecular mass of 196. The chromatograms obtained using a GTCB

Table 3. Henry constants calculated for tri- and dichlorobiphenyls at 500 K and the internal rotation angles (α) used for the calculations.⁶⁶

Molecule	α /deg	$\ln K_1$ (cm ³ m ⁻²)
2,6,2'-Trichlorobiphenyl	65	2.88
2,3'-Dichlorobiphenyl		
<i>syn</i>	53	3.34
<i>anti</i>	127	2.91
2,3,2'-Trichlorobiphenyl		
<i>syn</i>	60	3.38
<i>anti</i>	120	2.97
2,5,2'-Trichlorobiphenyl		
<i>syn</i>	60	3.15
<i>anti</i>	120	3.48
2,6,3'-Trichlorobiphenyl	60	3.62
2,4,2'-Trichlorobiphenyl		
<i>syn</i>	60	3.70
<i>anti</i>	120	3.30
2,4'-Dichlorobiphenyl	53	3.94
2,4,6-Trichlorobiphenyl	60	4.15
2,6,4'-Trichlorobiphenyl	60	4.32
2,3,6-Trichlorobiphenyl	60	4.57
3,3'-Dichlorobiphenyl		
<i>syn</i>	38	4.85
<i>anti</i>	142	4.50
2,5,4'-Trichlorobiphenyl	53	4.87

column (Fig. 6) show that the retention time of these compounds is close to the retention time of 2,4-dimethylbiphenyl. On the basis of analysis of the regular features of retention on GTCB, one can state that compounds with higher molecular masses can have

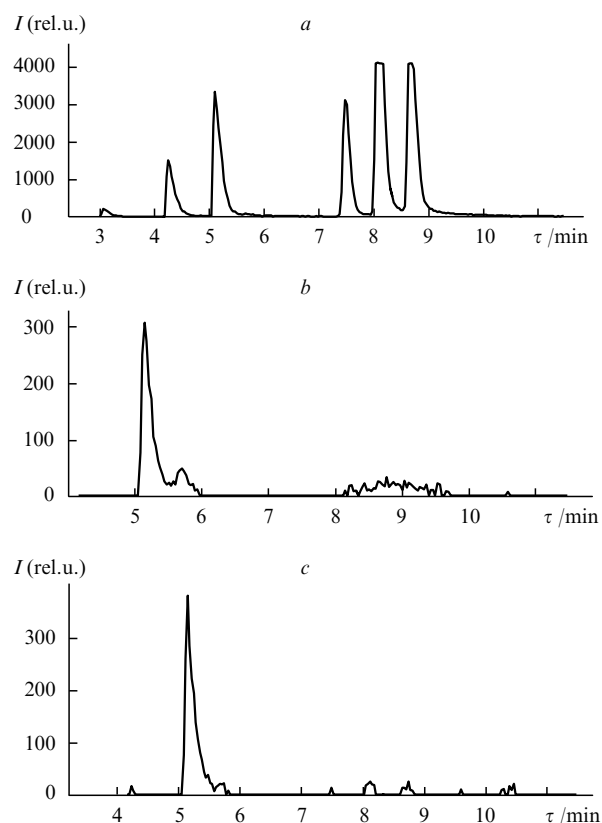


Figure 6. Characteristic-ion mass chromatograms of dimethylbiphenyls (a) and impurities (b, c) obtained on a micropacked GTCB column.⁸⁸ The characteristic ion has $m/z = 182$ (a), 196 (b), 104 (c).

shorter retention times only when their molecules are nonplanar, in particular, for large internal rotation angles. A dimethylbiphenylmethane or *ortho*-substituted trimethylbiphenyl structure can be proposed for these compounds. In this case, identification of the impurities using mass spectra confirmed the validity of the assumption. Analysis of the recorded mass spectra provides the conclusion that the isomer whose spectrum contains a large peak with $m/z = 104$ (Fig. 7 *a*) corresponds to the group of dimethylbiphenylmethanes. The mass spectrum of the other compound (Fig. 7 *b*) resembles most closely the spectrum of trimethylbiphenyl but this assignment can hardly be confirmed on the basis of library search, as the published data are scarce. In order to identify this compound, molecular-statistical calculations of $\ln K_1$ ($\text{cm}^3 \text{m}^{-2}$) were carried out for all possible trimethylbiphenyl isomers containing at least one methyl group in the *ortho*-position relative to the bond connecting the benzene rings. The results of these calculations are presented below.

Substituent position	$\ln K_1$	Substituent position	$\ln K_1$
2,3,2'	3.32	2,5,4'	3.53
2,3,3'	8.16	2,6,2'	3.67
2,3,4'	10.14	2,4'	4.24
2,4,2'	3.93	2,6,3'	4.29
2,4,4'	10.1	3,3'	5.42
2,5,2'	3.64	2,6,4'	4.86
2,5,3'	7.24		

Yet another example of utilisation of the method in question for compound identification is analysis of an industrial mixture of chlorobiphenyls for the most toxic, 'dioxin-like' isomers.^{66,67,89} The results of chromatographic separation of this mixture on micropacked and capillary columns showed that the degree of separation obtained on a micropacked column for a mixture containing tri- and tetrachlorobiphenyls is adequate for the molecular-statistical identification of isomers by comparison with characteristic-ion mass chromatograms of tri- and tetrachlorobiphenyls (Fig. 8). The results of calculation of the Henry

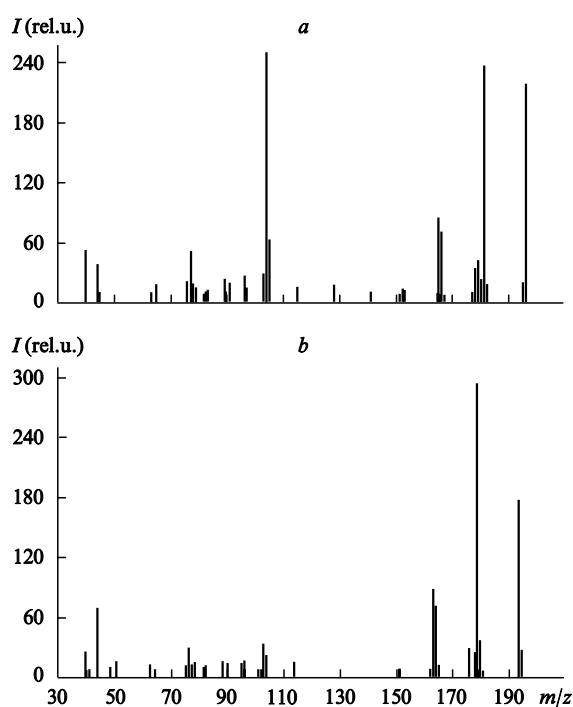


Figure 7. Mass spectra of various impurities with identical molecular ions detected in the reaction mixture resulting from catalytic dimerisation of toluene.^{67,88}

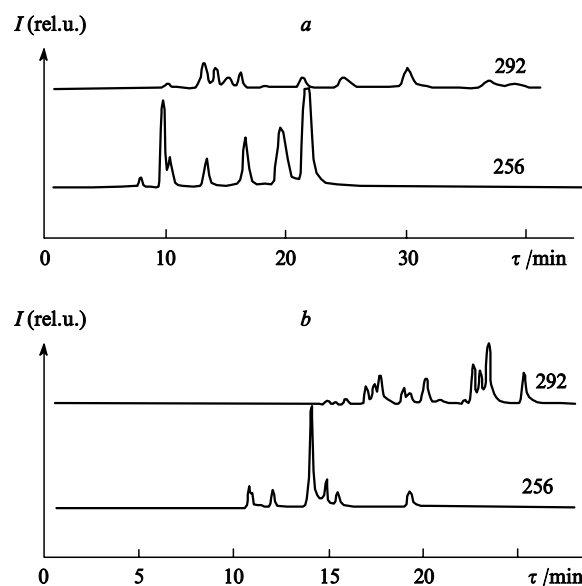


Figure 8. Molecular-ion mass chromatograms of trichloro- ($m/z = 256$) and tetrachlorobiphenyls ($m/z = 292$) obtained on a micropacked GTCB column (*a*) and on a capillary column (*b*).^{67,89}

constants for tetrachlorobiphenyl isomers were compared with this constant for 4,4'-dichlorobiphenyl, present in the mixture and used as the standard. This comparison made it possible to find out that the retention times of all tetrachlorobiphenyls present in the mixture are shorter than that of the 4,4'-substituted isomer, whereas the retention time of the 'dioxin-like' 3,4,3',4'-tetrachlorobiphenyl is longer. Thus, the mixture under study does not contain the most toxic *ortho*-unsubstituted isomers.

* * *

The gas chromatography – mass spectrometry method considered in this review, which was used for mixture identification, appears to be the only reliable method known to date suitable to identify the belonging of isomers to a particular class of compound. Naturally, the examples cited do not cover all the possible fields of GC-MS application but they demonstrate that in combination with molecular-statistical calculations, this method provides the most reliable results. When discussing the semiempirical molecular-statistical theory, one should note one substantial limitation, namely, that the theory is applicable only to adsorption on the GTCB surface. Nevertheless, the experience accumulated for decades demonstrates high potency of this theory in complex situations, which often arise during chromatographic identification of organic compounds.

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Nucleophilic attack on the unsubstituted carbon atom of azines and nitroarenes as an efficient methodology for constructing heterocyclic systems

O N Chupakhin, D G Beresnev

Contents

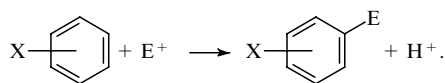
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Abstract. Data on new methods for the synthesis of fused azines by nucleophilic attack on the unsubstituted carbon atom of azines and nitroarenes are generalised. The review surveys tandem reactions of azines with binucleophiles comprising nucleophilic addition A_N-A_N , nucleophilic addition–substitution $A_N-S_N^{ipso}$, and nucleophilic substitutions $S_N^H-S_N^{ipso}$ and $S_N^H-S_N^H$. Intramolecular S_N^H reactions of azines and nitroarenes and other methods for the synthesis of fused heterocycles based on S_N^H nucleophilic substitution are also discussed. The bibliography includes 69 references.

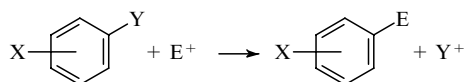
I. Introduction

The main procedures for the functionalisation of aromatic compounds involve electrophilic (S_EAr) and nucleophilic (S_NAr) substitution reactions. The S_EAr reactions, typical primarily of carbocyclic compounds, proceed predominantly as the electrophilic substitution of hydrogen. Strictly speaking, these transformations would be more correctly designated as S_E^HAr because less common reactions accompanied by the displacement of non-hydrogen groups (CO_2R , NO_2 , NR_2 , etc.) are conventionally symbolised by $S_E^{ipso}Ar$.

Transformation S_EAr (S_E^HAr):



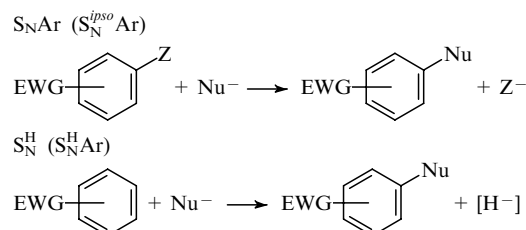
Transformation $S_E^{ipso}Ar$:



E is an electrophile.

Nucleophilic aromatic substitution reactions involve most often the *ipso*-substitution ($S_N^{ipso}Ar$) at the C_{Ar} atom bound to the

Hal, N, O, P or S atoms.¹ Some S_NH reactions have long been used in industry (synthesis of nitrophenols, alizarin, 2-aminopyridine). The preparation of *p*-phenylenediamine from nitrobenzene and benzamide is currently one of the most advanced organic syntheses used in industrial processes.²



Nu is a nucleophile; EWG is an electron-withdrawing group.

Presently, the S_N^{ipso} and S_N^H reactions and related processes are used as the main procedures for the modification of π -electron-deficient aromatic systems.^{1,3} It should be noted that methods based on nucleophilic attack on the unsubstituted carbon atom of aromatic compounds have some advantages. Thus, the preliminary introduction of nucleofuges (Cl, NO_2 , SO_3H , etc.) into the ring is not needed here and the hydride ion serves formally as the leaving group. In many reactions, water is removed from the reaction mixture as a by-product, which is of importance for the commercial use of these reactions in connection with increasing industrial requirements for environmental safety.

It should be noted that an aromatic substrate must be activated to be involved in the S_N^H processes. In reactions with arenes, this is most often achieved by the introduction of an electron-withdrawing substituent, for example, the nitro group, into the ring. In the reactions with heterocyclic compounds, the presence of the aza group is often quite sufficient. This group is comparable to NO_2 in its electron-withdrawing effect and also directs nucleophilic attack at positions 2 and 4.¹

The present review surveys the data on the use of nucleophilic attack on the unsubstituted carbon atom of azines and nitroarenes for the construction of new heterocyclic systems.

II. Main transformation paths of σ^H adducts

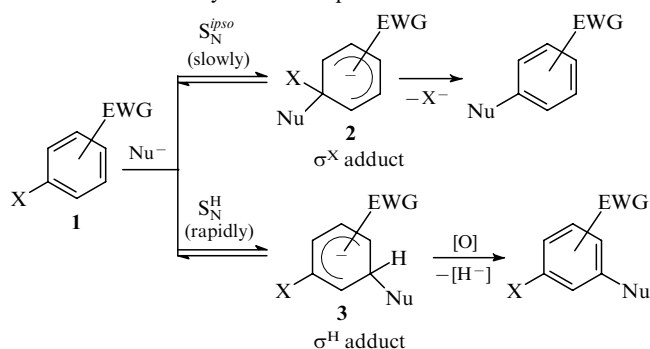
According to the modern notion of nucleophilic aromatic substitution reactions proceeding as 'addition–elimination', the first step of the nucleophilic attack on activated aromatic substrate **1** gives rise to intermediates of two types, viz., σ^X adducts (Meisenheimer complexes) **2** or σ^H adducts (Servis complexes) **3**. Even in the presence of a leaving group in the ring, the *ipso*-substitution is

O N Chupakhin, D G Beresnev Institute of Organic Synthesis, Urals Branch of the Russian Academy of Sciences, ul. S Kovalevskoi 20, 620219 Ekaterinburg, Russian Federation. Fax (7-343) 274 11 89. Tel. (7-343) 274 11 89. E-mail: chupakhin@ios.uran.ru (O N Chupakhin). Tel. (7-343) 249 30 58. E-mail: beresnev@ios.uran.ru (D G Beresnev)

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always preceded by the rapid and reversible formation of σ^H adducts as kinetically controlled products.⁴



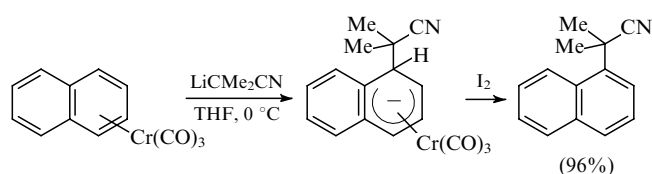
X is a leaving group; EWG is N_2 , NO_2 , NO , CO_2R , etc.

The σ^H adducts **3** differ substantially in stability. Thus, both unstable short-lived species and stable anionic complexes and dihydro compounds are known.¹ In the nitroarene series, the stability of σ^H adducts increases as the number of electron-withdrawing groups in the nucleus is increased. Thus, the existence of σ^H adducts, viz., di- and trinitrobenzene derivatives, was unambiguously proved, whereas the corresponding mononitrobenzene derivatives were not, to our knowledge, detected.

The σ^H intermediates derived from azines can be stabilised both by the introduction of electron-withdrawing groups, including the aza group, and through protonation of anionic forms and their transformations into neutral dihydro compounds. Clearly, the σ^H adducts generated from cationic forms of azines do not bear a charge. On the whole, σ^H adducts (Servis complexes) are generally more stable than their σ^X analogues (Meisenheimer complexes). The nature of the leaving group is the main factor responsible for the high stability of σ^H adducts. Unlike good leaving groups, such as Hal , CN , NO_2 , SO_3H , etc., which are readily solvated as X^- anions, the hydride ion is not susceptible to solvation and it was not detected as a kinetically independent species in solutions. The occurrence of hydrogen in the form of the proton H^+ or the radical $H^\bullet$ is thermodynamically much more favourable than its occurrence as the hydride ion H^- . Therefore, aromatisation, which proceeds either through oxidative processes or with the involvement of auxiliary leaving groups (autoaromatisation) rather than *via* the direct abstraction of a hydride ion, is the bottleneck of S_N^H processes. Hence, nucleophilic attack on the unsubstituted carbon atom of arenes (hetarenes) affords (under particular conditions) S_N^H -reaction products. If none of the mechanisms of aromatisation takes place, σ^H adducts can undergo dissociation. This is particularly true for σ^H adducts generated from nitroarenes. The σ^H adducts derived from heteroarenes can be involved in alternative reactions resulting in the ring opening or recyclisation (for example, ANRORC transformations).^{5,6}

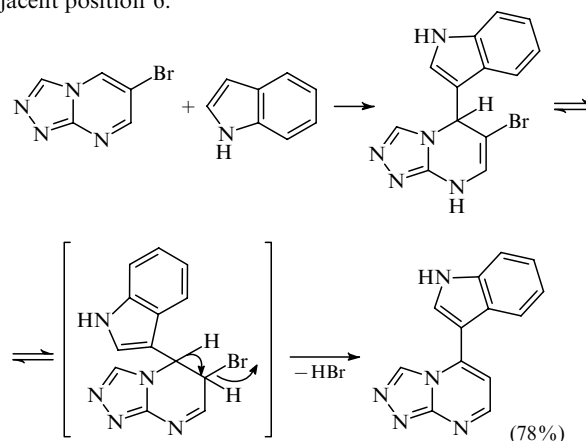
Oxidative aromatisation is a variation of the S_N^H reactions in which elimination occurs as a redox process.¹ In this type of reaction, both inorganic (atmospheric oxygen, halogens, hypohalogenites, sulfur, metal cations, etc.) and organic (quinones, triarylmethyl, tropylium and heterocyclic cations, etc.) reagents can be used as oxidisers. Besides, oxidative aromatisation can be performed electrochemically. In the absence of an oxidising agent, the starting π -electron-deficient arene (heteroarene) can serve as such a reagent. An oxidiser abstracts electrons from the σ^H adduct and hydrogen is most often eliminated as a proton.¹

As an example of the oxidative S_N^H processes, we refer to the reactions of naphthalene activated by chromium carbonyl with organolithium compounds. The resulting σ^H adduct undergoes aromatisation under the action of elemental iodine.⁷

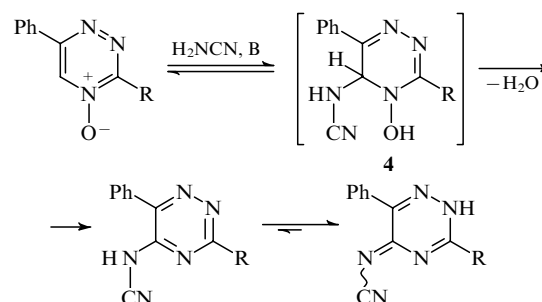


Autoaromatisation proceeds if the σ^H adduct contains a nucleofuge, which is initially present in either the substrate or the reagent. In this case, the nucleofuge group X (which is readily solvated) serves as an oxidiser and is eliminated together with the electron pair from the σ^H adduct as the X^- anion, whereas hydrogen leaves as a proton.

There are several types of autoaromatisation of σ^H adducts. If the leaving group is located in the aromatic ring in the *ortho* position with respect to the carbon atom subjected to the attack, these reactions are said to be *cine*-substitution reactions. Thus in the reactions of 6-bromoazolopyrimidines with indole and its derivatives,⁸ the hydrogen atom at position 7 of the triazolopyrimidine system is replaced and the bromine atom leaves the adjacent position 6.

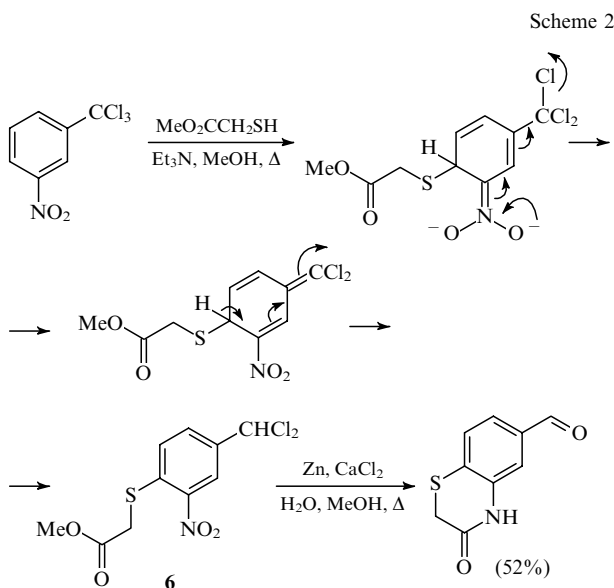
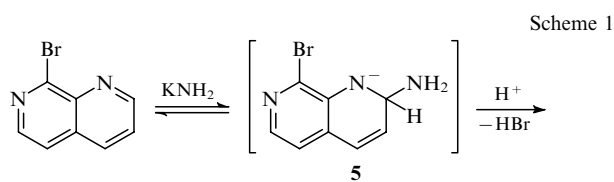


Numerous S_N^H reactions in the series of azine *N*-oxides and their derivatives (deoxygenative substitution of hydrogen)⁹ belong to the *cine*-substitution processes. In this case, the *N*-oxide, *N*-alkoxide or *N*-acyloxy functional group serves as the auxiliary leaving group in the second step involving elimination of the hydrogen atom from the σ^H adduct. For example, in the reactions of substituted 1,2,4-triazine *N*-oxides with cyanamide, σ^H adduct **4** undergoes aromatisation through 1,2-elimination of the water molecule.¹⁰



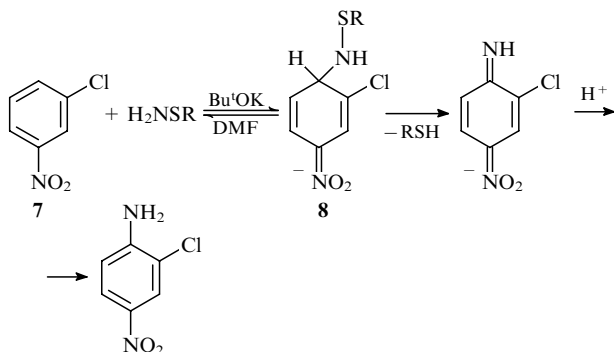
R = H, Et, Ph; B is a base.

If the reaction centre and the nucleofuge group X are separated by one or more atoms, the reactions are said to belong to *tele*-substitution processes. Here, the substituent X can be either bound to the aromatic nucleus (Scheme 1) or located in the side chain (Scheme 2). In the former case (see Scheme 1), the reactions proceed through the formation of σ^H adduct **5**, which undergoes aromatisation *via* 1,4-elimination of HBr with abstraction of the *tele*-arranged bromine atom.



In the latter case (see Scheme 2), aromatisation of the σ^{H} adduct is achieved through the abstraction of the chlorine atom from the trichloromethyl substituent. Reduction of $\text{S}_{\text{N}}^{\text{H}}$ -reaction product **6** with zinc led to the thiazine-ring closure.¹¹

The so-called vicarious nucleophilic substitution where a good leaving group X is present in the nucleophile residue belongs to well-studied autoaromatisation reactions of σ^{H} adducts.^{12–15} For example, the attack of sulfenamides on the unsubstituted carbon atom of 3-chloro-1-nitrobenzene (**7**) afforded adduct **8** whose structure allows the RSH group to undergo β -elimination.¹⁵



Vicarious autoaromatisation of σ^{H} adducts readily proceeds in the case of azoles,¹⁶ azines¹⁷ and nitroarenes¹⁷ and this process provides the basis for the construction of heteroaromatic systems, for example, of the indole^{18,19} and quinoline²⁰ rings.

III. Construction of azine-based heterocyclic systems

Azines containing two or more heteroatoms differ substantially from nitroarenes in that they can be subjected to the double nucleophilic attack. One-pot syntheses of fused heterocyclic

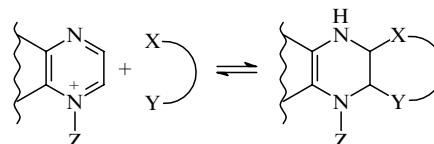
systems are based on the tendency of azines to form cycloadducts in reactions with bifunctional nucleophilic reagents.

1. Tandem reactions $\text{A}_{\text{N}}-\text{A}_{\text{N}}$

There are a large number of examples of the construction of fused heterocyclic systems by the replacement of two adjacent good leaving groups in pyridine, quinoline, pyrimidine, pyrazine, quinoxaline and other rings under the action of bifunctional nucleophiles.²¹ The main limitation of this method is that only azaaromatic compounds containing two nucleofuge groups at positions 1 and 2 can be used in such reactions.

The ability of unsubstituted azines to form cycloadducts in reactions with binucleophiles provides the basis for another procedure for the synthesis of fused heterocyclic systems.

It should be noted that although heterocyclic systems contain aza groups comparable to the nitro group in its electron-withdrawing properties, additional activation of the substrate is often required for the reaction to proceed. One of the commonly used procedures for the activation of azines in these transformations involves quaternisation of the nitrogen atoms in the ring. Some nucleophiles can react with azine salts. However, activation by acids is not necessarily applicable because it is accompanied by deactivation of the nucleophile. Another method involving alkylation of the azine ring is free from this drawback. The latter method was used in a large number of syntheses of fused heterocycles from N -alkylazinium salts. Thus, the *ortho*-cyclisation processes occurring in the reactions of 1,3-binucleophiles with quaternary 1,4-diazinium salts have been described.²⁰ One-pot syntheses of imidazopyrazines, imidazopteridines, furoquinoxalines, pyrroloquinoxalines, imidazoquinoxalines and thiazoloquinoxalines have been reported.²¹ Table 1 gives examples of the construction of fused azine-based heterocyclic systems using tandem reactions of the $\text{A}_{\text{N}}-\text{A}_{\text{N}}$ type. All these systems were prepared by cyclisation of triazinium (**9**), N -alkylquinoxalinium (**10**), N -alkylpyrazinium or N -alkylpteridinium salts with such 1,3-binucleophiles as β -diketones, thioamides, dithiocarbamates, thiourea derivatives, *etc.*



$\text{X} = \text{H}, \text{Alk}$; X, Y are nucleophilic groups.

Unlike the $\text{S}_{\text{N}}^{\text{ipso}}-\text{S}_{\text{N}}^{\text{ipso}}$ reactions in which thiourea derivatives act as N,S -binucleophiles,^{30–33} the $\text{A}_{\text{N}}-\text{A}_{\text{N}}$ reactions involve these derivatives exclusively as N,N' -binucleophiles.³⁴

An important characteristic feature of the $\text{A}_{\text{N}}-\text{A}_{\text{N}}$ reactions is the reversible formation of cyclic products. Due to the reversibility of the double addition and ambident character of the nucleophiles used, these reactions can yield regioisomeric cyclisation products. For example, tetrahydrothiazolo[4,5-*b*]quinoxaline **11** formed by the reaction of the N -alkylquinoxalinium salt **10** with thioamide **12** under kinetically controlled conditions in aprotic solvents can be subjected to different types of isomerisation. Upon heating in ethanol, compound **11**, containing the aryl group in the side chain ($\text{R}^2 = \text{Ph}$), underwent isomerisation to give thiazoloquinoxaline **13**. When $\text{R}^2 = \text{Me}$, isomerisation proceeded with the involvement of the methyl group to give pyrrolo[2,3-*b*]quinoxaline-2-thione **14** as the cyclisation product.²¹

Due to the tendency of cycloadducts to dissociation, not only regio- but also stereoisomers can be generated. An example is the construction of the tetrahydropyrrolo[2,3-*b*]quinoxaline ring. The reaction under the kinetically controlled conditions (activation of the nucleophile with a base) gave rise to stereoisomer **15** having the *exo* configuration, whereas the reaction in the absence of a base afforded both the *exo* isomer and the thermodynamically more stable *endo* isomer **16**, the rearrangement **15** $\rightarrow$ **16** being possible.³⁵

Table 1. Syntheses of fused heterocycles on the basis of 1,4-diazinium and triazinium salts with the use of A_N-A_N reactions.

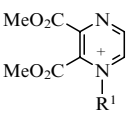
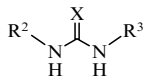
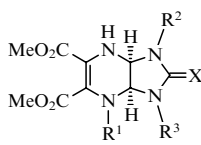
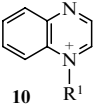
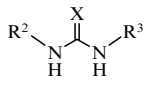
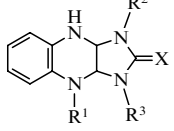
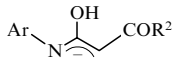
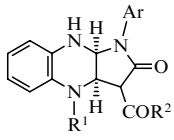
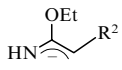
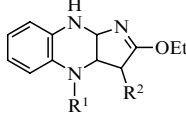
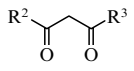
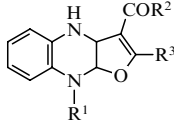
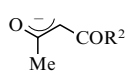
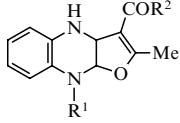
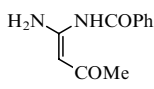
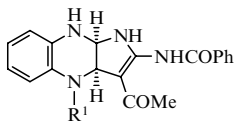
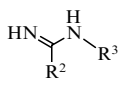
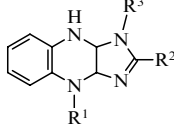
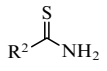
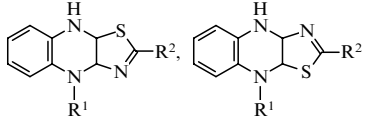
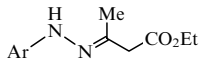
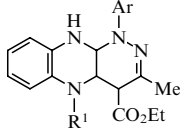
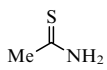
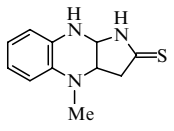
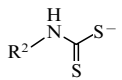
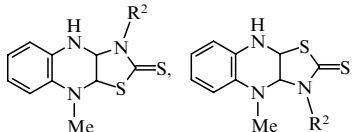
Substrate	Binucleophilic reagent	Product	Ref.
 R ¹ = Me, Et.	 R ² , R ³ = H, Me, Ph, NH ₂ , NHPh; X = O, S.		21
 R ¹ = Me, Et.	 R ² , R ³ = H, Me, Ph, NH ₂ , NHPh; X = O, S.		21
	 R ² = Me, Ph, 4-MeOC ₆ H ₄ , 2-Tol, 4-Tol, 4-ClC ₆ H ₄ .		21
	 R ² = Ph, 4-O ₂ NC ₆ H ₄ .		21
	 R ² , R ³ = Me, OEt.		21
	 R ² = Me, OEt, Bu ⁱ .		21
			21
	 R ² = Ph, 2-ClC ₆ H ₄ ; R ³ = Ph, 4-ClC ₆ H ₄ , 4-BrC ₆ H ₄ , 2-Py.		21
	 R ² = Me, Ph.		21
	 Ar = 4-O ₂ NC ₆ H ₄ , 2,4-(O ₂ N) ₂ C ₆ H ₃ .		21
10 (R ¹ = Me)			21
	 R ² = Bn, cyclo-C ₆ H ₁₁ , thiazol-2-yl.		21

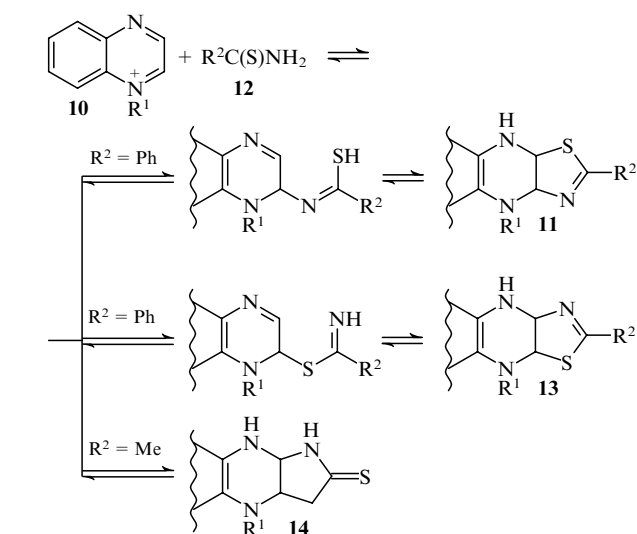
Table 1 (continued).

Substrate	Binucleophilic reagent	Product	Ref.
10 ($R^1 = \text{Me}$)			21
	$X = \text{NH, O.}$		
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	$X = \text{NH, O.}$		
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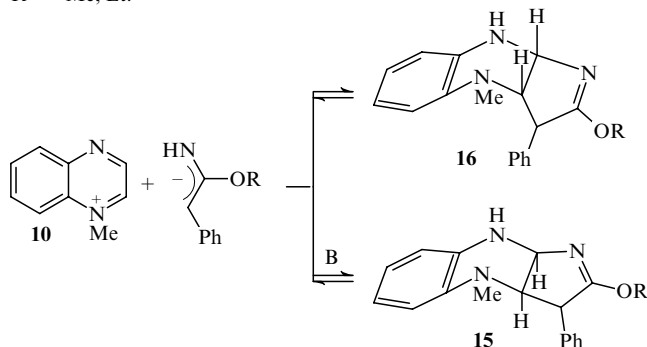
Table 1 (continued).

Substrate	Binucleophilic reagent	Product	Ref.
9 ($R^1 = \text{Et}$; $R^2 = \text{SMe, morpholinyl}$)			25
9 ($R^1 = \text{H}$; $R^2 = \text{SMe, NH}_2$)			26, 27
	Ar = Ph, 4-O ₂ NC ₆ H ₄ , 4-MeOC ₆ H ₄ . H ₂ N-C(=S)-R, Ac ₂ O R = Ph, Me.		28
	X = N, CCN; Y = N, CH, CCN, CSMe, CCF ₃ ; Z = N, CCO ₂ Et. HO-C ₆ H ₄ -OR R = H, Me.		29

Note. In all reactions, the yields of the products were higher than 80%.

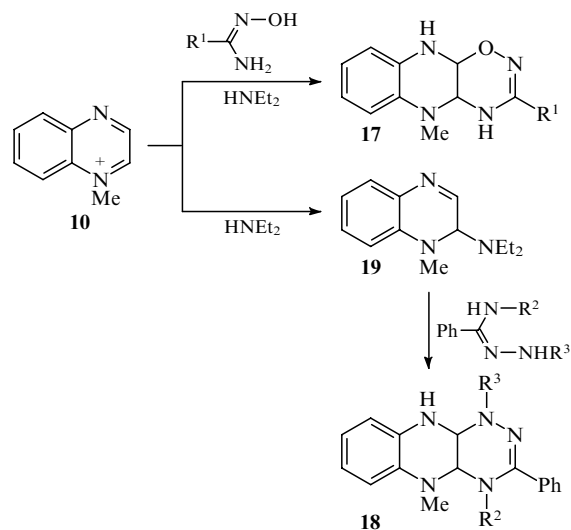


$R^1 = \text{Me, Et}$.



The reactions of 1,4-diazinium salts with 1,4-bifunctional nucleophiles are very similar to the annelation of five-membered rings to the pyrazinium ring. The reactions of *N*-alkyl-1,4-diazinium salts with 1,4-binucleophiles afforded a series of tetrahydropyrazines and tetrahydroquinoxalines fused with different

heterocycles, such as pyrazine, oxazine, thiadiazine and triazine rings (see Table 1). For example, cyclisation of quinoxalium salts with amide oximes and amidrazones afforded partially hydrogenated derivatives of new heterocyclic systems, viz., 1,2,4-oxadiazino- (**17**) and 1,2,4-triazolo[5,6-*b*]quinoxalines (**18**).²²



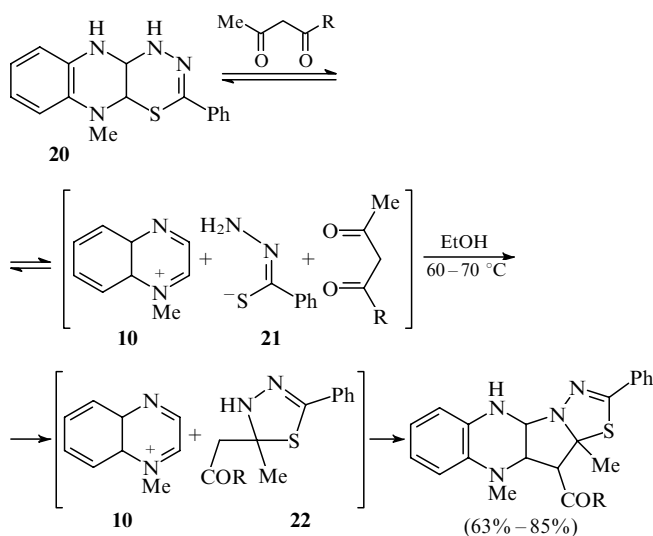
$R^1 = \text{Me, Ph, Bn, 4-BrC}_6\text{H}_4$; $R^2 = \text{H, Ph}$; $R^3 = \text{H, COPh}$.

The reactions with amidrazones were carried out with pre-isolated adduct **19** prepared by the reaction of the *N*-methylquinoxalium cation **10** with diethylamine to prevent the formation of tetrazines from amidrazones in a basic medium.²²

Like the products obtained in the A_N-A_N reactions of 1,4-diazinium salts with 1,3-binucleophiles, cycloadducts prepared by the addition of 1,4-binucleophiles to 1,4-diazinium salts readily undergo dissociative destruction and isomerisation in protic solvents in the presence of catalytic amounts of acids.³⁶

Dissociation of the cycloadducts is initiated both by mineral acids³⁷ and CH-acids, in particular, by acetylacetone and acetoacetic esters. In the latter case, the reactions afforded new fused heterocyclic systems.³⁸ First, the starting thiadiazinoquinoxaline

20 dissociated to yield the quinoxalinium cation **10** and thiobenzhydrazide (**21**). The latter reacted with a β -dicarbonyl compound to give hydrazone, which underwent intramolecular cyclisation to form thiadiazole **22**. The final step involved the tandem reaction A_N-A_N in which the compound **22** acted as a binucleophile.

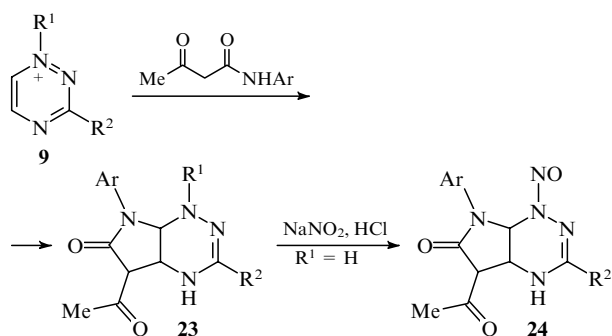


R = OAlk.

To prevent dissociation of the cycloadducts, the NH group of the tetrahydropyrazinium ring can be subjected to acylation.²¹ The acyl derivatives are much more stable than the starting cycloadducts and do not dissociate even in acidic solutions.

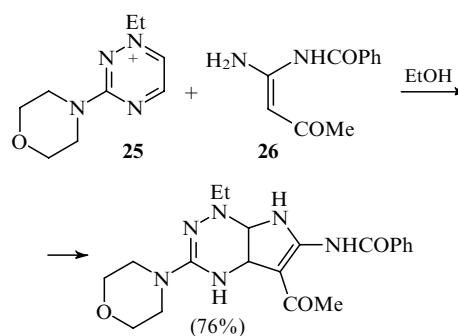
Another way of stabilising hydrogenated σ^H adducts is based on abstraction of hydrogen atoms together with the electron pair from the reaction centres in the presence of oxidising agents^{1,12} (oxidative S_N^H process). In some reactions, σ^H adducts are produced in quasistationary concentrations. Here the presence of an oxidising agent in the reaction mixture is a necessary condition for an arene to interact with a nucleophile. This type of reaction will be considered below.

1,2,4-Triazines are similar to 1,4-diazines in reactivity. In the reactions with binucleophilic reagents, these compounds are prone to form addition products at the *ortho*-atoms. For instance, protonated 1,2,4-triazines and their alkyl derivatives **9** readily reacted with acetoacetamides to give tetrahydropyrrolo[1,2,4]triazines.^{24,25} Cycloadducts **23** derived from protonated 1,2,4-triazines are unstable and can be isolated only as salts of trifluoroacetic acid. Dissociation of these compounds can be prevented by nitrosation of the nitrogen atom adjacent to the reaction centre. *N*-Nitroso derivatives **24** are more stable and could be isolated as free bases.²⁴

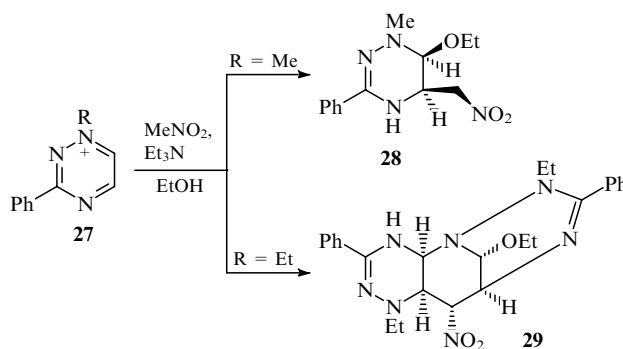


R¹ = H, Et; R² = SMe, morpholinyl.

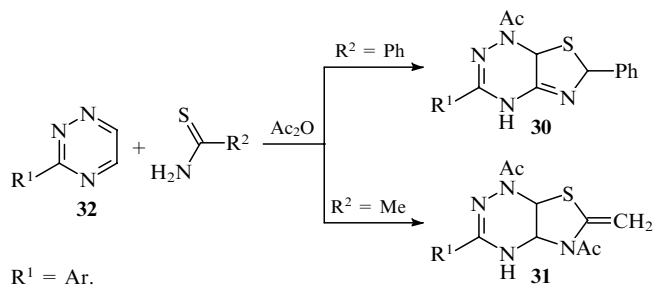
Another procedure for the synthesis of pyrrolotriazines involves the reaction of 1,2,4-triazine derivative **25** with ketene aminal **26**. These reagents, which are widely used in the inverse-electron demand Diels–Alder reactions,³⁹ react with triazinium salts as C,N-binucleophiles.⁴⁰



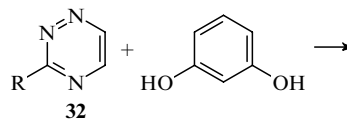
The reactions of 1-alkyl-3-phenyl-1,2,4-triazinium salts **27** with nitromethane in the presence of triethylamine are extraordinary processes. Depending on the nature of the *N*-alkyl group, either one or two molecules of the triazinium salt can participate in these reactions giving rise to adduct **28** or cage compound **29**, respectively.⁴¹ The reactions are accompanied by the addition of the solvent molecule (EtOH). In the latter reaction, nitromethane acts as a 1,1-binucleophile. This is a rare example of one-step syntheses of complex cage heterocycles.

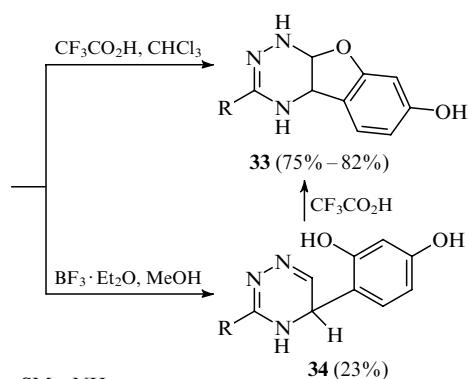


In addition to *N*-alkyltriazinium salts, *N*-acyl derivatives can also react with binucleophiles, activation by acylation often being advantageous over activation by alkylation.²⁸ Thus, a new approach to the synthesis of thiazolo[4,5-*e*][1,2,4]triazines **30** and **31** was proposed on the basis of the tandem nucleophilic addition of alkyl- and arylthioamides to 1,2,4-triazine derivatives **32** in acetic anhydride.²⁸ Attempts to prepare thiazolo[4,5-*e*][1,2,4]triazines from 1-alkyl-1,2,4-triazinium salts failed.



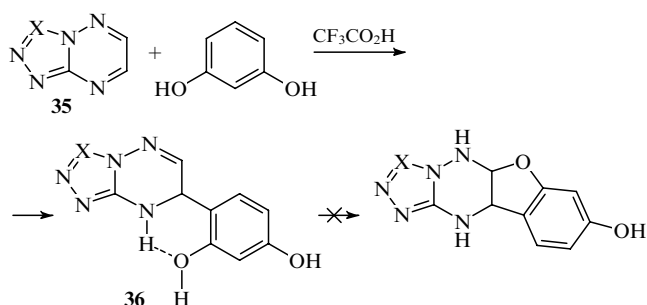
Aromatic ambident C-nucleophiles can participate in the A_N-A_N reactions with 1,2,4-triazinium salts.²⁶ For instance, 3-methylthio- and 3-amino-1,2,4-triazines **32** reacted with resorcinol in the presence of trifluoroacetic acid. The addition of the aromatic ring of resorcinol at the C(5) atom of the triazine followed by nucleophilic attack of the oxygen atom on the C(6) atom afforded benzofurotriazines **33**. Intermediate monoaddition product **34** was isolated only with the use of a softer activating agent, *viz.*, boron trifluoride etherate.²⁶





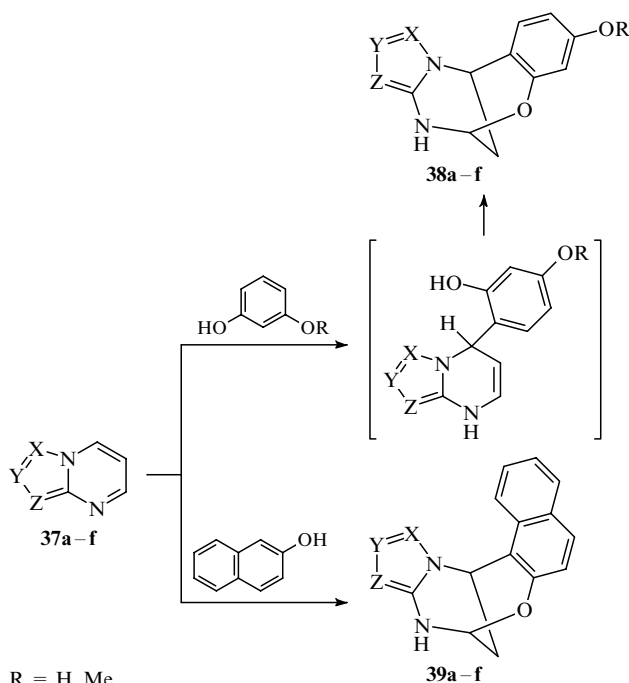
R = SMe, NH₂.

In the reactions with binucleophilic resorcinol, azolo-annealed 1,2,4-triazines **35** are more inert and their reactions stop at the stage of formation of monoaddition products.



X = CH, N.

This is attributable to the fact that the adduct **36** occurs predominantly in the conformation unfavourable for cyclisation, the conformation being stabilised by an intramolecular hydrogen bond.²⁷



R = H, Me.

Compounds 37 , 38 , 39	X	Y	Z
a	N	CH	CCO ₂ Et
b	CCN	CCN	N
c	N	CH	N
d	N	CSMe	N
e	N	CCF ₃	N
f	N	N	N

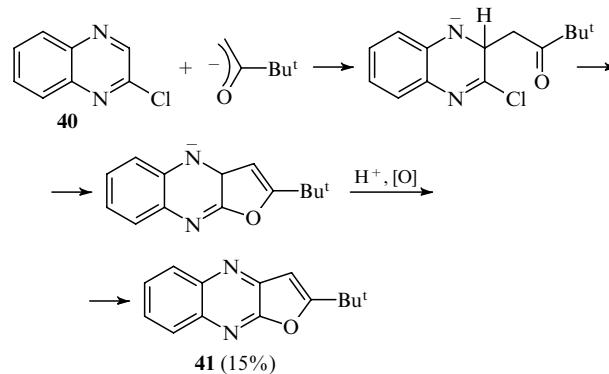
A different situation occurs when azines with the 1,3-arrangement of the heteroatoms are used as the substrate. These compounds tend to add binucleophiles at the atoms located in the *meta* positions of the heteroaromatic ring with respect to one another. Actually, the reactions of azolopyrimidines **37a–f** with 1,3-binucleophilic phenols gave rise to cage structures **38a–f** and **39a–f**.²⁹

To summarise, it should be noted that the nature of the interactions of azinium cations with binucleophiles depends on the relative arrangement of the aza groups. The presence of heteroatoms at positions 1 and 4 (pyrazine, quinoxaline or 1,2,4-triazine rings) is most favourable for the formation of fused heterocycles. The reactions of diazines containing heteroatoms at positions 1 and 2 or at positions 1 and 3 are often accompanied by side reactions.²¹ Examples of the construction of new heterocyclic systems *via* the addition of binucleophiles at the *ortho* or *meta* positions are few in number.^{29, 42}

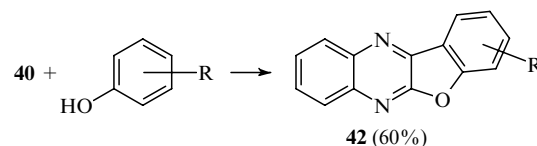
It should also be remembered that the A_N–A_N reactions are often complicated by the dissociation of primary cycloadducts formed under kinetically controlled conditions and their transformations into thermodynamically more stable compounds. These processes can be accompanied by changes not only in the regioorientation but also in the nature of the annelated ring. The A_N–S_N^{ipso} and S_N^H–S_N^{ipso} reactions considered in the following section lack this property.

2. Tandem reactions A_N–S_N^{ipso} and S_N^H–S_N^{ipso}

Azaaromatic compounds containing heteroatoms at positions 1 and 4 can add binucleophiles to the unsubstituted carbon atoms at positions 2 and 3.²¹ Let us consider the reactions of azines bearing a leaving group in one of these positions. The use of these substrates substantially increases the preparative potential of the reactions with binucleophiles due to a combination of the A_N, S_N^H and S_N^{ipso} processes. The transformations of this type can involve both non-activated azines and their quaternary salts. For example, the reactions of 2-chloroquinoxaline (**40**) with enolates led to the addition of the carbanion to the unsubstituted C(3) atom. The replacement of the chlorine atom in the resulting adduct followed by oxidation under the reaction conditions gave rise to furoquinoxaline **41**.⁴³

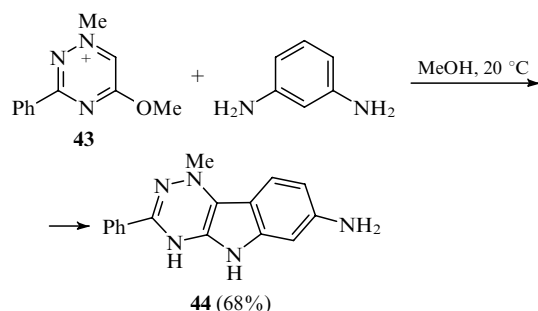


The reactions of 2-chloroquinoxaline with aromatic nucleophilic reagents proceed as the tandem sequence S_N^H–S_N^{ipso} (apparently, with the involvement of hydrogen) to form benzofuroquinoxalines **42**.⁴⁴

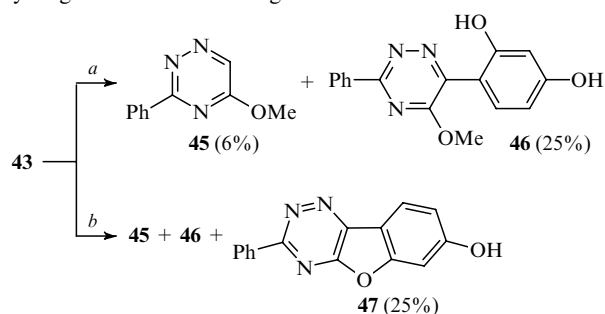


The presence of a leaving group possessing the electron-donating properties (for example, the methoxy group) in the azine ring leads to a decrease in the electrophilicity of the ring. The reactions with such non-activated substrates often do not take place. In this case, the azine ring can be activated with the use of a

conventional approach, *viz.*, by quaternisation of the nitrogen atoms of the heterocycle. Thus, 5-methoxy-1-methyl-3-phenyl-1,2,4-triazinium tetrafluoroborate (**43**) is more reactive than its non-quaternised analogue and its reaction with *m*-phenylenediamine at 20 °C proceeded by the tandem process $A_N-S_N^{ipso}$ to form triazacarbazole **44**.⁴⁵

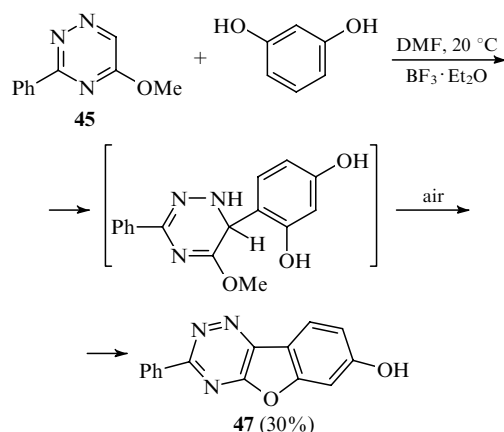


The reaction of the triazinium salt **43** with resorcinol proceeded through a cascade of transformations. This reaction was complicated by dequaternisation of the triazine ring to yield 5-methoxy-3-phenyl-1,2,4-triazine (**45**). The reaction afforded 6-(2,4-dihydroxyphenyl)-5-methoxy-3-phenyl-1,2,4-triazine (**46**) as the major product generated *via* the nucleophilic substitution of hydrogen in the triazine ring.⁴⁵



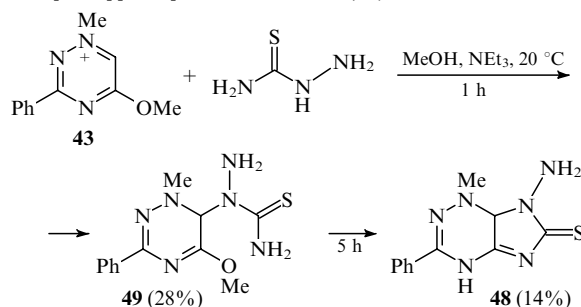
(a) resorcinol, methanol, Δ ; (b) resorcinol, DMF, 20 °C.

The reaction performed in dimethylformamide afforded benzofurotriazine **47** as the major product generated through several reactions, *viz.*, dequaternisation, S_N^H and S_N^{ipso} . It is most likely that the reaction involves dequaternisation as the first step followed by the attack of the nucleophile on the C(6) atom. In the final step, the methoxy group at position 5 is replaced and cyclisation occurs. This assumption was confirmed by a special experiment in which non-quaternised 5-methoxy-3-phenyl-1,2,4-triazine was used as the substrate (**45**). The latter reacted with resorcinol in the presence of boron trifluoride etherate to give benzofurotriazine **47**.



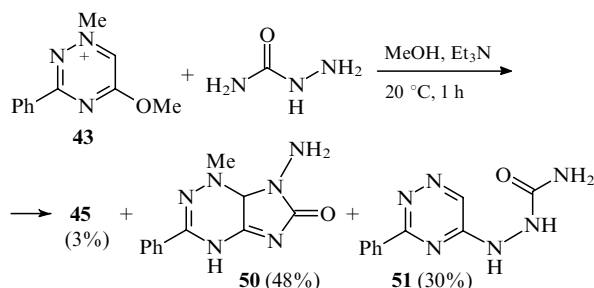
Analogously, triazinium salts react with *N,N*-binucleophiles.⁴⁵ The reaction of the salt **43** with thiosemicarbazide

proceeded through the A_N and S_N^{ipso} transformations to yield imidazo[4,5-*e*][1,2,4]triazine-6-thione (**48**).



The isolation of intermediate **49** has been reported.⁴⁵ This is additional evidence that the unsubstituted carbon atom of the triazine ring is subjected to the initial nucleophilic attack, whereas the substitution of the nucleofuge (OMe) is a secondary process resulting in cyclisation.

It should be noted that the reaction can also follow the 'traditional' (S_N^{ipso}) pathway. The reaction of the salt **43** with semicarbazide afforded imidazotriazine **50** along with triazine **51**, which is a product of *ipso*-substitution of the methoxy group in 5-methoxy-3-phenyl-1,2,4-triazine **45** generated through dequaternisation of the substrate.⁴⁵

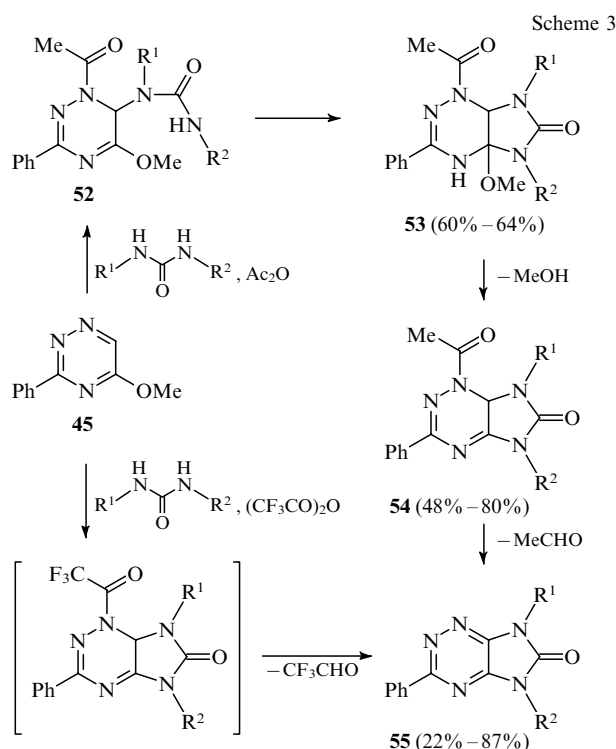


It is noteworthy that the nucleophilic attack in all the reactions under consideration occurs primarily on the unsubstituted carbon atom, although the methoxy group would be expected to be replaced according to the classical theory of nucleophilic aromatic substitution. Moreover, the methoxy group is located at position 5 of the 1,2,4-triazine ring, which is most reactive⁴⁶ with respect to nucleophiles. However, steric effects play the key role in these reactions¹ and σ^H adducts are initially generated in all processes. In the salt **43**, the methyl group at the N(1) atom adjacent to the reaction centre is responsible for substantial stabilisation of the compound **49**, which was isolated in the crystalline state. The reactions of the triazine **45** with nucleophiles (in particular, with semicarbazide) also can afford σ^H adducts upon attack on the C(6) atom. However, this process is reversible due to the absence of the methyl group at the nitrogen atom adjacent to the reaction centre and *ipso*-substitution of the methoxy group giving rise to compound **51** prevails.

The preparation of 6-azapurine derivatives by the reactions of 5-methoxy-1,2,4-triazines, for instance, of the compound **45**, with urea derivatives (Scheme 3) provides another example of the use of the $A_N-S_N^{ipso}$ and $S_N^H-S_N^{ipso}$ tandem reactions in the synthesis of fused heterocycles. In these reactions, acetic and trifluoroacetic anhydrides were used for activation of the substrate.⁴⁶

The reactions of *N*-acyl-1,2,4-triazinium salts generated *in situ* with urea derivatives include a series of successive steps. Depending on the nature of the reagents and reaction conditions, both open-chain adducts **52** and their cyclisation products **53**–**55** can be isolated (see Scheme 3).⁴⁷

The use of acylating reagents makes it possible, first, to activate the triazine ring to nucleophilic attack and, second, to stabilise a σ^H adduct. Besides, the acyl substituent can serve as an auxiliary group responsible for the occurrence of the S_N^H reaction. For example, the final step of the reaction of the 1,2,4-triazine **45**



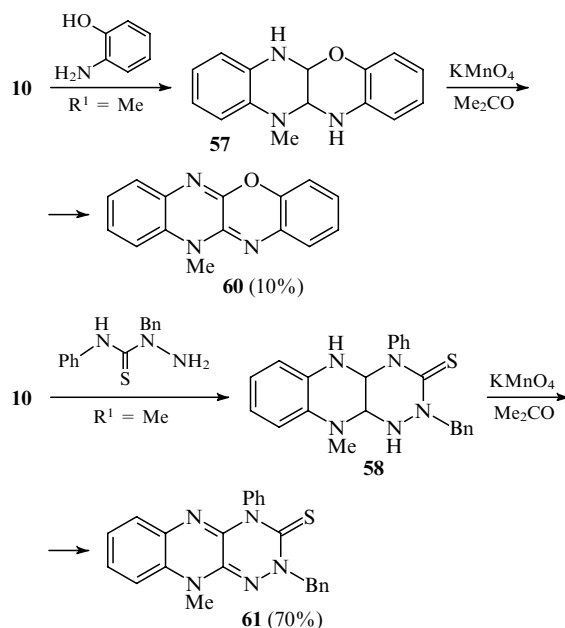
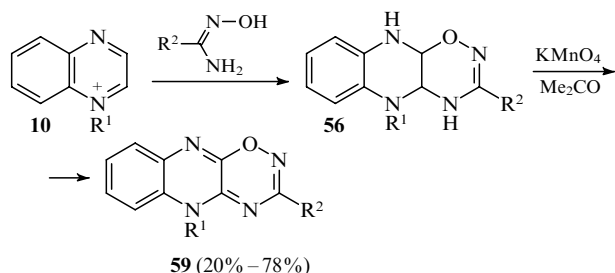
with urea derivatives involves elimination of acetic or trifluoroacetic aldehyde from the σ^H adduct, *i.e.*, the process as a whole can be considered as a variation of *cine*-substitution reactions.

Note also that the reaction of compound **45** with dimethylurea at 20 °C stopped at the stage of formation of adduct **53**, which is a cyclic Meisenheimer complex. The latter was isolated in the crystalline state. This is a rare example of a reaction proceeding according to the S_N^{iso} scheme in which an intermediate was isolated.²

To summarise, combination of the A_N and S_N^H strategies with *ipso*-substitution is, undoubtedly, a powerful tool for the construction of various fused heterocyclic systems. The only limitation is that there is a need to synthesise a substrate containing a leaving group in the position required for cyclisation. However, this drawback is compensated by the high stability of the resulting products and the fact that they cannot undergo dissociation, which is often observed in the A_N – A_N reactions.

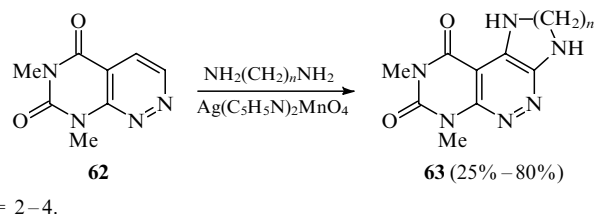
3. Tandem reactions S_N^H – S_N^H

Only a few examples of the double nucleophilic substitution of hydrogen are known. All these reactions involve oxidative aromatisation of σ^H adducts.^{48,49} Thus, oxidation of cycloadducts **56**–**58**, which were prepared by the A_N – A_N reactions of quinoxalinium salts, by potassium permanganate led to their aromatisation.⁴⁸



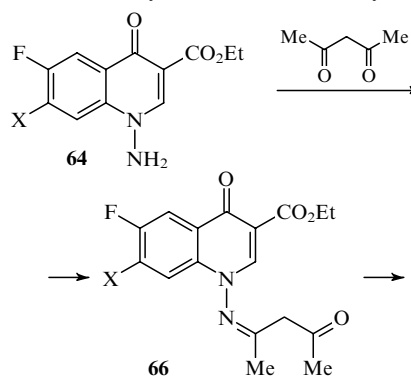
In this case, the S_N^H process is a convenient way of stabilising σ^H adducts. Compounds **59**–**61**, unlike their partially hydrogenated analogues, cannot undergo dissociation at all.

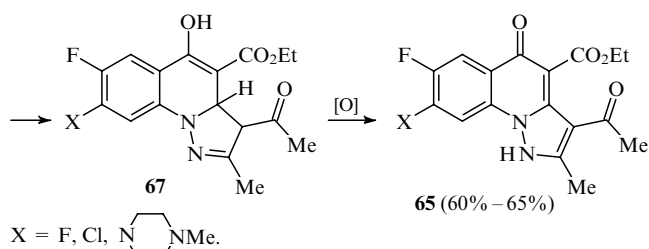
To our knowledge, the reactions of pyrimido[4,1-*c*]pyridazines **62** with diamines in the presence of an oxidising agent are the only examples of the tandem reactions S_N^H – S_N^H proceeding *in situ* without isolation of intermediate σ^H adducts.⁴⁹ The reactions involve the addition of the nucleophile at position 4 of the heterocyclic system followed by intramolecular cyclisation to form tricyclic product **63**.



4. Intramolecular S_N^H reactions

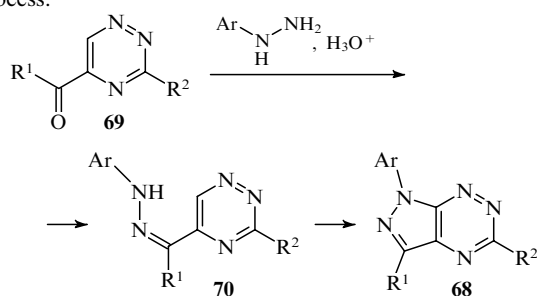
New heterocycles are often generated by the intramolecular attack of a nucleophilic functional group present in the side chain of the heterocyclic substrate. The intramolecular S_N^H reactions were used for structural modifications of fluoroquinolone antibiotics.^{50,51} For example, the reactions of 1-amino-substituted fluoroquinolones **64** with acetylacetone afforded tricyclic compound **65**.⁵⁰





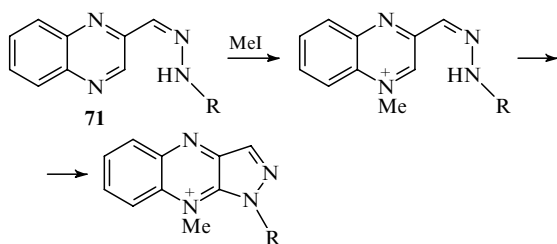
The mechanism of formation of the tricyclic product **65** involves condensation of the *N*-aminoquinolone **64** with acetylacetone followed by the intramolecular nucleophilic attack on the C(2) atom of the resulting diketone **66** and oxidation of σ^{H} adduct **67** with atmospheric oxygen.

The synthesis of pyrazolo[4,3-*e*][1,2,4]triazines **68** using the reactions of 5-acyl-1,2,4-triazines **69** with arylhydrazines in an acidic medium is another example of the intramolecular $\text{S}_{\text{N}}^{\text{H}}$ process.⁵²



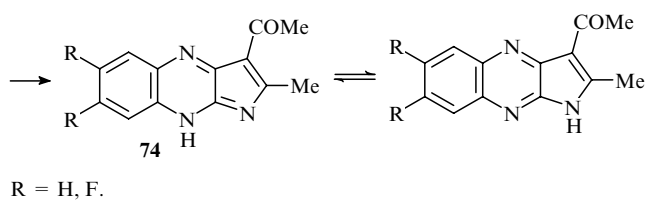
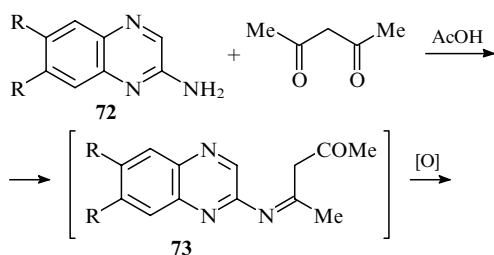
$\text{R}^1 = \text{Me}, \text{Et}, \text{Pr}^n; \text{R}^2 = \text{Ph}, \text{SMe}; \text{Ar} = \text{Ph}, 4\text{-Tol}, 4\text{-ClC}_6\text{H}_4, 2,4\text{-Cl}_2\text{C}_6\text{H}_3$.

This synthesis involved the successive formation of hydrazones **70** and intramolecular substitution of hydrogen.⁵² Analogous transformations were also observed upon alkylation of quinoxaline-3-carbaldehyde hydrazones **71**. These reactions led to the intramolecular nucleophilic substitution of hydrogen at the α position with respect to the quaternary nitrogen atom.⁵³

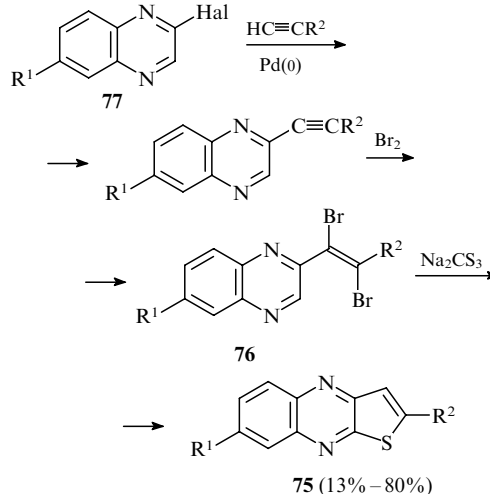


$\text{R} = \text{H}, \text{Me}, \text{Ph}, \text{Bn}, 4\text{-O}_2\text{NC}_6\text{H}_4, 4\text{-O}_2\text{CC}_6\text{H}_4$.

Yet another example of the intramolecular oxidative nucleophilic substitution of hydrogen is the reaction of 2-aminoquinoxaline **72** with acetylacetone or cyclohexanone.⁵⁴ Schiff's bases **73** generated in the course of the reactions underwent spontaneous cyclisation to pyrrolo[2,3-*b*]quinoxaline derivatives **74**.

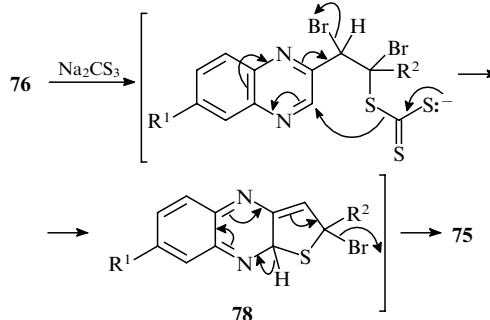


The intramolecular *tele*-substitution to form thienoquinoxalines **75** was observed upon treatment of compounds **76** derived from chloro- or iodoquinoxaline derivatives **77** with sodium trithiocarbonate.⁵⁵

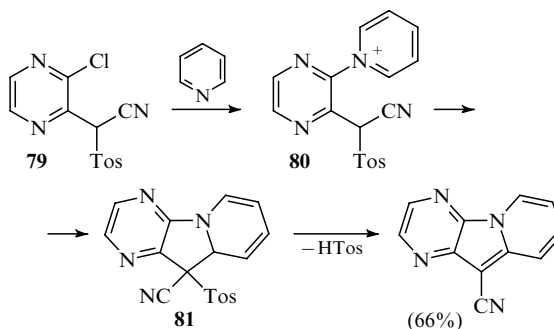


$\text{R}^1 = \text{H}, \text{Cl}; \text{R}^2 = \text{H}, \text{SiMe}_3, \text{Bu}^n, \text{Bu}^t, 4\text{-MeOC}_6\text{H}_4, 4\text{-O}_2\text{NC}_6\text{H}_4, 4\text{-ClC}_6\text{H}_4, 4\text{-IC}_6\text{H}_4, 5\text{-F}_3\text{CC}_5\text{H}_3\text{N}$.

Aromatisation of σ^{H} adduct **78** occurred through elimination of the bromine atom from the thiophene ring that formed.

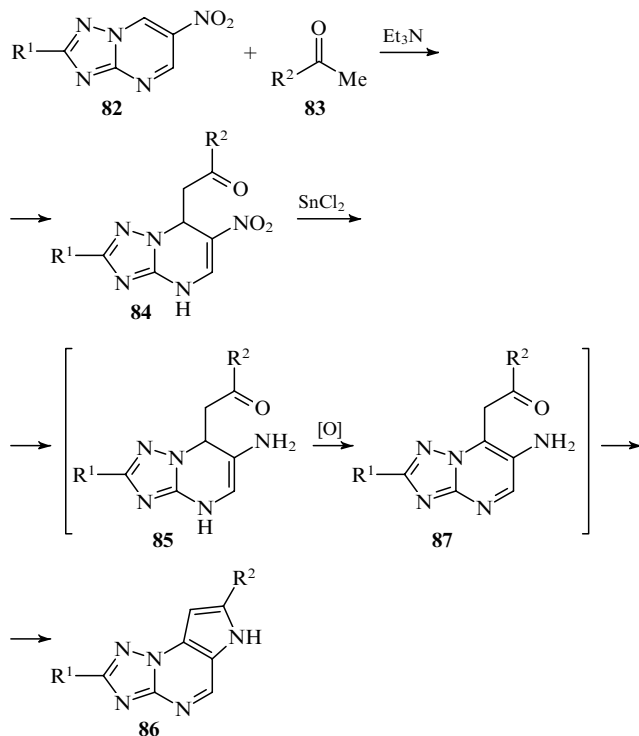


The reaction of pyrazine **79** with pyridine provides an interesting example of an intramolecular $\text{S}_{\text{N}}^{\text{H}}$ reaction.⁵⁶



This reaction was not completed by the formation of product **80** by the *ipso*-substitution of the chlorine atom. Under the action of an excess of pyridine, the carbanionic centre was generated in the side chain of the pyrazine ring and intramolecular cyclisation took place. Cycloadduct **81** underwent aromatisation through elimination of the proton together with the tosyl substituent.

For nitroarenes, commonly used procedures for the construction of heterocycles are based on the nucleophilic substitution of hydrogen followed by cyclisation of the S_N^H -reaction product involving the *ortho*-substituent.¹⁴ This strategy, as applied to compounds of the heterocyclic series, is exemplified only by the reactions of 6-nitrotriazolo[1,5-*a*]pyrimidines **82** with acyl derivatives **83** of aromatic and heteroaromatic compounds giving rise to products of addition at the C(7) atom (**84**).⁵⁷



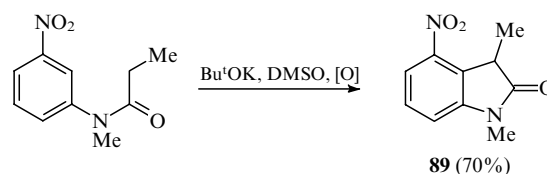
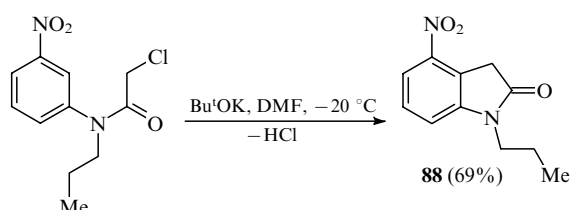
$R^1 = H, Me; R^2 = Ph, 4-HalC_6H_4, 2-thienyl, 2-furyl$.

Reduction of the nitro group in the adducts **84** by tin(II) chloride did not stop at the formation of the corresponding amine **85** and afforded triazolopyrrolopyrimidine **86** as a result of oxidative aromatisation of the amine **85** followed by intramolecular cyclisation of product **87**.

IV. Construction of nitroarene-based heterocyclic systems

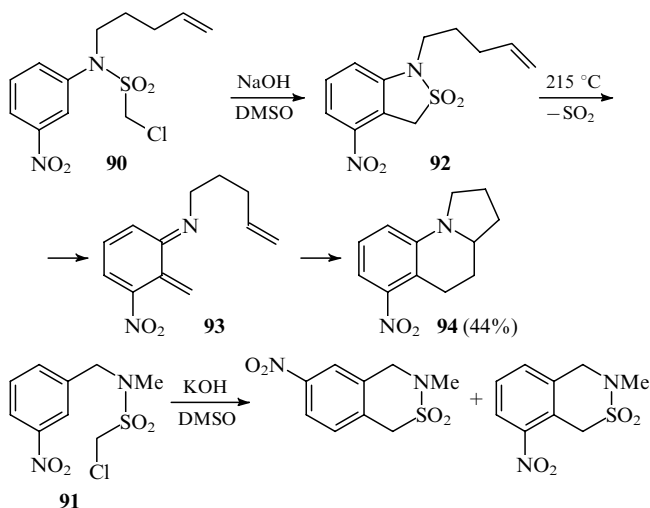
Most of the procedures for the direct annelation of heterocycles to nitroarenes consist in intramolecular S_N^H processes followed by cyclisation. In spite of the fact that the ring closure is not necessarily associated with the nucleophilic attack on the unsubstituted carbon atom, the S_N^H reactions of nitroarenes with binucleophiles are the key steps in these syntheses. These methods open up approaches to a wide range of biologically active indoles and quinolines, including those of natural origin. Since these methods have been surveyed in the recent review,¹⁴ we consider these questions only briefly.

Procedures for annelation of five- and six-membered heterocycles to nitroarenes are based on oxidative and intramolecular vicarious nucleophilic substitution of hydrogen. The syntheses of nitroxyindoles **88**⁵⁸ and **89**¹⁴ are examples. In the former case,



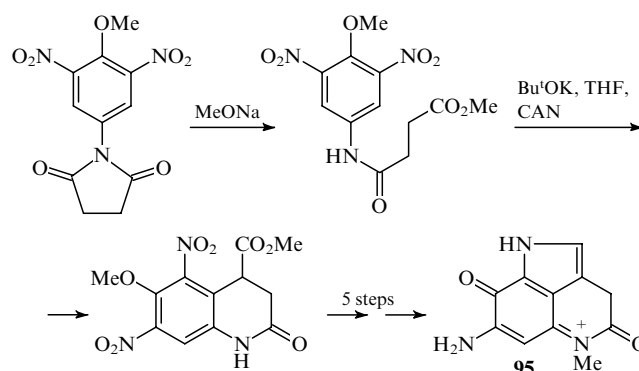
aromatisation of the σ^H adduct proceeds through the vicarious mechanism. The latter reaction involves oxidative aromatisation.

The intramolecular vicarious substitution of hydrogen in nitrophenyl- (**90**) and nitrobenzylchloromethylsulfonamides (**91**) led to annelation of five- and six-membered rings, respectively, to the arene ring.^{59–62}



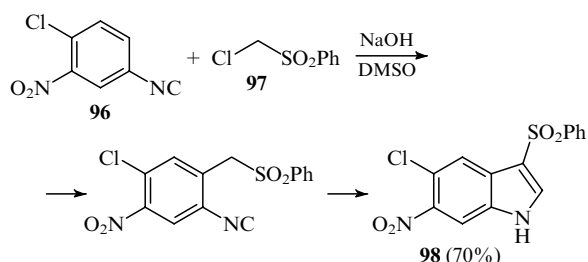
Interestingly, the initially formed cyclisation product **92** can be readily transformed into the quinoline derivative. Thermolysis of the compound **92** led to SO_2 extrusion with the formation of azaxylene **93**. The subsequent intramolecular [4 + 2]-cycloaddition afforded tetrahydroquinoline **94**.^{59–62}

The intramolecular S_N^H reactions can be employed for the preparation of the key compounds used in the syntheses of some natural substances. For instance, the synthesis of the natural antitumour drug makaluvamine C (**95**) found in marine sponges involved the closure of the six-membered ring on the basis of the oxidative S_N^H reaction.^{63, 64}

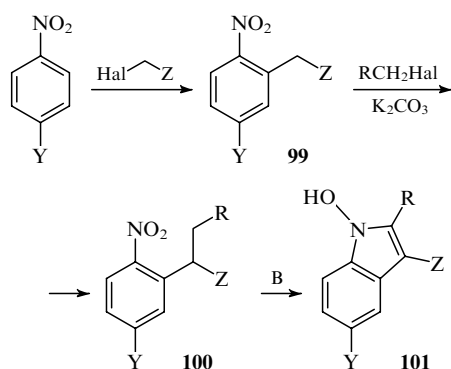


$CAN = (NH_4)_2Ce(NO_3)_6$.

The reactions of nitroarenes with bifunctional nucleophilic reagents can be accompanied by intramolecular cyclisation with the participation of such substituents in the aromatic substrate, as CN, NO_2 , etc. For example, the presence of the amino group in substituted *m*-nitroanilines made it possible to synthesise indole derivatives by its reactions with acetophenones⁶⁵ or phenylacetonitrile.⁶⁶ Isocyanonitrobenzenes can also be involved in analogous transformations. Thus, the product of the S_N^H reaction of compound **96** with α -chloromethyl sulfone **97** underwent spontaneous cyclisation to give nitroindole **98**.⁶⁷

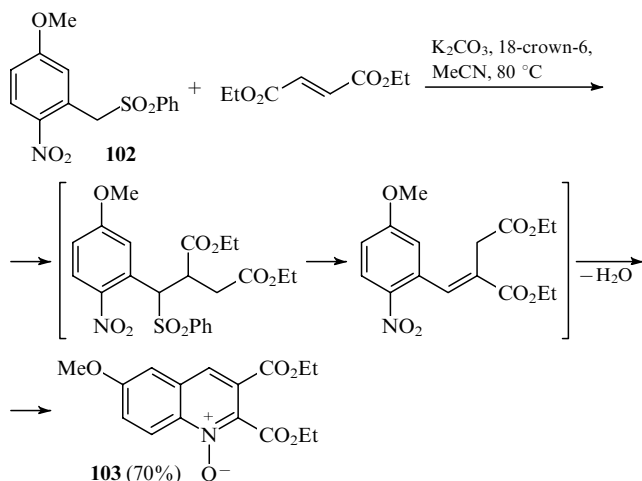


In some cases, cyclisation of nitroarenes proceeds with the involvement of the nitro group itself. For instance, nitrophenyl-acetonitriles **99** (Z = CN) generated by the S_N^H reactions can be readily alkylated. The resulting compounds **100** contain the nucleophilic centre in the side chain. In the presence of bases, these compounds undergo cyclisation involving the nitro group to yield *N*-hydroxyindole derivatives **101**.^{19, 68, 69}

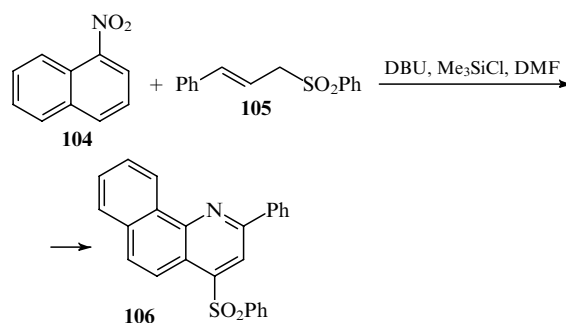


Y = Cl, Br, OMe; Z = CN, CO₂Bu, Tos, SO₂Ph;
R = Et, n-C₇H₁₅, CH = CH₂, CO₂Et, CONMe₂.

This approach can also be used in the annelation of a six-membered ring to an arene ring. For example, benzyl sulfone **102** was subjected to Michael condensation with α,β-unsaturated esters of carboxylic acids. In the presence of bases, the intermediate generated in this process underwent a series of transformations involving the nitro group to form quinoline *N*-oxide **103**.¹⁴

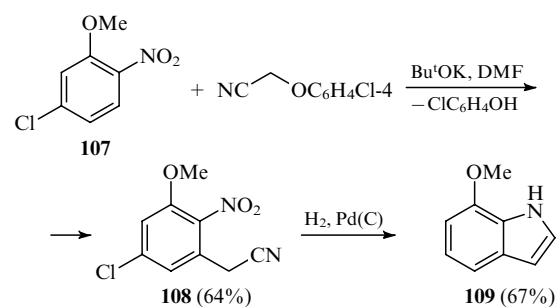


The reactions in which the heterocycle closure takes place *in situ* without isolation of intermediates are of particular interest.²⁰ For example, the reaction of nitronaphthalene **104** with sulfone **105** was not completed by the formation of the σ^H adduct. Under the reaction conditions, this adduct underwent aromatisation through an intramolecular redox process and cyclisation to give quinoline derivative **106**.

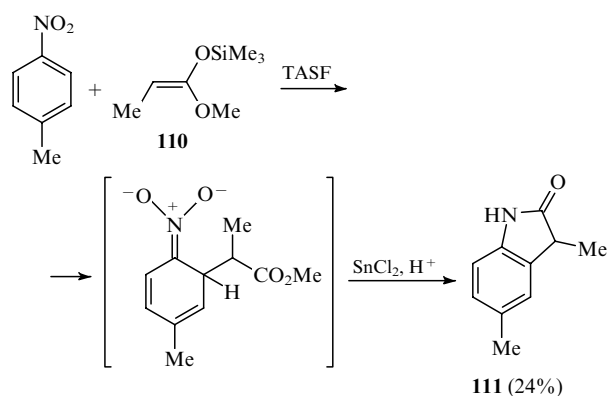


DBU is 1,8-diazabicyclo[5.4.0]undec-7-ene.

The syntheses in which annelation of the heterocycle proceeds with the participation of the amino group generated by reduction of the nitro group of nitroarenes can be considered separately. In these syntheses, acetonitrile and acetophenone derivatives, silyl ethers of ketones, CH-active derivatives of carboxylic acids and other polyfunctional derivatives are used as nucleophiles. Both S_N^H-reaction products and σ^H adducts can be subjected to reductive cyclisation. For example, the reaction of *o*-nitroanisole **107** with (4-chlorophenoxy)acetonitrile was accompanied by vicarious nucleophilic substitution S_N^H to produce cyanomethyl derivative **108**. Reduction of the latter led to annelation of the pyrrole ring to the anisole ring to give methoxy-substituted indole **109**.⁶⁸



Examples of reductive cyclisation of σ^H adducts of nitroarenes have been reported. Thus, the σ^H adduct formed in the course of the fluoride-induced addition of trimethylsilyloxyethylene **110** to nitroarenes underwent cyclisation into indolin-2-one **111** under the action of tin(II) chloride.⁶⁹



TASF = (Me₂N)₃S(Me₃SiF₂).

V. Conclusion

In the present review, we generalised and analysed the reactions of azines and nitroarenes containing at least one unsubstituted aromatic carbon atom with bifunctional nucleophilic reagents. These transformations were considered in the context of the construction of fused heterocycles. All the above-considered syntheses share a common trait, *viz.*, the initial attack of a nucleophile on the unsubstituted carbon atom of azine or nitroarene to give σ^H adducts, which are generated rapidly and

reversibly regardless of the presence of nucleofugal groups in the substrate. Subsequent transformations of σ^H adducts depend on the nature of the substrate and nucleophilic reagent.

The formation of cyclisation products is most typical of azines containing heteroatoms at positions 1 and 2, 1 and 3 or 1 and 4. Cycloadducts prepared by the A_N-A_N reactions can be subjected to dissociation and isomerisation. These products can be stabilised by acylation, nitrosation, alkylation or further S_N^H -transformations. Fused heterocycles prepared in the tandem reactions $A_N-S_N^{ipso}$ and $S_N^H-S_N^{ipso}$ are more stable and are not prone to isomerisation.

To construct heterocycles from nitroarenes, it is most often necessary to introduce an additional functional group into the aromatic ring although the nitro group by itself can be of use.

To summarise, the data surveyed in this review provide evidence that nucleophilic attack on the unsubstituted carbon atom of azines and nitroarenes is a powerful tool for the synthesis of fused heterocycles.

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

^b — *Chem. Heterocycl. Compd. (Engl. Transl.)*

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^d — *Dokl. Chem. (Engl. Transl.)*

1,3- and 1,4-Substituted tetrazolium salts

S V Voitekhovich, P N Gaponik, O A Ivashkevich

Contents

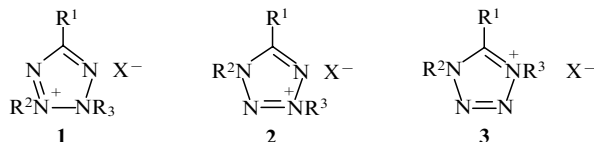
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Abstract. The published data on the synthesis, physicochemical properties, structures and reactions of 1,3-(1,3,5)- and 1,4-(1,4,5)-substituted tetrazolium salts are systematised and generalised. Their applications as starting compounds in the preparative chemistry of heterocyclic derivatives and some other branches of science and technology are reviewed. The bibliography includes 122 references.

I. Introduction

Compounds containing positively charged tetrazole rings have been known since the end of the 19th century, since the first description of 2,3-substituted tetrazolium salts **1**. Later, these compounds were given considerable attention in connection with their reduction into brightly coloured formazane under the action of various reagents. At present, practical applications of 2,3-substituted tetrazolium salts are based on chemical, biochemical, electrochemical and radiochemical reduction. These compounds proved to be especially useful in biochemical, microbiological, histochemical and cytochemical studies, analytical chemistry and clinical analysis as well as components of ionising radiation monitors and photosensitive materials, germination indicators of grain crops and phase-transfer catalysts.^{1–5} Other types of tetrazolium salts which differ in the positions of substituents at the nitrogen atoms have not received much attention until recently.

The situation has changed in the past decade owing to the appearance of a great number of publications devoted to 1,3- (**2**) and 1,4-substituted (**3**) tetrazolium salts.



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In many respects, this is due to the development of synthetic methods including selective procedures, which make possible direct synthesis of tetrazolium salts **2** and **3** with predetermined compositions and structures which can be used in organic chemistry and some other branches of science and technology. However, systematised data on the synthesis, properties and applications of these compounds are still absent in the literature. Previously published reviews^{1–5} deal with the description of mostly 2,3-substituted tetrazolium salts. The reviews devoted to the chemistry of tetrazoles^{6–8} and some of its particular aspects^{9–11} published in the past decade provide separate and, sometimes,^{8,10,11} very scarce data on 1,3- and 1,4-substituted tetrazolium salts.

The aim of the present review is to generalise the information on 1,3- and 1,4-substituted tetrazolium salts over the past 10–15 years in order to highlight current trends in their synthesis with special emphasis on the availability of tetrazolium salts and their efficacy in organic synthesis. Earlier publications that have not been cited in other reviews and monographs are also surveyed.

Depending on the nature of the substituent at C(5), tetrazolium salts **2** and **3** can be divided into two groups, viz., 1,3- and 1,4-disubstituted tetrazolium salts containing a labile hydrogen atom at the carbon atom of the heterocycle and 1,3,5- and 1,4,5-trisubstituted tetrazolium salts where $R^1 \neq H$. Yet another class of 1,3,5-trisubstituted tetrazolium salts, viz., compound **2** with the substituent R^1 represented by an anionic group [O^- , NH^- , $-C(CN)_2$, etc.], are referred to as mesoionic tetrazoles.¹² As the behaviour of these internal salts differs drastically from that of ordinary tetrazolium salts, they are not considered in the present review.

II. Methods for the synthesis of tetrazolium salts

All currently known approaches to the synthesis of 1,3- and 1,4-substituted tetrazolium salts can be classified into two main groups: (1) transformations of tetrazoles and (2) heterocyclisation of polynitrogenous linear structures.

The first group includes a broad range of processes, in the first place, direct exhaustive alkylation of tetrazoles at the endocyclic nitrogen atoms, i.e., quaternisation. Reactions involving exocyclic atoms of mesoionic tetrazoles and 1,4-dihydrotetrazoles and reactions affecting both endo- and exocyclic atoms of functionalised tetrazoles leading to the formation of annelated tetrazolium salts are also related to this group. Conversions of some tetrazolium salts into other ones do not have as a rule any preparative

significance and are considered in the section devoted to the chemical properties of tetrazolium salts.

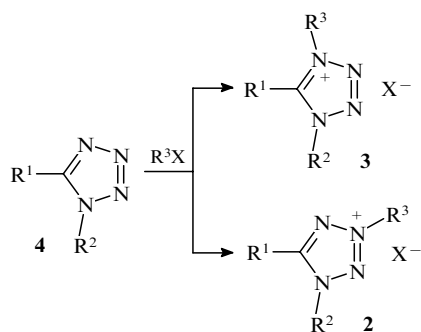
The second group includes few heterocyclisation reactions the main advantage of which is that they exclude the use of tetrazoles in the synthesis of tetrazolium salts.

Quaternisation of tetrazoles is the most popular and simple procedure for the synthesis of 1,3- and 1,4-substituted tetrazolium salts. This method is based on two approaches which differ in the nature of the alkylating reagents and the reaction media. The practical significance of quaternisation reactions has increased considerably in the past decade owing to the ready availability of diverse tetrazole derivatives.^{6–10}

1. Quaternisation of tetrazoles in organic media

In the early 1950's, it was shown for the first time that *N*-substituted tetrazoles, particularly 1-aryl-5-methyltetrazoles, react with methyl iodide to yield quaternary salts.¹ Later, it was established that quaternisation is largely a general process which involves all isomeric *N*-substituted tetrazoles^{13–37} including fused ones;^{16, 20, 24, 34} the role of alkylating reagents is played by alkyl halides, alkyl sulfates, oxonium salts and related compounds of which methylating and ethylating reagents^{13–37} as well as α -halogeno carbonyl compounds (bromoacetone^{18, 35, 37} and phenacyl bromides^{21, 27, 35, 37}) are studied most extensively. The mechanisms of quaternisation of *N*-substituted tetrazoles still remain obscure. It can be assumed, however, that similar to other azoles, quaternisation of tetrazoles occurs by an S_N2 mechanism. The azole molecule, which plays the role of a nucleophilic reagent with respect to alkyl halide, passes into a quaternised form. This reaction is accompanied by the Walden inversion.^{38, 39}

Quaternisation of tetrazoles for the synthesis of tetrazolium salts poses certain problems. In the first place, this is due to the non-selectivity of this reaction due to the ambident character of the tetrazolium ring^{3, 6, 7} and the necessity to separate the mixtures of isomeric tetrazolium salts formed. Thus quaternization of 1-mono- and 1,5-disubstituted tetrazoles **4** yields a mixture of isomeric tetrazolium salts **2** and **3**.^{13, 15–25, 27, 28, 31, 32–37}



In the case of 1-monosubstituted tetrazoles **4** ($R^1 = H$), the predominant reaction is the attack at the N(4) atom^{13, 15, 18, 21, 28, 33} manifesting the highest basicity (proton affinity) irrespective of the nature of the R^2 substituent.^{6, 8, 40} The presence of a substituent at C(5) increases the content of the 1,3-substituted tetrazolium salt **2** which becomes predominant in the presence of bulky substituents R^1 . Individual salts can be isolated from the mixtures owing to differences in the solubilities of the isomers. In most cases, 1,4,5-isomers are soluble in water and lower alcohols less readily than 1,3,5-isomers. Sometimes, individual salts **3** precipitate immediately.^{14, 22, 25, 32} This approach is largely used in the synthesis of 1,4-substituted tetrazolium salts (Table 1).

The use of 2-mono- and 2,5-disubstituted tetrazoles for the synthesis of 1,3-substituted tetrazolium salts seems to be more appropriate, since the quaternisation of the latter proceeds selectively at the N(4) atom (Table 2). However, by reason of the lower basicity of this type of tetrazole,⁴¹ their quaternisation requires more drastic conditions (elevated temperatures and

sometimes high pressure) than that for tetrazoles **4**.^{3, 17, 18, 21, 23, 27–29, 35–37}

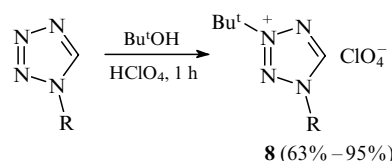
The use of tetrazole and its 5-monosubstituted derivatives **5** as starting compounds in the synthesis of tetrazolium salts is rather attractive, since the methods for the preparation of compounds **5** have been well developed.⁴² Nevertheless, exhaustive alkylation of this type of tetrazole has been studied for a limited number of compounds only. Thus the methylation of 5-methyltetrazole with an excess of methyl iodide (40 °C, 10 days) yields a mixture of 1,4,5- and 1,3,5-trimethyltetrazolium iodides in a 68 : 32 ratio.¹⁴ Later, it was found that tetrazoles with substituents in position 5 react with an excess of dimethyl sulfate upon heating to give 1,3- (**6**, $X = \text{MeSO}_4^-$) and 1,4-dimethyl-5-*R*-tetrazolium methyl sulfates (**7**, $X = \text{MeSO}_4^-$) (Table 3).^{32, 33} The ratio of the isomers formed depends on the nature of the substituent at the C(5) atom; owing to steric factors, the proportion of the 1,3,5-isomer **6** increases in the following order: $R = \text{Me, Et, Ph, Bu}^t$ (19%, 31%, 55% and 91%, respectively).³² The isolation of the main isomer is achieved by precipitation of the corresponding perchlorates³² and picrates³³ (see Table 3).

To conclude, special mention should be made of a study²⁶ which represents an approach to the mathematical estimation of the feasibility of quaternisation and alkylation of some azoles including tetrazoles. The authors attempted to correlate the sum of normalised potentials with pK_a values of azoles and demonstrated the applicability of these principles in several reactions.

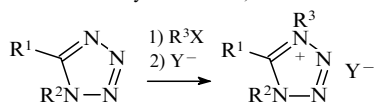
2. Quaternisation of tetrazoles in acidic media

The methods for the synthesis of tetrazolium salts based on quaternisation of tetrazoles with alcohols in acidic media were proposed in the past decade^{22, 30, 33, 36, 43–49} and are being intensively developed at present. The studies into the alkylation of 5-*R*-tetrazoles in strong acids which, contrary to the reactions occurring in neutral media, proceed selectively at the N(2) atom, formed the basis for these methods.^{50–52} Kinetic studies and an analysis of reaction mechanisms revealed that the selectivity is due to blocking of the most nucleophilic N(4) atom because of its protonation.^{53, 54} Later, it was found that the regioselectivity of the tetrazole alkylation in acidic media remains in the quaternisation. This allowed development of efficient procedures for the synthesis of tetrazolium salts and enlargement of their range by virtue of quaternising reagents that made it possible to introduce branched substituents onto the 'pyridine' nitrogen atom. It is now established that quaternisation of tetrazoles can be effected by alcohols that generate stable carbocations (*e.g.*, *tert*-butyl^{17, 22, 33, 36, 45–49} and diacetone alcohols,^{46, 47} 2,5-dimethylhexane-2,5-diol,³⁶ isopropyl alcohol,⁴⁹ 1-phenylethanol,⁴⁹ adamantan-1-ol⁴³ and α -ferrocenyl-substituted alcohols) in acidic media.⁴⁴ These reactions are usually carried out in strong mineral acids (*e.g.*, perchloric, sulfuric, tetrafluoroboric)^{33, 36, 45–49} or biphasic systems consisting of an organic solvent (ether, dichloromethane) and an acid.^{17, 22, 44} The direction of quaternisation cannot always be predicted unequivocally, since it depends on many factors, such as the nature of the substrate and the alkylating reagent, medium acidity and reaction time.

1,3-Disubstituted tetrazolium salts **8** and **9** were obtained in high yields by quaternisation of 1-monosubstituted tetrazoles with *tert*-butyl^{36, 45, 47} and isopropyl⁴⁹ alcohols in 72% perchloric acid at 20 °C and contained no admixtures of the corresponding 1,4-isomers.

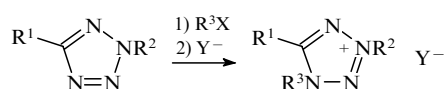


$R = \text{Me, Et, Bu}^t, \text{Bn, cyclo-C}_6\text{H}_{11}.$

Table 1. The synthesis of 1,4-substituted tetrazolium salts by quaternisation of 1-mono- and 1,5-disubstituted tetrazoles.

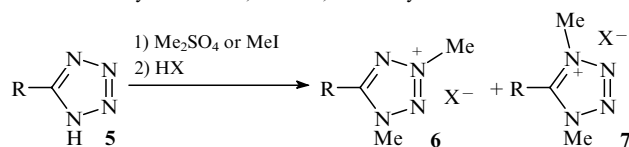
R ¹	R ²	R ³ X	Quaternisation conditions		Y	Yield (%)	M.p. /°C	Ref.
			T /°C	t /h				
Me	Me	Me ₂ SO ₄	20–25	216	I	50	266	18
Me	Me	Me ₂ SO ₄	120	1	ClO ₄	59	205–206	22
Et	Me	Me ₂ SO ₄	120	1	ClO ₄	51	146–147	22
Pr ⁱ	Me	Me ₂ SO ₄	120	1	ClO ₄	41	155–157	22
Pr ⁱ	Me	Me ₂ SO ₄	120	1	PF ₆	28	177–178	22
Me	Bu ^t	Me ₂ SO ₄	120	1	BF ₄	21	112–114	22
CH ₂ Bu ^t	Me	Me ₂ SO ₄	120	1	ClO ₄	41	185–186	22
CH ₂ Bu ^t	Me	Me ₂ SO ₄	120	1	BF ₄	22	166–168	22
Bn	Me	Me ₂ SO ₄	120	1	BPh ₄	44	207–210 ^a	22
Pr ⁱ	Ph	Me ₂ SO ₄	120	1	PF ₆	30	144–145	22
CH ₂ Bu ^t	Ph	Me ₂ SO ₄	120	1	PF ₆	44	237 ^a	22
Me ₂ NCH=CH	Ph	Me ₂ SO ₄	80	4	ClO ₄	58	160–161	25
Me ₂ NCH=CH	Ph	MeI	100	24	ClO ₄	60	160–161	25
Me ₂ NCH=CH	4-MeC ₆ H ₄	Me ₂ SO ₄	80	4	ClO ₄	69	154–155	25
Me ₂ NCH=CH	4-PhC ₆ H ₄	Me ₂ SO ₄	80	4	ClO ₄	85	166–167	25
Me ₂ NCH=CH	4-MeOC ₆ H ₄	Me ₂ SO ₄	80	4	ClO ₄	55	153–154	25
Me ₂ NCH=CH	4-FC ₆ H ₄	Me ₂ SO ₄	80	4	ClO ₄	61	168–169	25
Me ₂ NCH=CH	4-FC ₆ H ₄	Et ₂ SO ₄	90	8	ClO ₄	22	116–117	25
Me ₂ NCH=CH	4-ClC ₆ H ₄	Me ₂ SO ₄	80	4	ClO ₄	65	193–194	25
Me ₂ NCH=CH	4-ClC ₆ H ₄	Et ₂ SO ₄	90	8	ClO ₄	28	126–127	25
Me ₂ NCH=CH	4-BrC ₆ H ₄	Me ₂ SO ₄	80	4	ClO ₄	70	208–209	25
Me ₂ NCH=CH	4-BrC ₆ H ₄	Et ₂ SO ₄	90	8	ClO ₄	32	146–147	25
Me ₂ NCH=CH	4-IC ₆ H ₄	Me ₂ SO ₄	80	4	ClO ₄	84	209–210	25
Me ₂ NCH=CH	4-IC ₆ H ₄	Et ₂ SO ₄	90	8	ClO ₄	43	157–158	25
MeS	Me	Me ₂ SO ₄	70–80	0.5	BF ₄	69	141–143	17
MeS	Bu ^t	Me ₃ OBf ₄	40	12	BF ₄	95	121–123	17
H	Me	BrCH ₂ COPh	80	96	Br	90	145–148	21
Me	Me	BrCH ₂ COC ₆ H ₄ Br-4	70–75	96	Br	70	170–171	27
Me	Me	BrCH ₂ COC ₆ H ₄ NO ₂ -4	70–75	120	Br	35	130–135	27
Me	Pr ⁿ	BrCH ₂ COPh	70–75	72	Br	79	156–157	27
Me	Pr ⁱ	BrCH ₂ COPh	70–75	48	Br	84	157–158	27
Me	Bu ⁱ	BrCH ₂ COPh	70–75	24	Br	79	155	27
Me	cyclo-C ₆ H ₁₁	BrCH ₂ COPh	70–75	5	Br	75	182–184	27
NH ₂	CH ₂ COMe	Me ₂ SO ₄	20–25	48	Br	14	240 ^a	35
NH ₂	Me	BrCH ₂ COPh	90	8	Br	88	220 ^{a, b}	35
CH ₂ COMe	Me	BrCH ₂ COMe	50–55	288 ^c	BF ₄	33	124–127	37
H	CH ₂ COMe	MeI	50	5.5 ^d	I	35	130	18
Me	CH ₂ COMe	MeI	50	5.5 ^d	I	43	162–163	18
Me	Me	BrCH ₂ COMe	50	6 ^d	Br	65	157–158	18
Ph	Me	Me ₂ SO ₄	35	15	ClO ₄	78	159–160	23
C ₆ H ₄ NO ₂ -3	Me	Me ₂ SO ₄	35	15	ClO ₄	83	135–137	23
		Me ₂ SO ₄	82	1	BF ₄	75	131–135	24
		Me ₂ SO ₄	82	1	BF ₄	80	267–269	24
		Et ₃ OBf ₄	20	20	BF ₄	65	185–187	24

^a With decomposition; ^b M.p. of the corresponding semihydrate; ^c the reaction was carried out in the presence of AgBF₄; ^d the reaction was carried out under high pressure.

Table 2. The synthesis of 1,3-substituted tetrazolium salts by quaternisation of 2-mono- and 2,5-disubstituted tetrazoles.

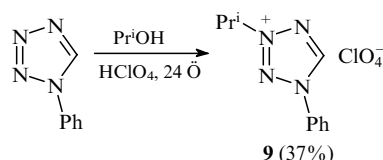
R ¹	R ²	R ³ X	Quaternisation conditions		Y	Yield (%)	M.p. /°C	Ref.
			T /°C	t /h				
CH ₂ COMe	Me	BrCH ₂ COPh	60	14 ^a	BF ₄	57	159–161	37
CH ₂ CO ₂ Me	Me	BrCH ₂ COPh	60	10 ^a	BF ₄	81	123–124	37
CH ₂ CO ₂ Me	Me	BrCH ₂ COC ₆ H ₄ Br-4	60	10 ^a	BF ₄	82	107–109	37
CH ₂ COMe	Me	BrCH ₂ COMe	60	10 ^a	BF ₄	57	oil	37
CH ₂ CO ₂ Me	Me	BrCH ₂ COMe	60	7 ^a	BF ₄	60	145	37
CH ₂ COMe	Ph	BrCH ₂ COPh	60	14 ^a	BF ₄	80	210–211	37
CH ₂ COMe	Ph	BrCH ₂ COMe	60	14 ^a	BF ₄	60	145	37
NH ₂	Me	BrCH ₂ COMe	60	5	Br	45	140–170	35
NH ₂	Me	BrCH ₂ COPh	90	2.9	Br	60	230	35
H	Me	BrCH ₂ COPh	60	2 ^a	Br	69	138–140	21
H	Me	BrCH ₂ COC ₆ H ₄ Br-4	60	2 ^a	Br	55	171–172	21
H	Me	BrCH ₂ COC ₆ H ₄ NO ₂ -4	60	2 ^a	Br	62	153–154	21
Me	Me	BrCH ₂ COPh	60	2	Br	57	142–146	21
H	CH ₂ COPh	Me ₂ SO ₄	20	2	Br	91	121–122	21
H	CH ₂ COC ₆ H ₄ Br-4	Me ₂ SO ₄	20	2	Br	78	135–137	21
H	CH ₂ COC ₆ H ₄ NO ₂ -4	Me ₂ SO ₄	20	2	Br	82	132–134	21
Me	CH ₂ COPh	Me ₂ SO ₄	20	2	Br	96	115–117	21
Ph	Ph	Me ₂ SO ₄	80	8	ClO ₄	85	209–210	29
C ₆ H ₄ Me-4	Ph	Me ₂ SO ₄	80	8	ClO ₄	86	224–226	29
C ₆ H ₄ OMe-4	Ph	Me ₂ SO ₄	80	8	ClO ₄	87	228–230	29
C ₆ H ₄ Cl-4	Ph	Me ₂ SO ₄	80	8	ClO ₄	90	255–257	29
Ph	C ₆ H ₄ NO ₂ -4	Me ₂ SO ₄	80	8	ClO ₄	87	272–273	29
Ph	C ₆ H ₄ Me-4	Me ₂ SO ₄	80	8	ClO ₄	82	243–245	29
Ph	C ₆ H ₄ OMe-4	Me ₂ SO ₄	80	8	ClO ₄	88	230–232	29
Ph	C ₆ H ₄ Cl-4	Me ₂ SO ₄	80	8	ClO ₄	91	265–267	29
H	CH ₂ COMe	MeSO ₃ F	20	0.17	FSO ₃	92	84–86	18
Me	CH ₂ COMe	MeI	50	0.23 ^b	I	46	144	18
C ₆ H ₄ OMe-4	Me	Me ₂ SO ₄	60	1.25	ClO ₄	68	144–145	23
C ₆ H ₄ Me-4	Me	Me ₂ SO ₄	60	1.25	ClO ₄	73	142–144	23
C ₆ H ₄ Me-3	Me	Me ₂ SO ₄	60	1.25	ClO ₄	62	103–104	23
Ph	Me	Me ₂ SO ₄	60	1.25	ClO ₄	78	129–131	23
C ₆ H ₄ I-4	Me	Me ₂ SO ₄	60	1.25	ClO ₄	77	140–142	23
C ₆ H ₄ Br-3	Me	Me ₂ SO ₄	60	1.25	ClO ₄	69	165	23
C ₆ H ₄ NO ₂ -3	Me	Me ₂ SO ₄	60	1.25	ClO ₄	87	138–139	23
C ₆ H ₄ NO ₂ -4	Me	Me ₂ SO ₄	60	1.25	ClO ₄	87	204	23

^a The reaction was carried out in the presence of AgBF₄; ^b the reaction was carried out under high pressure.

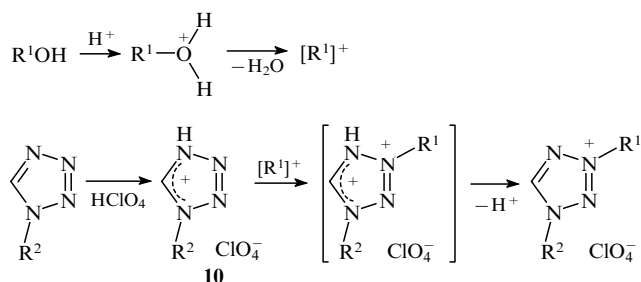
Table 3. The synthesis of 1,3- and 1,4-dimethyl-5-R-tetrazolium salts **6** and **7** by quaternisation of 5-R-tetrazoles **4**.

Salt	R	Alkylating reagent	X	Quaternisation conditions		Yield (%)	M.p. /°C	Ref.
				T /°C	t /h			
6	Me	MeI	I	40	240	26	266 ^a	14
6	Bu ^t	Me ₂ SO ₄	ClO ₄	90	1	72	149–150	32
7	Me	MeI	I	40	240	51	130 ^a	14
7	Me	Me ₂ SO ₄	ClO ₄	90	1	69	204–205	32
7	Me	Me ₂ SO ₄	2,4,6-(NO ₂) ₃ C ₆ H ₂ O	90	2	35	164–166	33
7	Et	Me ₂ SO ₄	ClO ₄	90	1	60	144–146	32

^a With decomposition.

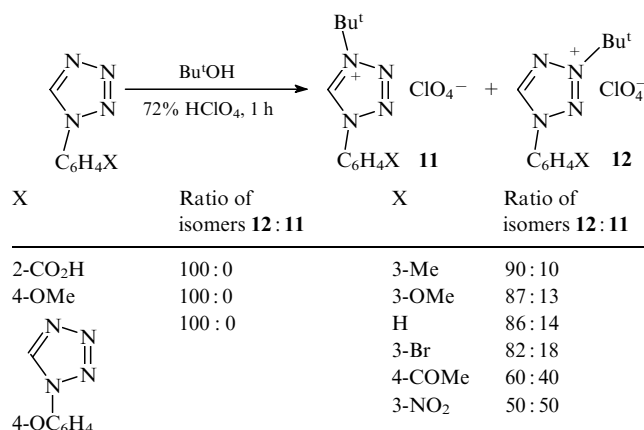


The regioselectivity of quaternisation is achieved by virtue of complete protonation of 1-*R*-tetrazole at the most nucleophilic nitrogen atom N(4) with the formation of the 1-*R*-4*H*-tetrazolium cation **10** in which the N(2) and N(3) atoms are susceptible to electrophilic attack. The attack at the N(2) atom is sterically hindered due to the presence of a substituent at the N(1) atom. Therefore, the carbocation generated from the alcohol, attacks the tetrazolium cation at the N(3) atom.⁴⁵

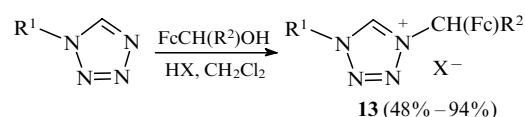


The assumption of a reaction of the azolium cation with the carbocation is unusual at first glance; however, the results of quantum-chemical calculations^{45, 53} suggest that such a reaction is possible, since the N(2) and N(3) atoms of the 1-*R*-4*H*-tetrazolium cation **10** retain sufficiently high π -electron density.

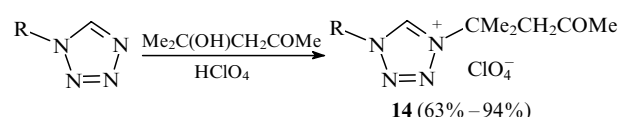
Selective preparation of 1,3-disubstituted tetrazolium salts demands special conditions to be met, which ensure complete protonation of the starting tetrazoles⁴⁵ and exclude the possibility of isomerisation of 1,3-substituted tetrazolium salts into the corresponding 1,4-isomers in the course of the reaction.^{45, 55} Moreover, quaternisation occurs smoothly only in the case of 1-alkyltetrazoles.⁴⁵ 1,4-Disubstituted tetrazolium salts **11** are formed as reaction products in the quaternisation of some 1-aryltetrazoles with *tert*-butyl alcohol. Their proportion increases in the presence of electron-withdrawing groups in the aryl substituent,^{36, 45, 47, 49} which is explained⁴⁹ by lower basicity of 1-aryltetrazoles in comparison with their alkyl analogues.⁴¹



Under certain conditions, individual 1,4-disubstituted tetrazolium salts **13** and **14** can also be prepared by quaternisation of 1-*R*-tetrazoles with α -ferrocenyl-substituted⁴⁴ or diacetone alcohols.^{46, 47}



$R^1 = \text{Bn, Ph, 4-MeOC}_6\text{H}_4, 4\text{-BrC}_6\text{H}_4, 4\text{-NO}_2\text{C}_6\text{H}_4$; $R^2 = \text{H, Me, Ph}$;
Fc = $\text{C}_5\text{H}_4\text{FeC}_5\text{H}_5$; X = $\text{ClO}_4, \text{BF}_4$.

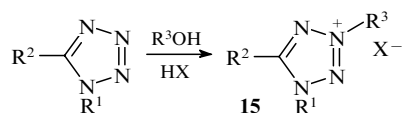


$R = \text{Me, Bn, cyclo-C}_6\text{H}_{11}, \text{Ph, 4-MeOC}_6\text{H}_4, 3\text{-NO}_2\text{C}_6\text{H}_4, 2\text{-HO}_2\text{CC}_6\text{H}_4, 2\text{-HO-4(5)-NO}_2\text{C}_6\text{H}_3$.

Because of steric hindrances, the aforementioned isomerisation of tetrazolium salts is not realised in the quaternisation of 1,5-disubstituted tetrazoles, which allows selective preparation of 1,3,5-trisubstituted tetrazolium salts **15** (Table 4).

1,3-Disubstituted tetrazolium salts **16** ($R^2 = \text{H}$) are formed in high yields upon quaternisation of 2-monosubstituted tetrazoles with alcohols in the presence of acids (Table 5). The yields of 1,3,5-trisubstituted derivatives in the reaction of 2,5-disubstituted

Table 4. The synthesis of 1,3,5-trisubstituted tetrazolium salts **15** by quaternisation of 1,5-disubstituted tetrazoles with alcohols in acidic media.



R^1	R^2	R^3	Quaternisation conditions		Yield (%)	M.p. /°C	Ref.
			HX	t /h			
Me	MeS	Bu ^t	54% HBF ₄ ^a	15	67	131–133	17
Bu ^t	MeS	Bu ^t	54% HBF ₄ ^a	15	64	154–155	17
Me	Pr ⁱ	Bu ^t	54% HBF ₄ ^a	15	48	129–131	22
Me	Me	Bu ^t	54% HBF ₄ ^a	15	52	149–150 ^b	22
Me	Me	Bu ^t	48% HBF ₄	48	40	151–152	30
Me	Me	Bu ^t	40% HClO ₄	48	46	140–141	30
CH ₂ =CH	Me	Bu ^t	48% HBF ₄	48	40	50 ^b	30
Me	Me	CM ₂ CH ₂ C(O)Me	72% HClO ₄	12	75	115–117	46

^a Solution in diethyl ether; ^b with decomposition.

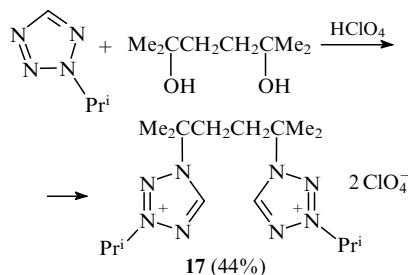
Table 5. The synthesis of 1,3- and 1,3,5-substituted tetrazolium salts **16** by quaternisation of 2-mono- and 2,5-disubstituted tetrazoles with alcohols in acidic media.

$\text{R}^1-\text{N} \begin{array}{c} \diagup \text{N} \diagdown \\ \diagdown \text{N} \diagup \end{array} \text{R}^2 \xrightarrow[\text{HX}]{\text{R}^3\text{OH}} \text{R}^1-\text{N}^+ \begin{array}{c} \diagup \text{N} \diagdown \\ \diagdown \text{N} \diagup \end{array} \text{R}^2 \text{X}^-$			Quaternisation conditions		Yield (%)	M.p. /°C	Ref.
			HX	<i>t</i> /days			
Me	H	Bu ^t	72% HClO ₄	2	95	150 ^a	48
Me	H	Bu ^t	48% HBF ₄	3	56	155–156	30
Et	H	Bu ^t	72% HClO ₄	2	80	133–135	48
Et	H	Bu ^t	48% HBF ₄	3	72	136–137	30
Pr ⁱ	H	Bu ^t	72% HClO ₄	2	96	130–131	48
Bu ^t	H	Bu ^t	72% HClO ₄	3	74	120–122	48
CH ₂ =CHCH ₂	H	Bu ^t	72% HClO ₄	2	89	143–145	48
CH ₂ =CHCH ₂	H	Bu ^t	48% HBF ₄	3	62	105–107	30
CH ₂ =CMe	H	Bu ^t	72% HClO ₄	2	88	145 ^a	48
CH ₂ BrCHMe	H	Bu ^t	72% HClO ₄	2	75	78–80	48
MeC(O)CH ₂ CH ₂	H	Bu ^t	72% HClO ₄	2	70	97–99	48
Me	H	CMe ₂ CH ₂ C(O)Me	72% HClO ₄	2	94	133–135	46
Et	H	CMe ₂ CH ₂ C(O)Me	72% HClO ₄	2	63	79–81	46
Pr ⁱ	H	CMe ₂ CH ₂ C(O)Me	72% HClO ₄	2	70	69–71	46
Ad	H	Ad ^b	74% H ₂ SO ₄	9	21 ^c	240–241	43
Me	CH ₂ =CH	Bu ^t	48% HBF ₄	3	45	50 ^a	30
Bu ^t	CH ₂ =CH	Bu ^t	48% HBF ₄	3	50	138–140 ^a	30
Et	Me	Bu ^t	48% HBF ₄	3	33	130–132	30

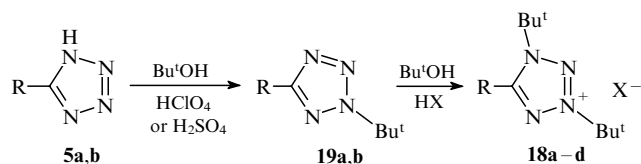
^a With decomposition; ^b Ad is 1-adamantyl; ^c isolated as perchlorate.

tetrazoles with *tert*-butyl alcohol in the presence of HBF₄ (see Ref. 30) do not exceed 50% (see Table 5), apparently due to steric hindrances preventing the introduction of the substituent into position N(4).

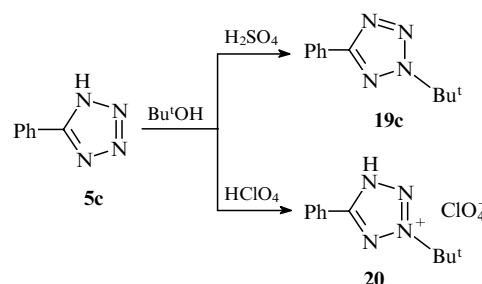
The synthesis of the salt **17** shows that quaternisation can successfully involve diols, which opens up new opportunities for the selective synthesis of binuclear tetrazolium salts.³⁶



1,3-Di-*tert*-butyl-5-*R*-tetrazolium salts **18a–d** were prepared by exhaustive alkylation of tetrazole (**5a**) and 5-methyltetrazole (**5b**) with *tert*-butyl alcohol in the presence of strong acids.^{33, 45} The selectivity of alkylation is explained by the intermediate formation of 2-*tert*-butyl-5-*R*-tetrazoles **19a,b** in which only the



Compound 18	R	X	Yield (%)	Ref.
a	H	ClO ₄	80	45
b	Me	ClO ₄	59	45
c	H	2,4,6-(NO ₂) ₃ C ₆ H ₂	62	33
d	Me	2,4,6-(NO ₂) ₃ C ₆ H ₂	10	33

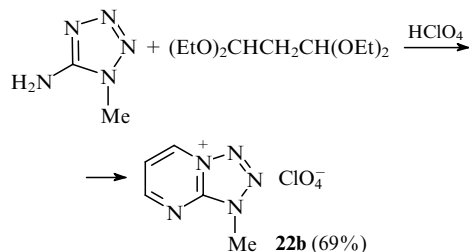
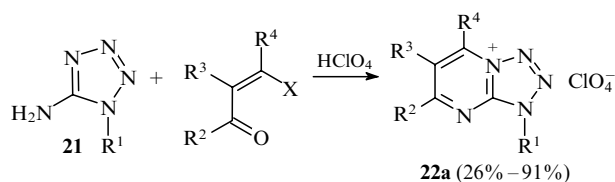


N(4) atom is accessible for quaternisation. In the case of 5-phenyl-tetrazole (**5c**), the expected tetrazolium salts are not formed, presumably due to steric hindrances. In this case, 2-*tert*-butyl-5-phenyltetrazole (**19c**)³³ or its protonated form, viz., 3-*tert*-butyl-5-phenyl-1*H*-tetrazolium perchlorate (**20**), was isolated as the alkylation product.⁴⁵

It may be expected that the methods for the synthesis of tetrazolium salts based on quaternisation of tetrazoles in the presence of strong acids will be developed further. Their attractiveness is due both to the availability of the starting compounds and the selectivity and simplicity of the reactions. The use of novel functionalised reagents in the quaternisation reaction will enable one to extend the range of available tetrazolium salts.

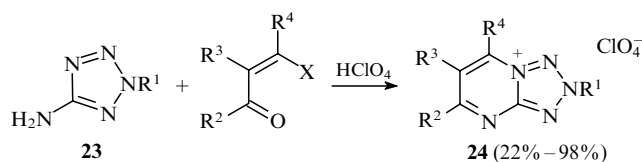
3. Miscellaneous methods based on the transformations of tetrazole derivatives

Disubstituted tetrazoles containing reactive groups at the C(5) atom react with bifunctional reagents to give annelated tetrazolium salts. It was shown, in particular,⁵⁶ that the condensation of 1-substituted 5-aminotetrazoles **21** with β-diketones, β-chloro-vinyl ketones and aldehydes as well as with malonaldehyde acetals yields 1-substituted tetrazolo[1,5-*a*]pyrimidinium salts **22a,b**. This reaction proceeds at 20 °C or upon short-term heating of solutions of the reactants in acids (*e.g.*, acetic, trifluoroacetic, perchloric) or in ethanol in the presence of perchloric acid.



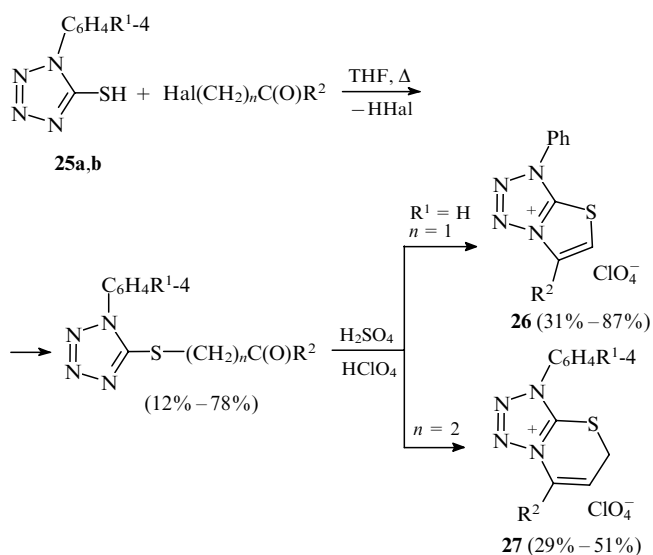
$\text{R}^1 = \text{Me}, \text{CH}=\text{CH}_2, \text{CH}_2\text{CH}=\text{CH}_2, \text{Bn}, \text{Ph}, \text{HO}_2\text{CCH}_2$; $\text{R}^2 = \text{H}, \text{Me}, \text{Ph}$; $\text{R}^3 = \text{H}, \text{Me}$; $\text{R}^4 = \text{H}, \text{Me}, \text{Ph}$; $\text{R}^3-\text{R}^4 = (\text{CH}_2)_4$; $\text{X} = \text{Cl}, \text{OH}$.

2-Substituted 5-aminotetrazoles **23** generate 2-substituted tetrazolo[1,5-*a*]pyrimidinium salts **24** under analogous conditions.⁵⁶



$\text{R}^1 = \text{Me}, \text{CH}_2\text{CH}=\text{CH}_2, \text{Bn}$; $\text{R}^2 = \text{H}, \text{Me}, \text{Ph}, \text{CO}_2\text{H}$; $\text{R}^3 = \text{H}, \text{Me}$; $\text{R}^4 = \text{H}, \text{Me}, \text{Ph}$; $\text{R}^3-\text{R}^4 = (\text{CH}_2)_4$; $\text{X} = \text{Cl}, \text{OH}$.

1-Aryl-5-mercaptotetrazoles **25a,b** react with α - and β -halogeno ketones with heating to give tetrazolylthioalkyl ketones which undergo cyclisation under the action of sulfuric acid in the presence of HClO_4 to give thiazolo[3,2-*d*]tetrazolium (**26**) and tetrazolo[5,4-*b*][1,3]thiazinium perchlorates **27**, respectively.^{7, 57}

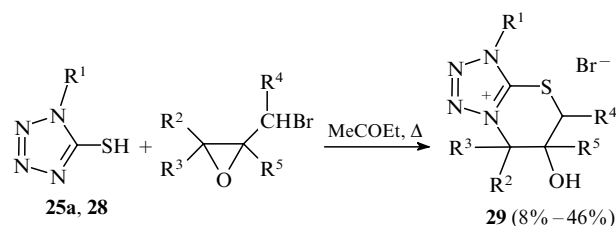


$\text{R}^1 = \text{H}$ (**25a**), Cl (**25b**);

26: $\text{R}^1 = \text{H}$; $\text{R}^2 = \text{Bu}^t, \text{Et}, \text{Ad}, \text{Ph}, 4\text{-MeOC}_6\text{H}_4, 4\text{-NO}_2\text{C}_6\text{H}_4, 4\text{-C}_6\text{H}_5\text{C}_6\text{H}_4, 4\text{-ClC}_6\text{H}_4, 4\text{-BrC}_6\text{H}_4$;

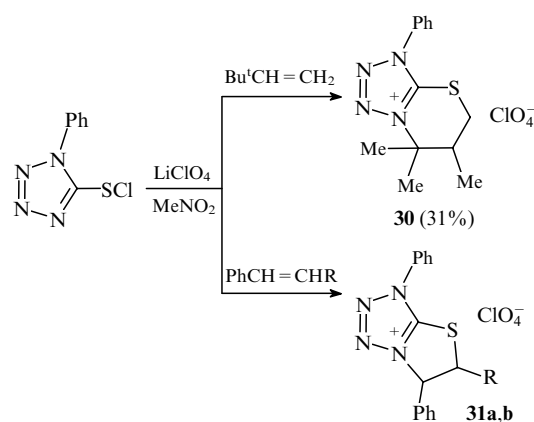
27: $\text{R}^1 = \text{H}, \text{Cl}$; $\text{R}^2 = \text{Ph}, 4\text{-ClC}_6\text{H}_4, 4\text{-BrC}_6\text{H}_4, 4\text{-FC}_6\text{H}_4$.

Treatment of 5-mercaptotetrazoles **25a** and **28** substituted by epoxy bromides in position N(1) with heating affords 6-hydroxy-1-*R*-6,7-dihydro-5*H*-tetrazolo[5,4-*b*][1,3]thiazinium bromides **29** in relatively low yields.⁵⁷



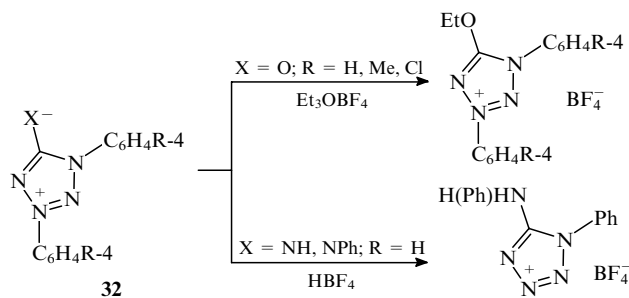
$\text{R}^1 = \text{Ph}, \text{cyclo-C}_6\text{H}_{11}$; $\text{R}^2, \text{R}^3, \text{R}^4, \text{R}^5 = \text{H}, \text{Me}$.

The reaction of 1-phenyltetrazol-5-ylsulfenyl chloride with 3,3-dimethylbut-1-ene in nitromethane in the presence of lithium perchlorate yields 7,8-dihydro-6,6,7-trimethyl-2-phenyl-6*H*-tetrazolo[4,5-*b*][1,3]thiazinium perchlorate (**30**). It has been shown that the heterocyclic compound **30** is formed in the A_{E} reaction of an alkene with sulfenyl chloride due to the tandem rearrangement–cyclisation occurring by a π -route.⁵⁸ The reaction of this sulfenyl chloride with styrene or 1-phenylpropene yields 2,3-dihydrothiazolo[3,2-*d*]tetrazolium salts **31a,b**.⁵⁹

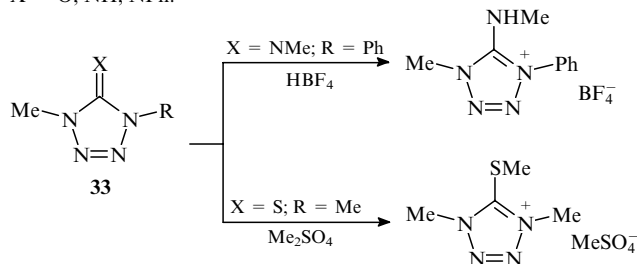


$\text{R} = \text{H}$ (**a**, 47%), Me (**b**, 52%).

1,3,5- and 1,4,5-Trisubstituted tetrazolium salts can be prepared in more than 70% yields from mesoionic tetrazoles **32**^{12, 60, 61} and 1,4-dihydropyridotetrazoles **33**,^{17, 62} in which the exocyclic atoms are readily involved in alkylation and protonation.

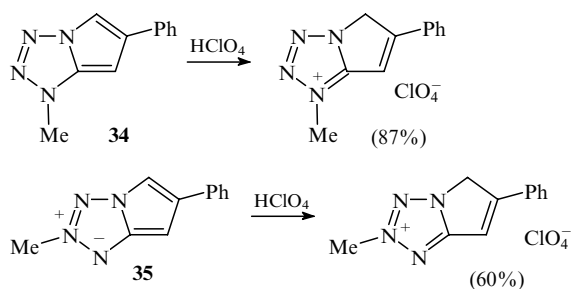


$\text{X} = \text{O}, \text{NH}, \text{NPh}$.

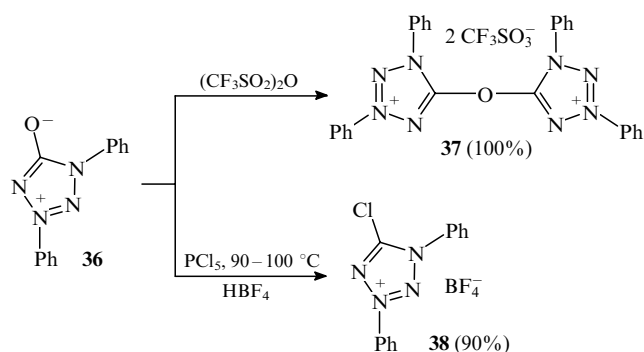


$\text{X} = \text{NMe}, \text{S}$.

Analogous reactions with fused tetrazole derivatives, with pyrrolotetrazoles **34** and **35** in particular, also proceed smoothly.⁶³

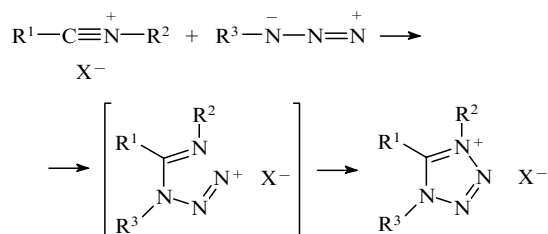


Special mention should be made of the reaction of readily available 1,3-diphenyltetrazolium-5-olate¹² (36) with phosphorus pentachloride⁶¹ and trifluoromethanesulfonic anhydride⁶⁴ which yields functionalised tetrazolium salts 37 and 38.



4. Heterocyclisation reactions

The main advantage of the synthesis of tetrazolium salts by heterocyclisation is that this excludes preliminary synthesis of tetrazole derivatives. Reactions of alkyl and aryl azides with nitrilium salts which proceed as [3 + 2]-cycloaddition and result in 1,4,5-trisubstituted tetrazolium salts in good yields have the greatest preparative significance (Table 6).^{22, 65, 66}



An intramolecular version of this reaction is also known. It was shown³¹ that cyclisation of the *in situ* generated *N*-methyl- ω -azidonitrilium triflates 39 is a rather convenient and efficient procedure for the synthesis of annelated 1,4,5-trisubstituted tetrazolium salts 40.

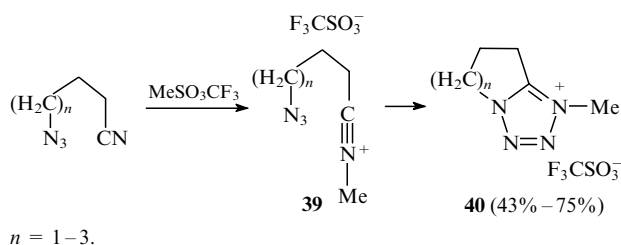
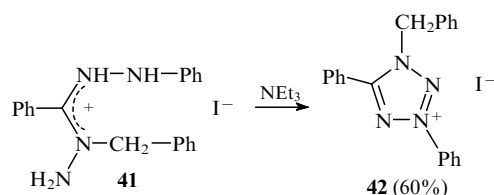


Table 6. The synthesis of 1,4,5-trisubstituted tetrazolium salts by the reaction of azides with nitrilium salts.

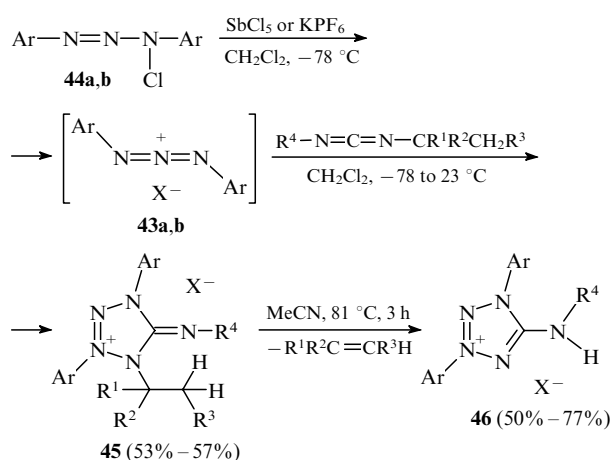
R ¹	R ²	R ³	X	Yield (%)	M.p. /°C	Ref.
Pr ⁱ	Me	Me	BF ₄	71	100–101	22
Bu ⁱ CH ₂	Pr ⁱ	Me	BF ₄	52	166–168	22
Me	Me	Me	FSO ₃	41	205–206	22
Me	Me	Me	FSO ₃	80	155–158	65
Me	Me	Ph	F ₃ SO ₃	87	210–211 ^a	22
Pr ⁱ	Me	Bu ⁱ CH ₂	BF ₄	77	144	22
Pr ⁱ	Me	Ad	FSO ₃	32	129–130	22
Me	Me	Bn	FSO ₃	71	oil	65
Me	Et	Et	FSO ₃	58	118–119	65
cyclo-C ₆ H ₁₁	Me	Bn	FSO ₃	60	128–129	65
Bu ⁱ	Me	Bn	FSO ₃	60	oil	65
Ph	Me	Me	FSO ₃	75	145–148	65
Ph	Me	Bn	FSO ₃	70	135	65
Ph	Et	Et	FSO ₃	55	165–167	65
Ph	Et	Et	SbCl ₆	55	204	65
Ph	Et	Et	BF ₄	53	130	65
Ph	Ph	Me	SbCl ₆	78	176	65
Ph	Ph	Bn	SbCl ₆	65	156	65
Ph	Ph	Ph	SbCl ₆	52	172	65
cyclo-C ₃ H ₅	Me	Me	PF ₆	97	219	66
All	Me	Me	PF ₆	51	100–101	66
(<i>E</i>)-MeCH=CHCH ₂	Me	Me	PF ₆	48	93	66
(<i>E</i>)-Bu ⁱ CH=CHCH ₂	Me	Me	PF ₆	57	133–134	66
(<i>E</i>)-PhCH=CHCH ₂	Me	Me	PF ₆	11	165–170	66
(<i>E</i>)-MeCH=CH	Me	Me	PF ₆	48	190–192	66
(<i>Z</i>)-EtCH=CH	Me	Me	PF ₆	60	77–79	66

^a With decomposition.

Heterocyclisation reactions can also be employed for the synthesis of 1,3,5-trisubstituted tetrazolium salts. The use of these reactions is limited due to the low availability of the starting reagents; it has been reported, however,⁷ that the hydrazinium salt **41** is converted into 1-benzyl-3,5-diphenyltetrazolium iodide (**42**) under the action of a base.

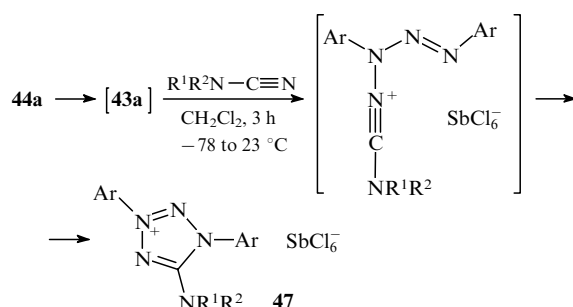


1,3-Diaza-2-azoniaallene salts **43a,b** [Ar = 2,4,6-Cl₃C₆H₂ (**a**), 4-ClC₆H₄ (**b**)] generated *in situ* from *N*-chlorotriazenes **44a,b** react with carbodiimides to give dihydrotetrazolium derivatives **45** which are converted into 5-alkylamino-1,3-diaryltetrazolium salts **46** upon heating.^{67, 68}



Ar	R ¹	R ²	R ³	R ⁴	X
2,4,6-Cl ₃ C ₆ H ₂	H	Me	H	Pr ⁱ	SbCl ₆
2,4,6-Cl ₃ C ₆ H ₂	H	(CH ₂) ₄	H	cyclo-C ₆ H ₁₁	SbCl ₆
2,4,6-Cl ₃ C ₆ H ₂	Me	Me	H	Bu ^t	SbCl ₆
4-ClC ₆ H ₄	H	Me	H	Pr ⁱ	PF ₆
4-ClC ₆ H ₄	H	(CH ₂) ₄	cyclo-C ₆ H ₁₁		PF ₆

The use of cyanamides in this reaction leads to 5-dialkylamino-1,3-diaryltetrazolium salts **47**.^{67, 68}



R ¹	R ²	Yield (%)
Bu ^t	H	34
Me	Me	61
Me	Pr ⁱ	65
Pr ⁱ	Pr ⁱ	71

III. Physicochemical properties and structures of tetrazolium salts

In the individual state and under normal conditions, tetrazolium salts are stable crystalline compounds (except for the salts containing the MeSO₄[−] anion) frequently isolated as viscous fluids (see, *e.g.*, Refs 23, 28, 32). 1,4-Dialkyltetrazolium perchlorates manifest higher melting temperatures than the 1,3-isomers.⁴⁵ Certain 1,3-dialkyltetrazolium perchlorates possess rather low (for ionic compounds) melting temperatures (~70–80 °C, see, *e.g.*, Refs 45, 46, 48). This allows the preparation of ionic fluids possessing unique properties presently established for other azolium salts.^{69, 70}

1. NMR spectra

NMR spectroscopy is one of the main techniques for the identification of tetrazolium salts. The chemical shift (CS) of the endocyclic carbon atom in the ¹³C NMR spectra strongly depends on the isomer type. The signals for carbon C(5) in 1,3-substituted tetrazolium salts **2** are downfield shifted by 7–16 ppm in comparison with the corresponding signals for 1,4-isomers^{71, 72} (Table 7). It is noteworthy that the nature of the substituents at the nitrogen atoms of the ring has little effect on the CS, being equal to ~147–151 ppm for 1,3-disubstituted, and ~138–142 ppm for 1,4-disubstituted tetrazolium salts. In the case of trisubstituted derivatives, the magnitude of the CS depends critically on the nature of the substituent at C(5). The signal of the C(5) atom characteristic of all ¹³C NMR spectra is shifted upfield in the following series of substituents: Prⁱ > Me > NH₂ > Cl > Br > I.^{15, 18, 21, 22, 28, 61, 71–75} A comparative study^{71, 72} of the NMR spectra of tetrazolium salts and related tetrazoles revealed that the quaternisation at the α-nitrogen atom of *N*-substituted tetrazoles little affects the magnitude of the CS of the C(5) atom (~1–4 ppm), while the quaternisation of the β-atom significantly changes it as can be evidenced from the downfield shift of 7–10 ppm. The slight change in the CS observed upon quaternisation of the N(4) atom is due to the oppositely directed effect of two factors, *viz.*, the electronegative group N= (the downfield shift) and the decrease in the order of the N–C bond in the cation formed as a result of polarisation (the upfield shift).

The ¹H NMR spectra of tetrazolium salts non-substituted in position 5 are characterised by a downfield shift of the signal for the proton at the endocyclic carbon atom and a significant (by ~20 Hz) increase in the spin–spin coupling constant (SSC) ¹J(¹³C–¹H) in comparison with the starting compounds.^{23, 30, 44, 71, 72} The CS value of the proton at C(5) strongly depends on the structure of the salt and the type of solvent. Chemical shifts of isomeric 1,3- and 1,4-disubstituted tetrazolium salts differ by ~0.5–1 ppm and even more.^{30, 43–49} Thus the CS of 1,4-dialkyltetrazolium perchlorates and tetrafluoroborates are 11.1–11.9 ppm, whereas those of 1,3-isomers are 10.2–10.9 ppm [in (CD₃)₂SO]. On going from DMSO to MeCN, the signal for the proton in the ¹H NMR spectrum is shifted upfield (10.6–10.9 ppm for 1,4-substituted and 9.6–10.1 ppm for 1,3-substituted derivatives).^{30, 43–49}

Identification of tetrazolium salts on the basis of ¹H NMR spectra often makes use of characteristic CS of the protons of the substituent owing to magnetic equivalence (or non-equivalence) of the groups. Thus the CS of the protons in the alkyl groups (Me, Et, Bu^t) in positions N(1) and N(4) differ considerably from those of the analogous substituents at the atoms C(5) and N(3).^{3, 14, 17, 18, 21, 35, 36, 49, 71}

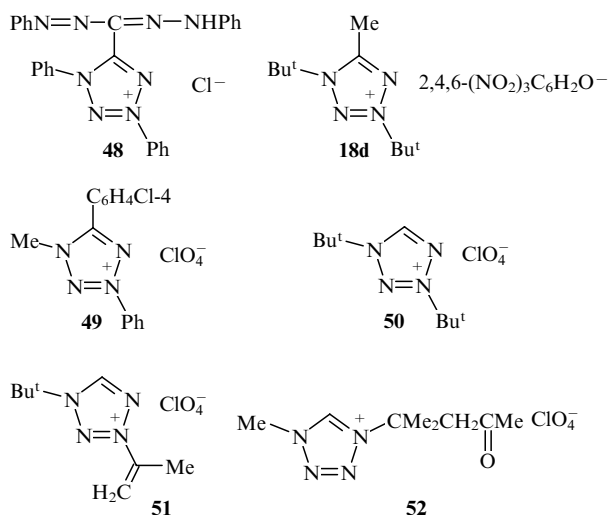
NMR spectroscopy allows both identification of tetrazolium salts and an analysis of the conjugation of the tetrazole fragment with the substituent. Thus the change in the CS of the carbon atoms of the vinyl group in the ¹³C NMR spectra upon quaternisation of vinyltetrazoles allows one to conclude that there is a decrease in the *p*,*π*-conjugation in *N*-vinyltetrazolium salts and an increase in the *p*,*π*-conjugation in *C*-vinyltetrazolium salts as compared to the starting tetrazoles.²⁸ These data are consistent with the results of quantum-chemical calculations of geometric

Table 7. The chemical shift values of the signals of C(5) atoms of 1,3- (**2**) and 1,4-substituted tetrazolium (**3**) salts determined from ^{13}C NMR spectra (δ).

R ¹	R ²	R ³	X	Solvent	Compound		Ref.
					2	3	
H	H	Ph	HSO ₄	H ₂ SO ₄	147.3	138.2	15
H	Et	Ph	BF ₄	(CD ₃) ₂ CO	148.3	140.3	15
NH ₂	Me	Me	Cl	(CD ₃) ₂ SO	158.1	148.5	73
NH ₂	CH ₂ COPh	Me	Br	(CD ₃) ₂ SO	158.7	148.9	35
CH ₂ =CH	Me	Me	MeSO ₄	CD ₃ OD	162.7	149.4	28
Me	Me	CH ₂ COMe	I	D ₂ O	161.7	154.7	18
H	Ph	Ph	BF ₄	(CD ₃) ₂ SO	147.5	—	60
NH ₂	Ph	Ph	BF ₄	(CD ₃) ₂ SO	157.7	—	61
N ₃	Ph	Ph	BF ₄	(CD ₃) ₂ SO	155.9	—	61
Cl	Ph	Ph	BF ₄	(CD ₃) ₂ SO	153.9	—	60
Br	Ph	Ph	BF ₄	(CD ₃) ₂ SO	143.2	—	60
I	Ph	Ph	BF ₄	(CD ₃) ₂ SO	117.3	—	60
Hg	Ph	Ph	BF ₄	(CD ₃) ₂ SO	183.3	—	60
EtO	Ph	Ph	BF ₄	(CD ₃) ₂ SO	160.6	—	74
EtS	Ph	Ph	BF ₄	(CD ₃) ₂ SO	162.7	—	74
MeS	Me	Me	Cl	(CD ₃) ₂ SO	162.4	—	73
Me	Me	Me	ClO ₄	(CD ₃) ₂ SO	—	152.7	22
Et	Me	Me	ClO ₄	(CD ₃) ₂ SO	—	154.9	22
H	Me	CH ₂ =CH	MeSO ₄	CD ₃ OD	—	142.1	28

2. X-Ray diffraction analysis

By now, crystal structures of eight tetrazolium salts, viz., 5-(1,5-diphenyl-3-formazany)-1,3-diphenyltetrazolium chloride (**48**),³ 1,3-di-*tert*-butyl-5-methyltetrazolium picrate (**18d**),³³ 5-(4-chlorophenyl)-1-methyl-3-phenyl- (**49**),²⁹ 1,3-di-*tert*-butyl- (**50**),⁴⁸ 1-*tert*-butyl-3-isopropenyl- (**51**),⁴⁸ 1-(2,2-dimethyl-4-oxopentyl)-4-methyltetrazolium perchlorates (**52**),⁴⁶ tetrazolo[4,5-*b*][1,3]thiazinium- (**30**)⁵⁸ and thiazolo[3,2-*d*]tetrazolium perchlorates **31b**, have been established.⁵⁹



The tetrazole rings in tetrazolium salts and other tetrazole derivatives are planar. The parameters of the tetrazole ring depend critically on the type of the salt. Thus the C(5)–N(1) [1.317(4) Å] and C(5)–N(4) [1.315(4) Å] bond lengths in the cation **52** are practically identical and intermediate between the double and ordinary bond lengths, N(2)–N(3) [1.276(4) Å] being the shortest bond and close to a double bond. The values of the bond angles at the N(2) and N(3) atoms practically coincide with that in a regular pentagon, while those at the N(1) and N(4) atoms approximate it. These data suggest that the structure of the 1,4-disubstituted tetrazole ring is close to that of a symmetrical ring with delocalisation of the excess positive charge over the N(4)–C(5)–N(1) fragment.⁴⁶ A similar structure is characteristic of the tetrazole ring of fused 1,4,5-trisubstituted tetrazolium salts **30** (see Ref. 58) and **31b** (see Ref. 59).

The heterocycles of 1,3-substituted tetrazolium salts are non-symmetrical. The N(2)–N(3) [1.287(3)–1.299(3) Å] bond in the cations **18d**, **48**–**51** is the shortest bond; the N(4)–C(5) [1.300(4)–1.314(3) Å] bond length differs from it only insignificantly. This suggests that the positive charge of 1,3-substituted tetrazolium salts is predominantly localised on the N(3) atom rather than on the N(1) atom which represents the quaternisation site.⁴⁸ The non-coincidence of the quaternisation site and the site of localisation of the positive charge in the case of some tetrazolium salts was established experimentally: the quaternisation of *N*-substituted tetrazoles differing in the positions of substituents gave identical compounds.^{30, 48} The exocyclic N–C bonds in the cations under study lie in the plane of the ring. Their lengths are rather similar and differ only insignificantly from the length of the corresponding ordinary bond N–C with the exception of the N(3)–C(Me) bond in the cation **51**. Its length [1.440 Å] is somewhat smaller than that of an ordinary bond, while its torsion angles deviate by no more than 10.6° from 0° or 180°, which is suggestive of the conjugation of the π -systems of the tetrazole ring with the C=C bond.⁴⁸

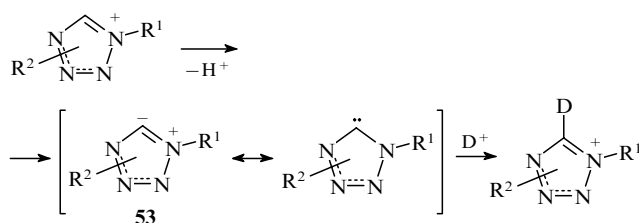
IV. Reactions of tetrazolium salts

Systematic studies of the chemical properties of 1,3- and 1,4-substituted tetrazolium salts were not carried out until recently. This section is devoted to the consideration of the most important

electrophilic and nucleophilic substitution reactions of tetrazolium salts at the carbon atom of the heterocycle and other transformations under the action of various reagents.

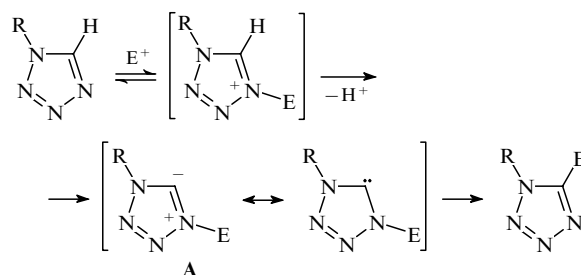
1. Substitution reactions at the carbon atom of the heterocycle

Only very few cases of substitution of the hydrogen atom in position C(5) of 1-monosubstituted tetrazoles were described before the 1980's. These include deuterium–hydrogen exchange, lithiation, mercuration and bromination.^{72, 80, 81} It was believed that the problems encountered in the electrophilic substitution of hydrogen were caused by the deactivation of position 5 by annular nitrogen atoms.⁸² With regard to disubstituted tetrazolium salts, the only known case was the isotope exchange in alkaline and acid media.



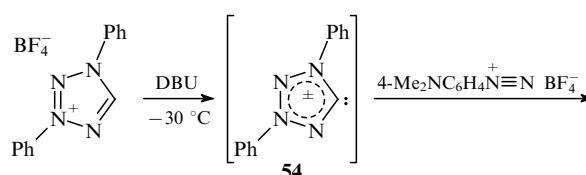
It is assumed that this exchange proceeds through the intermediate formation of ylide **53** or its isoelectronic analogue, carbene. It was shown that the kinetic CH-acidity changes in the following order: 2-R-tetrazoles < 1-R-tetrazoles < 1,3-disubstituted tetrazolium salts < 1,4-disubstituted tetrazolium salts.^{80, 81, 83–85}

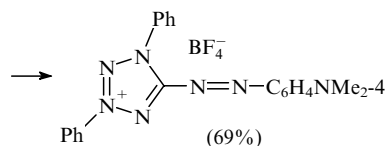
The first successful attempts at aminomethylation^{86, 87} and iodination of 1-R-tetrazoles were reported in the late 1980's–early 1990's.^{88, 89} The experimental data suggest that these reactions proceed through the intermediate formation of an ylide, which accounts for the introduction of a substituent into position 5. This reaction begins with an attack of an electrophilic reagent at the most nucleophilic N(4) atom and the formation of a tetrazolium cation, which is further deprotonated into the intermediate ylide (carbene) **A** stabilised by intramolecular rearrangement.



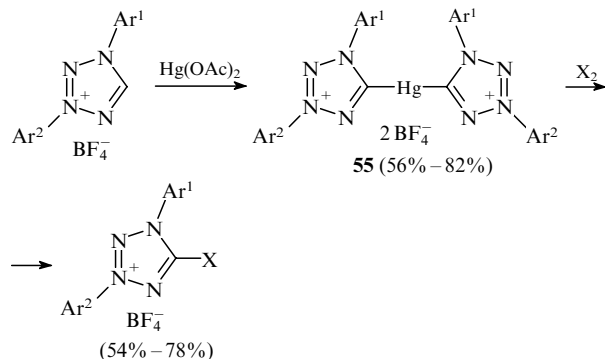
E = I, CH₂NAlk₂; R = Ar, Alk, H.

Simultaneously electrophilic substitution at the C(5) atom of tetrazolium salts was reported. It was shown, in particular, that the substitution of lithium for hydrogen in 2,3-diaryltetrazolium salts occurs under the action of *tert*-butyllithium or lithium bis(trimethylsilyl)amide.^{90, 91} The condensation of 1,3-diphenyltetrazolium tetrafluoroborate with a diazonium salt in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), which favours the formation of a mesoionic carbene, viz., 1,3-diphenyltetrazolyene (**54**), has been described.⁶⁰



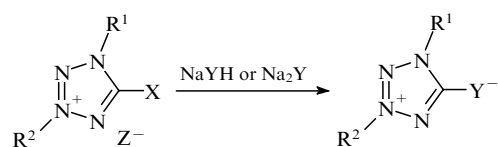


It was found that 1,3-diaryltetrazolium salts undergo mercuriation upon heating with mercury(II) acetate in dimethyl sulfoxide to yield bis(tetrazolio)mercury(II) salts **55** the mercury atom in which is easily replaced by a halogen.⁶⁰



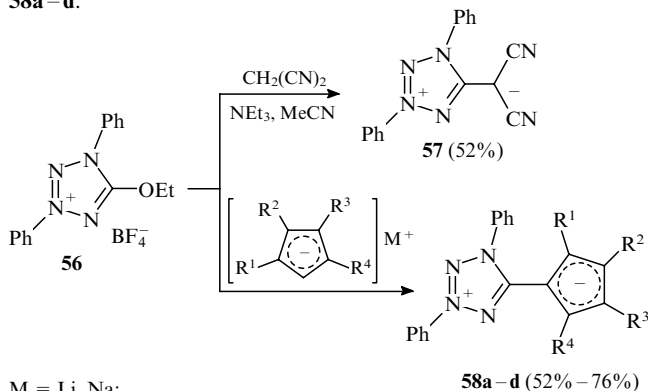
$\text{Ar}^1 = \text{Ph}, 4\text{-MeC}_6\text{H}_4$; $\text{Ar}^2 = \text{Ph}, 4\text{-MeOC}_6\text{H}_4$; $\text{X} = \text{Cl}, \text{Br}, \text{I}$.

Nucleophilic substitution at the C(5) atom of tetrazolium salts has been studied in more detail and is often employed in the synthesis of mesoionic tetrazoles. Thus it was shown that the ethoxy⁹² and the methylthio groups⁷³ and the chlorine atom⁶⁰ of 1,3,5-trisubstituted tetrazolium salts can be replaced by sulfide, hydroxide and selenide ions.



$\text{R}^1, \text{R}^2 = \text{Me}, \text{Ph}, 4\text{-MeC}_6\text{H}_4, 4\text{-ClC}_6\text{H}_4$; $\text{X} = \text{Cl}, \text{OEt}, \text{SMe}$;
 $\text{Y} = \text{O}, \text{S}, \text{Se}$; $\text{Z} = \text{BF}_4, \text{MeSO}_4$.

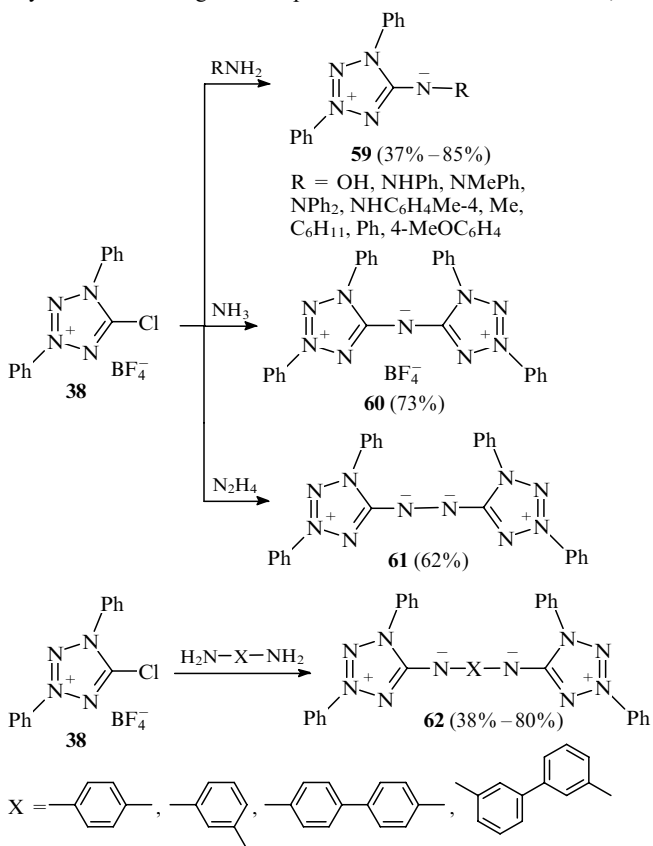
5-Ethoxy-1,3-diphenyltetrazolium tetrafluoroborate (**56**) reacts with C-nucleophiles, *e.g.*, malonic dinitrile,⁹³ lithium and sodium cyclopentadienide,^{94,95} indenide, fluorenyl and cyclopenta[def]phenanthrenide⁹⁵ to give mesoionic tetrazoles **57** and **58a–d**.



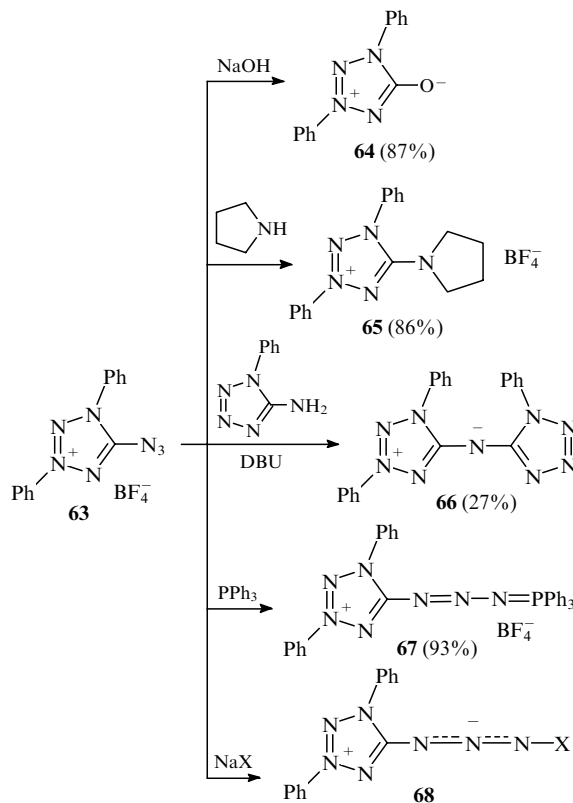
$\text{M} = \text{Li}, \text{Na}$;
 $\text{R}^1 = \text{R}^2 = \text{R}^3 = \text{R}^4 = \text{H}$ (**a**);
 $\text{R}^1 = \text{R}^2 = \text{H}, \text{R}^3\text{--R}^4 = \text{CH}=\text{CHCH}=\text{CH}$ (**b**);
 $\text{R}^1\text{--R}^2 = \text{CH}=\text{CHCH}=\text{CH}, \text{R}^3\text{--R}^4 = \text{CH}=\text{CHCH}=\text{CH}$ (**c**);
 $\text{R}^1\text{--R}^4 = \text{--CH--CH=C--CH=CH--C--CH=CH--CH=}$ (**d**).

Mesoionic tetrazolium amides **59** were prepared by the reaction of 5-chloro-1,3-diphenyltetrazolium tetrafluoroborate **38** with N-nucleophiles, such as aliphatic amines,⁹⁶ aniline, hydroxylamine, *N*-mono- and *N,N*-disubstituted hydrazines.⁶⁰

The reaction of the salt **38** with ammonia yielded bistetrazolio-amide **60** as the main product;⁶⁰ the reaction with hydrazine and arylendiamines⁹⁷ gave tetrapolar mesoionic bistetrazoles **61**, **62**.



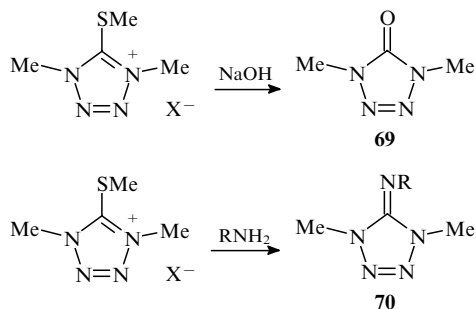
5-Azido-1,3-diphenyltetrazolium tetrafluoroborate (**63**) prepared by the reaction of sodium azide with the salt **38** has rich synthetic potential. The attack of strong nucleophiles, *e.g.*,



$\text{X} = \text{CN}$ (93%), $\text{SO}_2\text{C}_6\text{H}_4\text{Me-4}$ (46%).

sodium hydroxide or amines at the endocyclic carbon atom, yields substitution products. Weaker nucleophiles, such as the cyanide ion, *p*-toluenesulfonate anion, triphenylphosphine, *etc.*, attack the terminal nitrogen atom to give the addition products **67** and **68**.⁶¹

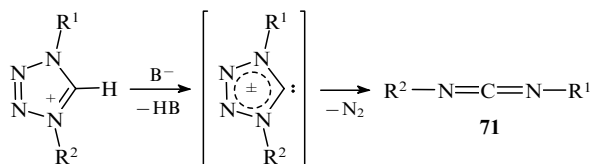
The nucleophilic substitution at the C(5) atom in 1,4,5-trisubstituted tetrazolium salts has been described exclusively for 1,4-dimethyl-5-(methylthio)tetrazolium salts. It was shown that they react with bases to give 1,4-dihydro-1,4-dimethyltetrazoles **69** and **70** (yields 27%–40%).^{7, 17, 62}



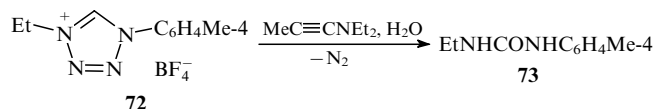
X = BF₄, MeSO₄; R = Me, PhNH.

2. The action of bases

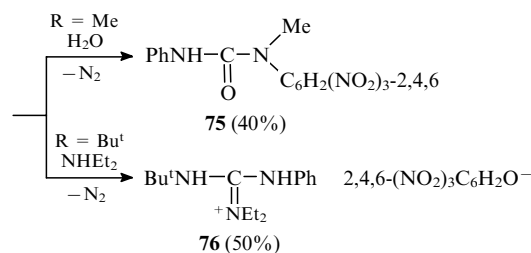
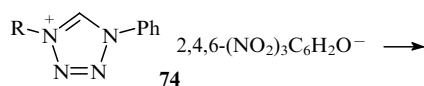
The majority of currently known tetrazolium salts are sensitive to bases. A base attacks predominantly the two carbon atoms with the lowest electron density, *viz.*, the C(5) atom and the carbon atoms in the α -position relative to the nitrogen atoms of the heterocycle, which leads to the opening of the tetrazole ring, dealkylation or self-condensation. The salts devoid of substituents at the C(5) atom are the most susceptible to bases. The abstraction of the hydrogen atom under the action of bases is accompanied by the formation of heteroaromatic carbenes, *viz.*, tetrazolidenes. The latter, in turn, undergo fragmentation the direction of which depends on the type of the salt used. It was shown^{13, 98} that 1,4-disubstituted tetrazolium salts are split into molecular nitrogen and carbodiimides **71** under the action of tertiary amines at 20 °C. Along with other reactions, this reaction is used in the synthesis of carbodiimides (see Ref. 99) and is the sole procedure in the synthesis of, *e.g.*, vinylcarbodiimides.¹³



The carbodiimides formed, being highly reactive compounds,⁹⁹ react with an excess of the base or the solvent, or undergo intramolecular cyclisation. Thus the reaction of 1-ethyl-4-(*p*-tolyl)tetrazolium tetrafluoroborate (**72**) with diethylpropynylamine in the presence of water gives *N*-ethyl-*N'*-(*p*-tolyl)-urea (**73**).⁹⁸

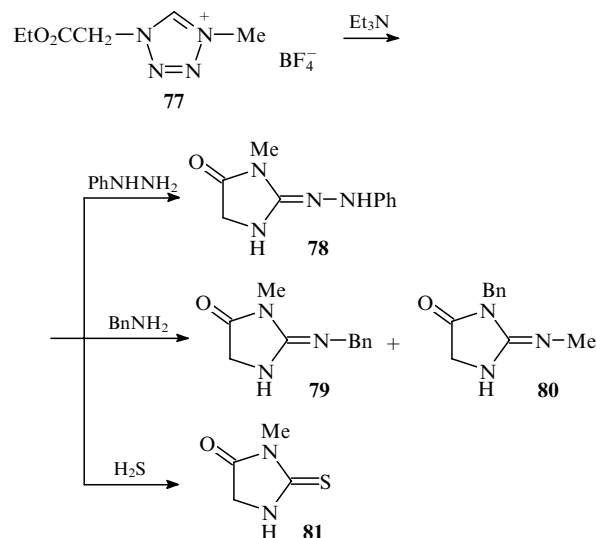


4-Alkyl-1-phenyltetrazolium picrates **74** are decomposed slowly in the presence of water to yield trisubstituted urea **75**; after treatment with diethylamine, they are converted into guanidinium picrate **76**.³³

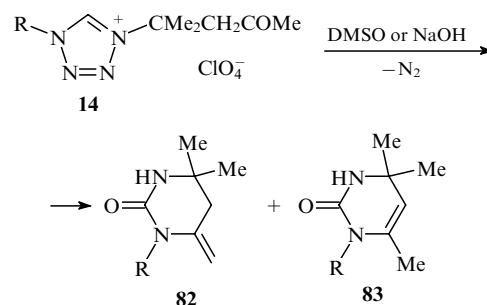


R = Me, Bu^t.

It has been reported¹³ that consecutive treatment of 1-(ethoxycarbonylmethyl)-4-methyltetrazolium tetrafluoroborate (**77**) with triethylamine and then with benzylamine, phenylhydrazine or hydrogen sulfide yields hydantoin **78**–**81**. Unfortunately, neither the methodology of these reactions, nor the yields of the target products have been reported.¹³

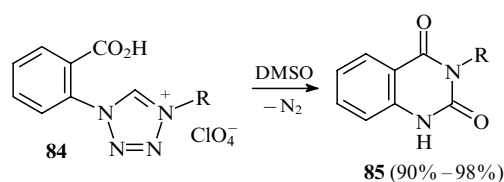


1-R-4-(2-Methyl-4-oxopent-2-yl)tetrazolium perchlorates **14** evolve nitrogen in the presence of bases to be transformed into 4,4-dimethyl-1-R-6-methylidene-3,4,5,6-tetrahydropyrimidin-2(1*H*)-ones **82** and 4,4,6-trimethyl-1-R-3,4-dihydropyrimidin-2(1*H*)-ones **83**, the latter being predominant.⁴⁷



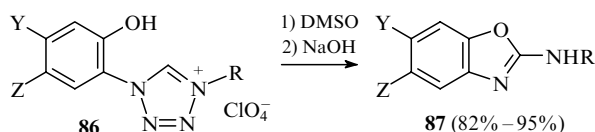
R = Ph, Bn.

3-Monosubstituted quinazoline-2,4(1*H*,3*H*)-diones **85** are formed in high yields on dissolution of 4-alkyl-1-(2-carboxyphenyl)tetrazolium perchlorates **84** in dimethyl sulfoxide.⁴⁷



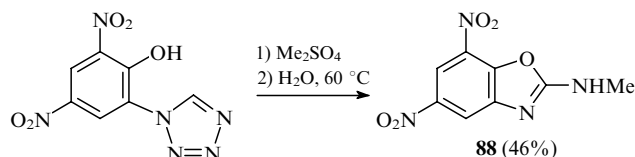
R = Bu^t, CMe₂CH₂COMe.

4-Alkyl-1-(2-hydroxyaryl)tetrazolium perchlorates **86** undergo recyclisation into 2-alkylaminobenzooxazoles **87** under the action of bases.⁴⁷

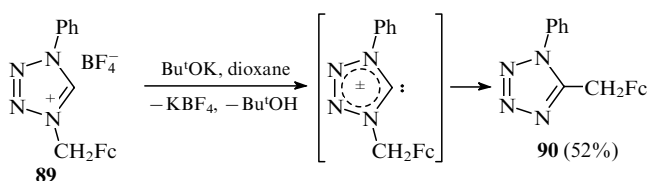


R = Bu^t, CMe₂CH₂COMe; Y = H, NO₂; Z = H, NO₂.

Preparation of 2-methylamino-5,7-dinitrobenzooxazole (**88**) is an example of a successful conversion of readily available 1-monosubstituted tetrazoles into benzooxazoles without the intermediate isolation of the tetrazolium salt.¹⁰⁰

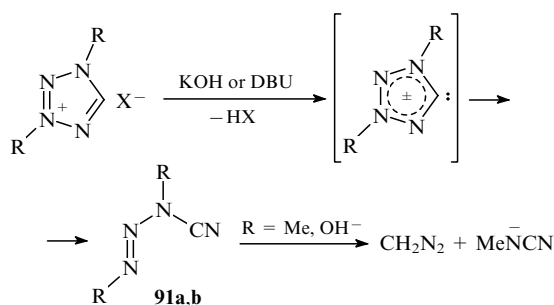


1-Aryl-4-ferrocenylalkyltetrazolium salts undergo dealkylation by aqueous ammonia or sodium carbonate at 20 °C to yield 1-aryltetrazoles and ferrocenylalkyl alcohols. 1-Ferrocenylmethyl-4-phenyltetrazolium tetrafluoroborate (**89**) undergoes the Stevens rearrangement in the presence of potassium *tert*-butoxide in dioxane to give 1,5-disubstituted tetrazole **90**.⁴⁴



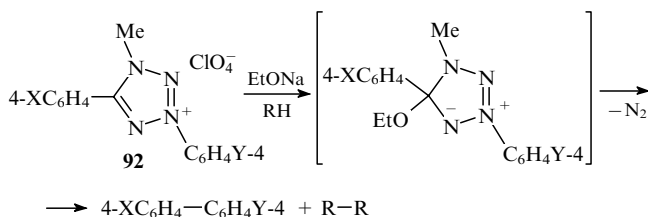
Fc = C₅H₄FeC₅H₅.

1,3-Disubstituted tetrazolium salts react with strong bases to give 1,3-disubstituted 3-cyanotriazenes **91a,b**.^{60, 82} Compound **91a** is decomposed under the action of the hydroxide ion resulting in diazomethane and methylcyanamide anion.



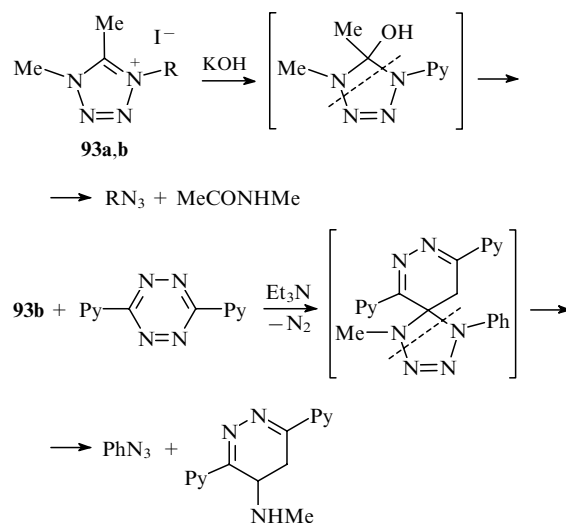
R = Me (a), Ph (b); X = Cl, BF₄.

3,5-Diaryl-1-methyltetrazolium salts **92** are resistant to the action of Et₃N in toluene at 20 °C, but react vigorously with sodium ethoxide in benzene or toluene to yield a complex mixture of reaction products among which biaryls are predominant.²⁹



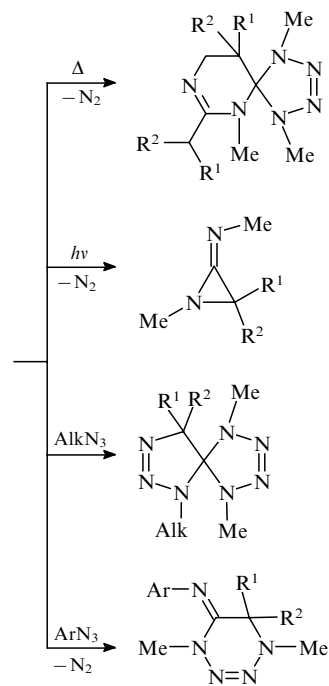
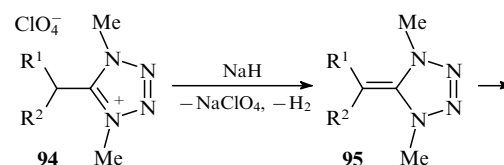
Y = H: X = H, Me, MeO, Cl; X = H: Y = H, NO₂, Me, MeO, Cl;
R = Ph, C₆H₄Me-4.

1,4,5-Trisubstituted tetrazolium salts **93a,b** undergo N-dealkylation⁹⁸ or fragmentation in the presence of bases,^{25, 101} and ring-opening products always contain alkyl or aryl azide.



R = Me (a), Ph (b).

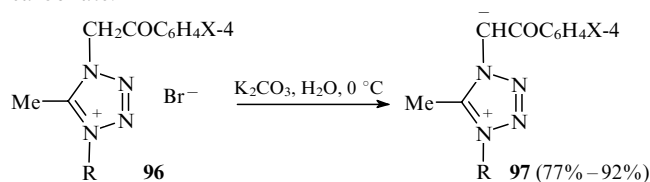
1,4,5-Trialkyltetrazolium salts **94** undergo deprotonation under the action of sodium hydride in tetrahydrofuran. This reaction has been studied in sufficiently great detail, since it allows one to prepare 1,4-dihydro-5-alkylenetetrazoles **95**, the starting compounds in the synthesis of iminoaziridines, tetrazines, and other nitrogen-containing heterocyclic systems.^{66, 102}



R¹, R² = H, Alk.

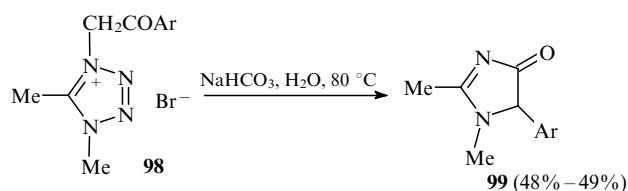
Some interesting conversions of *N*-acyl- and *N*-phenacyl-tetrazolium salts under the action of bases have been described.^{21, 27, 35, 103, 104} It was shown that tetrazolium salts can be converted into ylides, fused tetrazoles, and other heterocyclic molecules. The direction of these reactions depends on the nature

of the reagent and the substituents in the substrate. Thus 1-alkyl-5-methyl-4-phenacyltetrazolium bromides **96** are converted into ylides **97** under the action of aqueous solutions of potassium carbonate.²⁷

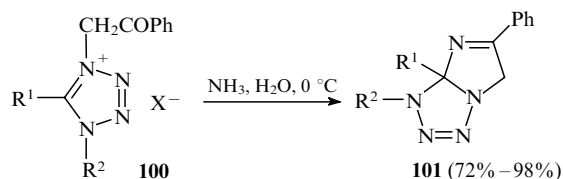


R = Me, Prⁿ, Prⁱ, Bu^t, CH₂Bu^t, cyclo-C₆H₁₁; X = H, Br, NO₂.

Similar conversions were observed in the case of 1,3-di- and 1,3,5-trisubstituted tetrazolium salts containing a phenacyl group at N(1) or N(3) atoms.²¹ 1,5-Dimethyl-4-phenacyltetrazolium salts **98** undergo recyclisation into 1,2,5-trisubstituted imidazol-4-ones **99** upon heating with aqueous sodium hydrogencarbonate.¹⁰³ Analogous salts **100** yield 3*a*,6-dihydro-3*H*-imidazo[1,2-*d*]tetrazoles **101** in a reaction with aqueous ammonia.¹⁰⁴



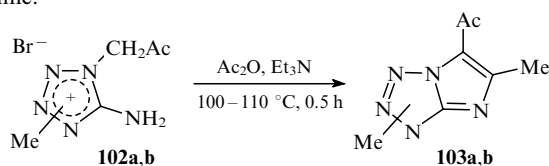
Ar = Ph, C₆H₄Br-4.



R¹ = Me, Et, Pr, Prⁱ, cyclo-C₆H₁₁, Ph, Bn, CH₂C₆H₄NO₂-4;

R² = Me, Et, Bn; X = Br, I, ClO₄, SbCl₆, PF₆.

1-Acetylmethyl-5-amino-3- (**102a**) and -4-methyltetrazolium bromides (**102b**) undergo cyclisation into 6-acetyl-2,5-dimethyl-2*H*- (**103a**) and 6-acetyl-3,5-dimethyl-3*H*-imidazo[1,2-*d*]tetrazoles (**103b**) under the action of acetic anhydride and triethylamine.³⁵

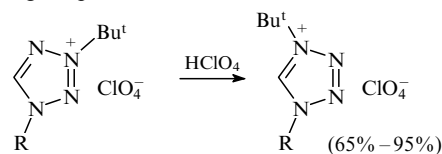


103a: 3-Me (86%); **103b**: 4-Me (51%).

3. The action of acids

The heterocycle in tetrazolium salts is usually resistant to acids. In reactions with acids, the modification affects only the substituents and is usually followed by their elimination and migration into another position of the ring.

It was found that 1-*R*-3-*tert*-butyltetrazolium perchlorates are slowly converted into 1-*R*-4-*tert*-butyltetrazolium perchlorates on storage in perchloric acid.^{45, 47, 55}



R = Me, Et, Bu^t, cyclo-C₆H₁₁, Ph, 2-HO₂C₆H₄,

2-HO-5-NO₂C₆H₃, 2-HO-4-NO₂C₆H₃.

Higher thermodynamic stability of 1,4-disubstituted tetrazolium salts in comparison with their 1,3-isomers is the driving force of this process as can be evidenced from the results of quantum-chemical calculations of the heats of formation and total energies of isomeric tetrazolium cations carried out with the use of semi-empirical^{28, 45} and *ab initio* methods (Table 9) with full optimisation of the cation geometry.

1-*tert*-Butyl-3-*R*-tetrazolium salts do not undergo isomerisation in perchloric acid, but partly lose their *tert*-butyl groups.⁴⁵ The conversion of 1-*R*-3-*tert*-butyltetrazolium salts into the corresponding 1,4-isomers is accompanied by a partial loss of the *tert*-butyl group.^{45, 55} Notwithstanding, storage of 1-*R*-3-*tert*-butyltetrazolium salts with perchloric acid has been employed for the synthesis of 1-*R*-4-*tert*-butyltetrazolium salts.^{45, 47}

In contrast to 1,3-disubstituted tetrazolium salts, 1,3,5-trisubstituted derivatives do not undergo isomerisation under similar conditions but are subject to dealkylation.⁴⁵ This property of 1,3,5-trisubstituted tetrazolium salts was used in the synthesis of mono- and binuclear 1,5-disubstituted tetrazoles where alkyl substituents are introduced into position N(1) of the tetrazole ring of 2,5-disubstituted tetrazoles with subsequent elimination of the *tert*-butyl substituent (the yields of the target products are 78%–94%).^{36, 106}

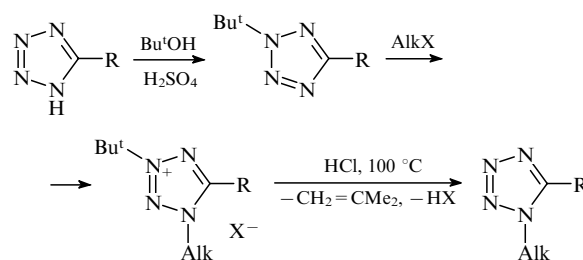
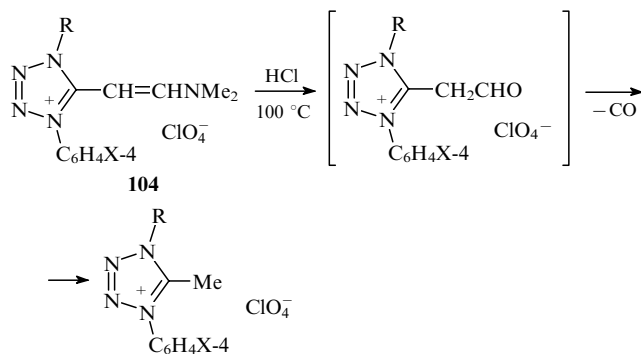


Table 9. The relative stability of tetrazolium cations (data from *ab initio* quantum-chemical calculations).

Compound	Method	Total energy of 1,4,5-isomer /kJ mol ⁻¹	Total energy of 1,3,5-isomer /kJ mol ⁻¹	Δ <i>E</i> /kJ mol ⁻¹	Ref.
Protonated 1 <i>H</i> ,5 <i>H</i> -tetrazole	STO-3G	–560438.6	–560416.0	22.6	105
	3-21G	–564290.9	–564267.5	23.4	105
	6-31G	–567204.6	–567189.5	15.1	105
	6-31G*//6-31G	–567545.4	–567537.7	7.7	105
	6-31G**	–567573.5	–567566.1	7.4	see ^a
	MP2/6-31G**	–567554.4	–567543.8	10.6	see ^a
Protonated 1-methyl-5 <i>H</i> -tetrazole	6-31G	–653363.5	–653350.6	12.9	78
<i>N</i> (1)-Methyltetrazolo[1,5- <i>a</i>]pyridine	GIAO-CHF	–1180387.0	–	76.7	34
<i>N</i> (3)-Methyltetrazolo[1,5- <i>a</i>]pyridine	GIAO-CHF	–	–1180310.3	76.7	34

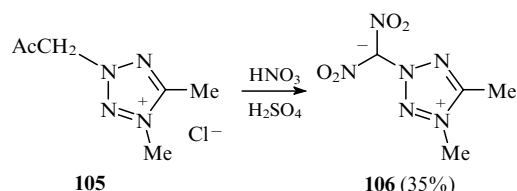
^a Original author's data.

Boiling of 1-alkyl-4-aryl-5-(2-dimethylaminovinyl)tetrazolium perchlorates **104** in hydrochloric acid leads to the modification of the substituent at the C(5) atom.²⁵

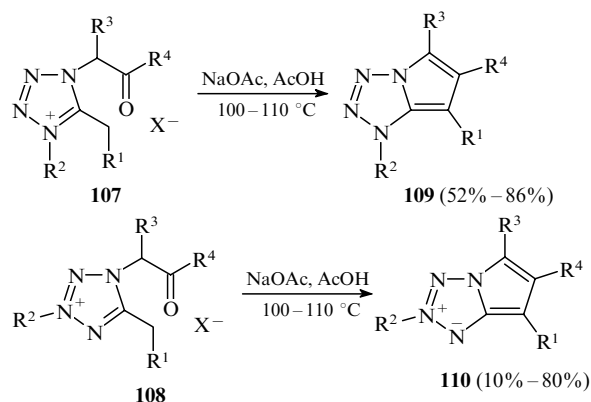


R = Me, Et; X = H, Me, F, Cl, Br, I.

Treatment of 3-acetylmethyl-1,5-dimethyltetrazolium chloride (**105**) with a nitrating mixture results in mesoionic tetrazole **106**.¹⁰⁷



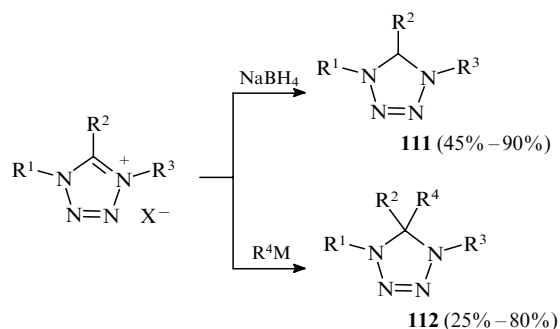
1,4,5- (**107**) and 1,3,5-trisubstituted tetrazolium salts (**108**) undergo cyclisation into 1*H*- and 2*H*-pyrrolotetrazoles **109** and **110** upon heating in acetic acid in the presence of sodium acetate.³⁷



R¹ = MeCO, CO₂Me; R² = Me, Ph; R³ = H, Me;
R⁴ = Me, Ph, 4-BrC₆H₄; X = BF₄, MeSO₄.

4. The action of reducing and oxidising reagents

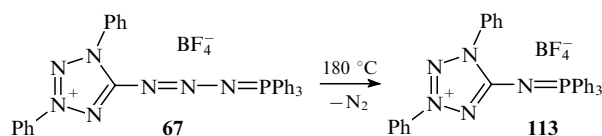
Tetrazolium salts are highly resistant to oxidising and reducing reagents; their heterocycles are not opened when treated with these reagents. Thus the oxidation of 1,3-diaryl-5-mercaptotetrazolium salts with concentrated nitric acid leads merely to the elimination of the substituent from position C(5) and the formation of 1,3-diaryltetrazolium salts,⁶⁰ while treatment of 5-azido-1,3-diphenyltetrazolium tetrafluoroborate (**63**) with hydroiodic acid or sodium sulfite results in the reduction of the azido group to the amino group.⁶¹ At the same time, 1,4,5-trialkyl(aryl)tetrazolium salts are reduced to trisubstituted dihydrotetrazoles **111** with sodium borohydride in ethanol. These salts undergo alkylation in reactions with organolithium compounds and vinylmagnesium bromide to give tetrasubstituted dihydrotetrazoles **112**.⁶⁵



R¹ = Me, Et, Oh; R² = Ph, Me, cyclo-C₆H₁₁, Bu^t; R³ = Me, Et, Bn, Ph;
R⁴ = Me, Ph, PhC≡C, CH₂=CH; M = Li, MgBr.

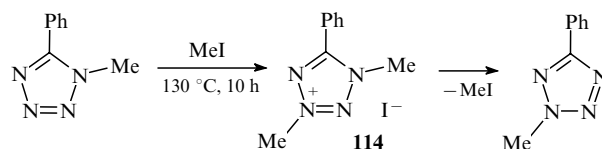
5. Thermolysis

The published data on the thermal stability of tetrazolium salts are rather scarce. It was shown^{6, 14} that of 1,3- and 1,4-dimethyl-5-*R*-tetrazolium iodides, the 1,4,5-isomers are more stable. Their decomposition begins at temperatures above 265 °C (R = Me) and 130 °C (R = Ph), whereas that of 1,3,5-isomers occurs even at 130 and 70 °C, respectively. *N*-Demethylation is the main process of thermolysis leading to the formation of disubstituted tetrazoles.^{6, 14} Thermolysis of 1,3,5-trisubstituted derivative **67** is accompanied by the evolution of nitrogen and the formation of the salt **113** in 94% yield.⁶¹



Recently, the thermal stabilities of 1-methyl-4-phenyl-, 1,4,5-trimethyl-, 1,3-di-*tert*-butyl-5-methyl- and 1,3-di-*tert*-butyltetrazolium picrates have been studied using differential scanning calorimetry and complex thermal analysis (heating rate 5 °C per min in a nitrogen atmosphere).³³ Among those, 1,4,5-trimethyltetrazolium picrate [initial temperature of intense decomposition (*T*_d) 215 °C] manifested the highest stability. 1-Methyl-4-phenyltetrazolium picrate (*T*_d = 100 °C) appeared to be the least stable, which may be attributed to the easy abstraction of proton from the carbon atom of the heterocycle. Special mention should be made of the enhanced thermal resistance of poly-*N,N'*-dimethyl-5-vinyltetrazolium perchlorate in comparison with poly-*N*-methyl-5-vinyltetrazole. According to complex thermal analysis data, the decomposition of polymeric tetrazolium perchlorate is observed at temperatures above 275 °C, whereas the non-quaternised polymer is decomposed at 230 °C.¹⁰⁸

2-Methyl-5-phenyltetrazole is the main reaction product in the attempted synthesis of tetrazolium salts by quaternisation of 1-methyl-5-phenyltetrazole with methyl iodide at 130 °C.⁶ The resulting isomerisation is due to the specificity of thermolysis of the initially formed tetrazolium salt **114**; its decomposition yields predominantly 2,5-disubstituted tetrazole.⁶

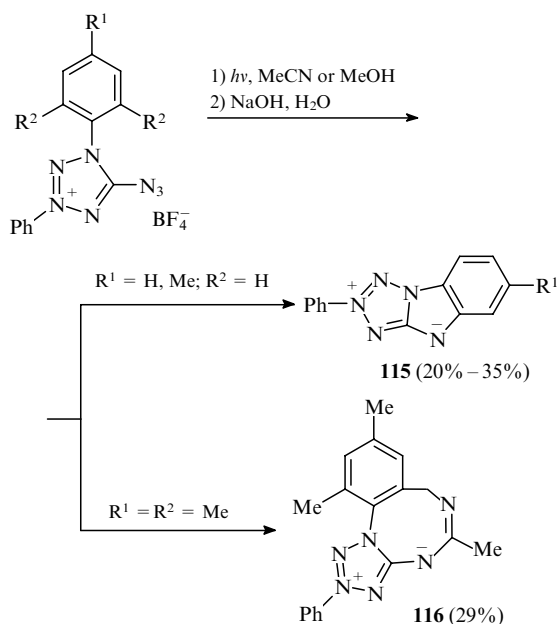


The formation of tetrazolium complexes is usually the key step in the isomerisation of *N*-substituted tetrazoles, which occurs under the action of alkylating reagents^{6, 109} or acids.^{43, 55, 110, 111}

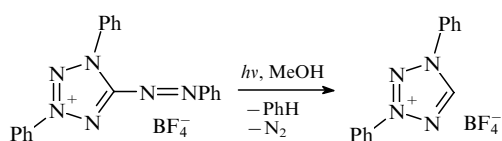
6. Photolysis

The photochemical conversions of some azido-, azo- and triazo-1,3-diaryltetrazolium derivatives have been studied recently.^{112–114} It was found^{112, 113} that the tetrazole rings of the

compounds under study are resistant to UV irradiation. Among other conversions, only the reactions of 5-azido-1,3-diaryltetrazolium salts, which yield hardly accessible tricyclic mesoionic compounds **115** and **116**, deserve special mention.

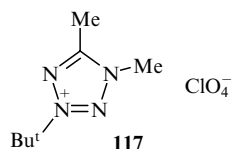


UV Irradiation of 1,3-diphenyl-5-phenyltetrazolium tetrafluoroborate is accompanied by the evolution of nitrogen and the formation of 1,3-diphenyltetrazolium tetrafluoroborate and benzene.¹¹⁴



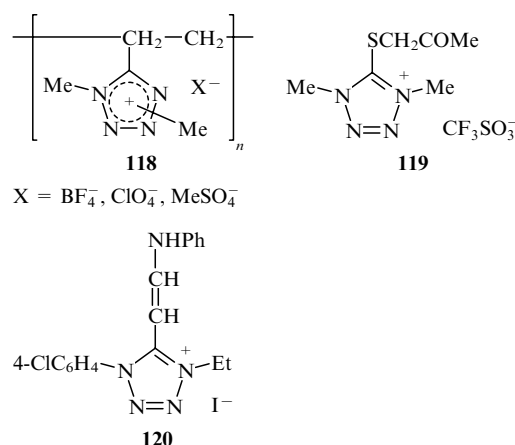
V. Applications of tetrazolium salts

Until recently, 1,3- and 1,4-substituted tetrazolium salts have not been sufficiently investigated due to their unavailability and data concerning their applications are virtually absent from the literature. However, the development of procedures for their synthesis have given strong impetus to their investigations, particularly in those areas where 2,3-substituted tetrazolium salts (*e.g.*, phase-transfer catalysts, reagents for the separation of metals, *etc.*) were conventionally used before. There is evidence of successful applications of 3-*tert*-butyl-1,5-dimethyltetrazolium perchlorate (**117**) as a phase-transfer catalyst in oxidation reactions catalysed by the permanganate ion.¹¹⁵

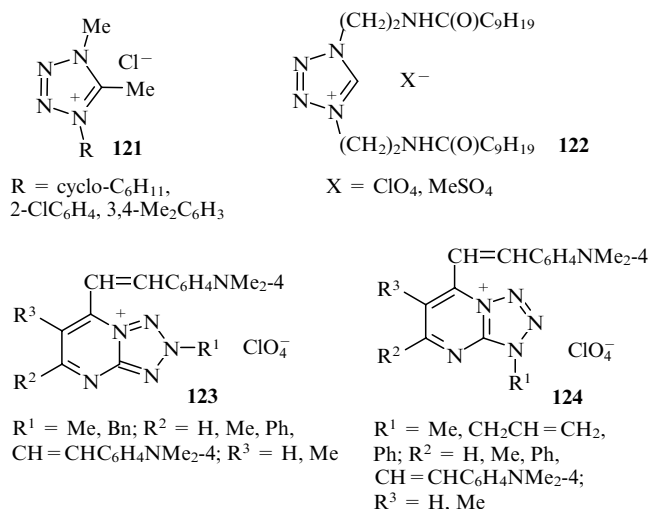


It is of note that 1,3-substituted tetrazolium salts have a number of advantages over 2,3-derivatives in such reactions.¹¹⁶ First, these methods allow one to obtain 1,3,5-trisubstituted tetrazolium salts with various types of substituents at the carbon and nitrogen atoms of the tetrazole ring and thus to vary their physicochemical properties (*e.g.*, thermal stability, solubility, *etc.*). The methods for the synthesis of 2,3-disubstituted tetrazolium salts exclude the introduction of alkyl substituents to the nitrogen atoms of the tetrazole ring, which limits the array of available derivatives.^{1–3} Of no less importance is the relative stability of 1,3-substituted tetrazolium salts in reductive media;

therefore, they can be used in phase-transfer reduction reactions, whereas 2,3-substituted derivatives are converted into formazanes even under the action of weak reducing agents.^{1–3} Recently, a series of poly-5-vinyltetrazolium salts **118** prepared by exhaustive methylation of poly-5-vinyltetrazole have been examined as sorbents for the extraction of palladium ions from various solutions in the form of $PdCl_4^{2-}$. These include an efficient adsorbent for the selective extraction of palladium ions from spent palladium electrolytes.¹⁰⁸ It was found that 1,4-dimethyl-5-[(2-oxopropyl)thio]tetrazolium triflate (**119**) inhibits transglutaminase,¹¹⁷ and 5-(2-anilinoethyl)-1-(4-chlorophenyl)-4-ethyltetrazolium iodide (**120**) manifests antiarrhythmic activity.¹¹⁸



The addition of 1-aryl- and 1-cyclohexyl-4,5-dimethyltetrazolium chlorides **121** to photographic dyes decreases the light sensitivity of photomaterials and enhances image sharpness.¹¹⁹ 1,4-Bis(2-decanoylaminoethyl)tetrazolium methylsulfate and perchlorate **122** have been patented as corrosion inhibitors and disinfectants.¹²⁰ Tetrazolo[1,5-*a*]pyridinium salts **123**, **124** have found application as sensitizers in the recording layers of electro-photographic materials.^{56, 121}



However, 1,3- and 1,4-substituted tetrazolium salts present the greatest interest as starting materials in the synthesis of various (including hardly accessible) heterocyclic systems. Condensation reactions of these salts are employed in the synthesis of annelated heterocycles. These reactions are specific and often the only way to the synthesis of imidazo-^{35, 103} and pyrrolotetrazoles.³⁷ It was shown that recyclisation of 1,4-substituted tetrazolium salts is a convenient procedure for the synthesis of three-, five- and six-membered nitrogenous heterocycles, such as iminoaziridines and tetrazines,^{66, 102} imidazolones,¹⁰³ benzooxazoles and quinazoline-diones.^{47, 100} The conversions of substituents at the carbon atom of the heterocycles of 1,3,5- and 1,4,5-trisubstituted tetrazolium

salts can be used in the high-yield synthesis of mesoionic tetrazoles,^{21, 27, 60, 94, 95, 112–114} The use of tetrazolium salts for the generation of N-heteroaromatic carbenes,^{44, 59, 122} which occupy a special place in the chemistry of carbenes by virtue of their peculiar structures and reactivities, especially holds great promise.^{83, 122}

VI. Conclusion

Significant progress has been achieved in the synthesis and investigation of physicochemical properties of 1,3-(1,3,5)- and 1,4-(1,4,5)-substituted tetrazolium salts in the past 10–15 years. The interest in these studies is largely due to the development of methods for selective functionalisation of the tetrazole ring, which permits direct introduction of substituents on the carbon and nitrogen atoms of the heterocycle, and the recently discovered isomerisation of 1,3-disubstituted tetrazolium salts into the corresponding 1,4-disubstituted derivatives. In turn, the availability of tetrazolium salts has stimulated the search for novel areas of their applications, particularly for synthetic purposes. Recyclisation and condensation reactions of tetrazolium salts and transformations of substituents at the carbon atom of the heterocycle proved to be useful tools in the synthesis of various organic compounds. Elucidation of the synthetic potentials of tetrazolium salts presents considerable interest for further progress in preparative chemistry of nitrogen-containing heterocyclic systems and organic chemistry on the whole. In-depth studies into the properties of novel 1,3-(1,3,5)- and 1,4-(1,4,5)-substituted tetrazolium salts will make it possible to extend the range of their practical applications, e.g., the design of polynitrogenous ionogenic polymers and ionic fluids resembling those of other azolium salts and possessing unique properties. Of no less importance are further studies into tetrazole quaternisation and possible involvement of functionalised C- and N-tetrazole derivatives and various alkylating reagents in this reaction. The knowledge of regularities underlying the formation of tetrazolium cations will enhance the potentialities of quaternisation and protonation reactions for the activation of the tetrazole ring in the substitution reactions occurring at the endocyclic carbon atom.

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Supramolecular chemistry of cucurbiturils

O A Gerasko, D G Samsonenko, V P Fedin

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Abstract. The main principles of the design of supramolecular compounds starting from organic macrocyclic cavitands, *viz.*, cucurbit[*n*]urils [C₆H₆N₄O₂]_{*n*} (*n* = 5–10), are considered. The presence of the hydrophobic inner cavity along with polar carbonyl groups forming the cucurbituril portals are responsible for high specificity of the formation of host–guest complexes. The unique ability of cucurbiturils to act as synthetic molecular containers is discussed. In these containers, bimolecular reactions between specially selected guests proceed with high regio- and stereoselectivity. The review surveys new data on the directed construction of supramolecular organic–inorganic compounds through the formation of an extensive network of hydrogen bonds between the portal oxygen atoms of cucurbiturils and water molecules of metal aqua complexes. The bibliography includes 108 references.

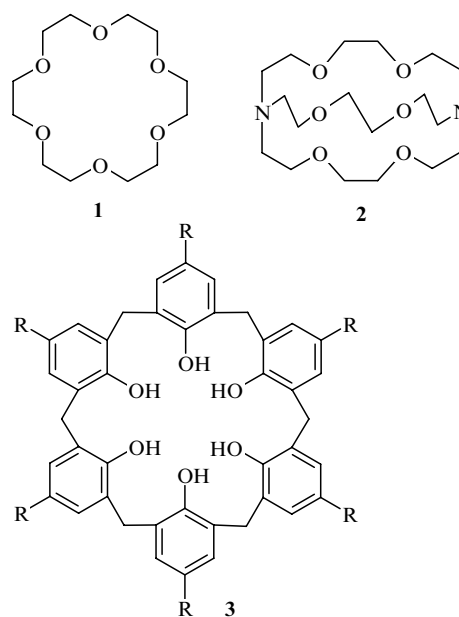
I. Introduction

Supramolecular chemistry is a new extensively evolving area of research focused on the association of individual molecules giving rise to more complex chemical systems formed through intermolecular (non-covalent) interactions.^{1–3} Supramolecular chemistry concerns various phenomena in different fields of science (organic, coordination and physical chemistry, biology, physics) and has a broad spectrum of possibilities due to the mutual enrichment of these areas of scientific exploration. Supramolecular chemistry deals with supramolecular ensembles, which are spontaneously self-assembled from complementary (*i.e.*, characterised by geometric and chemical compatibility) fragments in much the same fashion as spontaneous self-assembly of very complicated spatial structures in living cells. The directed construction of such systems and the design of highly ordered supramolecular compounds with desired structures and properties from molecular building blocks are fundamental problems of modern chemistry.

Intermolecular interactions holding the fragments together, *viz.*, Coulombic interactions, hydrogen bonds and van der Waals interactions, are, on the whole, much weaker than the covalent bonds in the molecule itself. To increase the strength of these bonds, their directionality and specificity, it is necessary to use rather large molecular building blocks capable of creating an extensive network of bonds due to a large contact interface.

Examples of compounds with a large number of bonded non-covalent interactions are host–guest complexes in which the inner cavity of the host molecule (or cavitand)⁴ can include a guest molecule of suitable size. Numerous complexes containing such macrocyclic organic molecules as crown ethers (**1**), cryptands (**2**), calixarenes (**3**) or cyclodextrins (**4**) as the host are presently available.

The encapsulation of inert gases, metal ions or organic molecules in the cavities of these molecules gives rise to stable compounds having unusual structures and exhibiting interesting properties. The present review surveys the synthesis and structures of supramolecular compounds prepared with the use of macrocyclic cavitands having the trivial name cucurbiturils.



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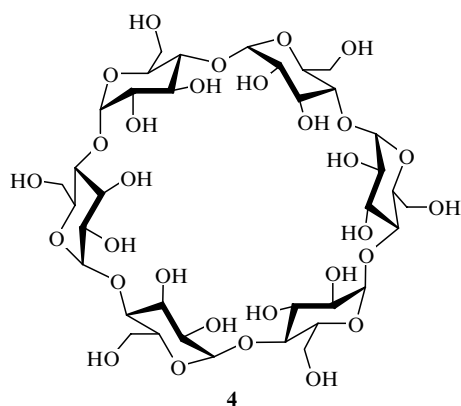
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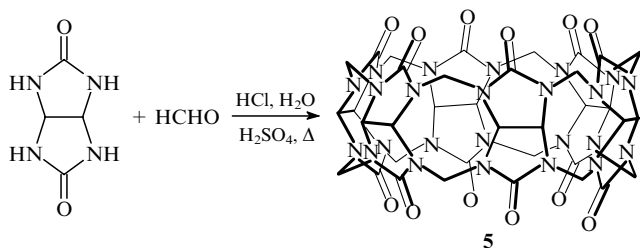
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Cucurbituril with composition $C_{36}H_{36}N_{24}O_{12}$ [cucurbit[6]uril (5)] consisting of six methylene-linked glycoluril fragments has been studied the most. This compound is the first example of cucurbiturils. It was prepared by Behrend *et al.*⁵ in 1905 by condensation of formaldehyde with glycoluril (condensation product of urea and glyoxal) in acidic medium. At that time, however, the procedures available did not allow one to determine correctly its composition and structure.



In 1981, Freeman, Mock and Shih⁶ reproduced the synthesis developed by Behrend and obtained a colourless crystalline compound whose structure was established by X-ray diffraction analysis. Cucurbituril **5** is a barrel-shaped macrocyclic cavitand containing carbonyl oxygen atoms (portals) at the top and bottom of the barrel. This cavitand received its trivial name for the visual similarity of its molecular shape to *Cucurbitaceae* (pumpkin family). According to the nomenclature of Chemical Abstracts, the systematic name of this compound is dodecahydro-1*H*,4*H*,14*H*,17*H*-2,16:3,15-dimethano-5*H*,6*H*,7*H*,8*H*,9*H*,10*H*,11*H*,12*H*,13*H*,18*H*,19*H*,20*H*,21*H*,22*H*,23*H*,24*H*,25*H*,26*H*-2,3,4*a*,5*a*,6*a*,7*a*,8*a*,9*a*,10*a*,11*a*,12*a*,13*a*,15,16,17*a*,18*a*,19*a*,20*a*,21*a*,22*a*,23*a*,24*a*,25*a*,26*a*-tetraoxazabispentaleno [1''',6''' : 5'',6'',7'']-cycloocta(1,2,3-*cd* : 5,6,7-*c'd'*)dipentaleno-1,4,6,8,10,12,14,17,19,21,23,25-dodecane. Hereinafter, cucurbiturils consisting of *n* glycoluril fragments will be abbreviated to *Qn* or referred to as cucurbit[*n*]uril.

The dimensions of the inner cavity of cucurbit[6]uril (**5**) (the height is 6 Å and the inner diameter is 5.5 Å) allow the molecule to accommodate small guest organic molecules or ions and the portals formed by the carbonyl groups (the diameters of the portals are 4 Å) can bind cations. The structure determination of Q6 gave impetus to investigations of its ability to act as a macrocyclic cavitand. Cucurbit[6]uril (**5**) whose cavity is similar in size to those of α -cyclodextrin and 18-crown-6 has higher negative charges on the donor oxygen atoms resulting in the enhancement of stability of its adducts with positively charged ions.^{7,8} Yet another difference between cucurbituril Q6 and other cavitands is its structural rigidity. Thus, this cucurbituril virtually retains its shape upon the inclusion of different guests and, consequently, exhibits higher selectivity in the formation of inclusion compounds.⁷

Cucurbit[6]uril (**5**) is a colourless crystalline compound, which is insoluble in water and organic solvents but is readily soluble in some mineral acids (HCl, H₂SO₄, CF₃SO₃H), carboxylic acids

(for example, HCOOH) and aqueous solutions of alkali salts. Cucurbit[6]uril serves as a convenient starting compound for the preparation of various supramolecular compounds due to its unique structure, the simplicity of the synthesis procedure and thermal stability (it does not decompose upon heating to 400 °C; see Ref. 9). Presently, cucurbit[6]uril is a readily available reagent (in particular, it can be purchased from Merck).

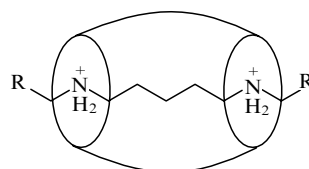
The results of studies devoted to the synthesis, examination of structures and properties of supramolecular compounds of cucurbiturils and investigations of thermodynamic and kinetic aspects of formation of these systems are summarised in reviews.^{7, 10–13} The present review surveys the recent advances in the chemistry of cucurbiturils achieved, primarily, in the latter half of the 1990s. Considerable attention is given to the studies aimed at the directed construction of supramolecular organic–inorganic hybrid materials, which have been performed in the last five years.

II. Host–guest cucurbit[6]uril compounds

The presence of the rather rigid inner cavity is responsible for the ability of cucurbit[6]uril (**5**) to accommodate small guest molecules. The formation of inclusion compounds was established by crystallographic methods as well as by different physicochemical methods because absorption, fluorescence and NMR spectra of guests are changed as the guest molecules go from the solvent environment (generally, from weakly acidic aqueous solutions) to the non-polar cavity of cucurbituril. Cucurbit[6]uril (**5**) forms stable inclusion compounds with amines, diamines, alkylammonium ions, benzylammonium ions and dye molecules.

1. Inclusion compounds with alkylammonium ions

Inclusion compounds of cucurbit[6]uril (**5**) with alkylammonium ions have received the most study. The hydrocarbon radical of the alkylammonium cation is encapsulated in the cavity of Q6 displacing the solvent molecules and is held in this cavity through van der Waals forces, whereas the nitrogen atom is fixed at the portal through Coulombic interactions of the cation with the oxygen atoms of the carbonyl groups. As a result, high specificity of binding of alkylammonium ions to cucurbit[6]uril is achieved.



X-Ray diffraction analysis of the supramolecular compound of Q6 with *p*-xylenediammonium chloride carried out by Freeman¹⁴ in 1984 showed that the hydrocarbon fragment of the diammonium cation $H_3N^+CH_2C_6H_4CH_2N^+H_3$ is located in the cavity, whereas two protonated nitrogen atoms are located at the portals of the macrocycle. The formation of host–guest compounds with composition 1:1 was also evidenced by X-ray diffraction data and solution NMR spectroscopic studies of supramolecular compounds of cucurbit[6]uril with alkyldiamines containing four, five or six methylene units between the nitrogen atoms.^{14–16}

The incorporation of alkylammonium cations into cucurbit[6]uril was examined by solution NMR spectroscopy in the 1980–1990s.^{15–20} It was found that the most stable inclusion compounds with cations of primary amines $H(CH_2)_nNH_3^+$ and diamines $H_3N^+(CH_2)_nNH_3^+$ are formed at *n* = 4 and *n* = 5, 6, respectively. An increase in the length of the hydrocarbon chain either hinders coordination of both amino groups of the alkyldiamine to the portals of cucurbit[6]uril or causes the hydrophobic alkyl fragment of the amine to interact with the second hydrophilic portals. A decrease in the length of the hydrocarbon chain leads to a decrease in the number of van der Waals contacts as a result of which two ammonium groups cannot be simultaneously

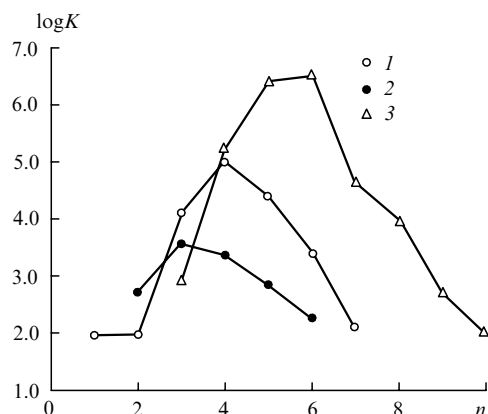
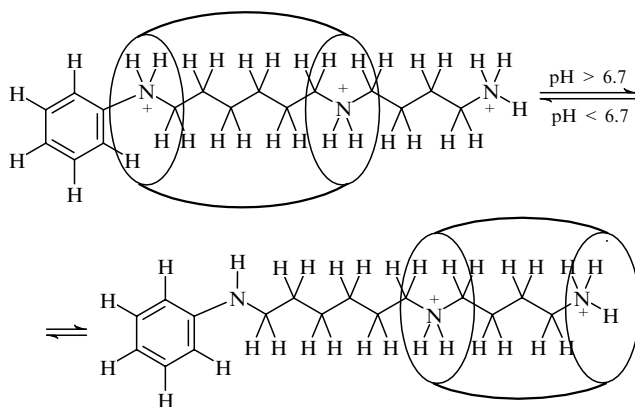


Figure 1. Logarithm of the formation constant (K) of inclusion compounds of cucurbit[6]uril with amines vs. the number of CH_2 groups in the chain; (1) alkylamines, (2) alkyldiamines, (3) amino alcohols.

located at the portals. The plots of the formation constants of inclusion compounds with composition 1:1 versus the chain length for alkylamines,¹⁷ alkyldiamines¹⁷ and amino alcohols¹⁸ are shown in Fig. 1. In the case of amino acids, no influence of the number of methylene groups on the stability constants was observed.¹⁸

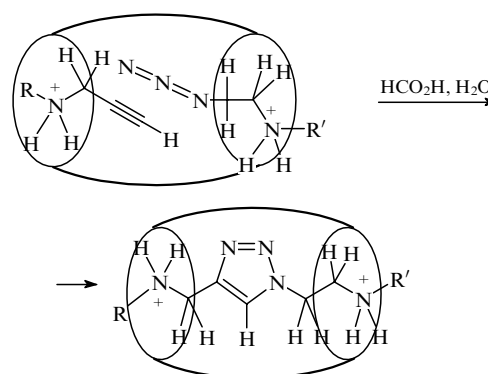
The $\text{PhNH}(\text{CH}_2)_6\text{NH}(\text{CH}_2)_4\text{NH}_2$ ligand containing three amino groups was specially synthesised and its binding with cucurbit[6]uril (**5**) was studied.¹⁹ An important characteristic feature of this guest molecule is the presence of two nitrogen atoms involved in the diaminoalkyl fragment. Their basicity is 10^6 times as high as that of the nitrogen atom bound to the phenyl group. In addition, the formation constant of the supramolecular compound of the hexanediammonium cation with cucurbit[6]uril is approximately 100 times larger than that for the butanediammonium ion, *i.e.*, different fragments of the triamine behave differently in binding to Q6. In aqueous solutions, the constant $\text{p}K_{\text{a}}$ of the nitrogen atom of the aniline fragment in this triamine is 4.7 and it is increased to 6.7 in the presence of stoichiometric amounts of Q6. The behaviour of each region of the triamine depends on pH. In acidic solutions, the hexanediammonium fragment (more complementary to the cavity in size) is located inside the cavitand. By contrast, the butanediammonium end of the triamine is bound to Q6 at $\text{pH} > 6.7$ because the nitrogen atom of the aniline fragment is deprotonated. This system is a molecular 'switch', *i.e.*, Q6 can be moved along the triamine molecule by changing the pH.



NMR spectroscopic studies demonstrated that the rate of formation of adducts with cucurbit[6]uril (**5**) depends on the diameter of the ammonium molecules and it is independent of thermodynamic stability of the resulting complexes.²⁰ Linear

hydrocarbon chains with a diameter that is no larger than the diameter of the portals of Q6, readily penetrate into the cavity, whereas the inclusion of cyclic or branched hydrocarbons is, apparently, accompanied by deviation of the oxygen atoms at the portals from their normal positions. Studies devoted to investigations of the thermodynamic and kinetic aspects of the inclusion of bulky ligands^{21–23} demonstrated that the formation of host–guest supramolecular compounds depends, in particular, on the acidity of the medium. The formation of compounds with cucurbit[6]uril is the first example of the pH-controlled kinetics of encapsulation of organic guests into the host cavity. The inclusion of a protonated guest into the cavity of the cavitand is slow due to formation of an intermediate upon interaction of the guest with the polar oxygen atoms at the portals, whereas an unprotonated molecule is encapsulated directly in the cavity and the rate constant of this reaction is 20 times larger.²³

High specificity of binding of Q6 with ammonium ions made it possible to perform unique azide–alkyne cyclisation in which both starting components, *viz.*, propargylamine and azidoethylamine, are included in the cavity of cucurbit[6]uril and cyclisation proceeds within the cavitand.^{24,25}



Under standard conditions, azide–alkyne cyclisation proceeds in solutions rather slowly ($k_0 \sim 10^{-6} \text{ mol}^{-1} \text{ s}^{-1}$) to give two isomeric products in equal amounts. Due to interactions of the ammonium groups of the starting reagents with the opposite portals of Q6, only a certain arrangement of the components in the cavity is possible resulting in regiospecificity of this reaction (only the 1,4-addition product is generated). Besides, the reaction is substantially accelerated in the presence of catalytic amounts of cucurbit[6]uril ($k_0 \sim 10^{-2} \text{ mol}^{-1} \text{ s}^{-1}$).

2. Inclusion of dye and other guest molecules

Examples of inclusion of other guest molecules into the cavity of cucurbit[6]uril (**5**) are few in number. The sizes of the cavity allow tetrahydrothiophene, tetrahydrofuran, benzene, cyclopentanone and furan to be accommodated, which was proved by shifts of the signals in the solution NMR spectra of these compounds.^{17,26} The *para*-substituted benzene ring can also be included into the cavity of cucurbit[6]uril (if the substituents are directed toward the portals). However, the size of this ring is somewhat larger than the size of the cavity resulting in distortions of both the guest and host molecules. Calorimetric titration showed that the stability of inclusion compounds of Q6 with aliphatic alcohols as well as with acids and nitriles is unaffected by the presence of polar groups and the number of methylene units in the guest molecule.²⁷

Various dye molecules form stable inclusion compounds with cucurbit[6]uril.^{7,28–30} Most of the dyes are hydrophobic and their molecules (or molecular fragments of suitable size) can interact rather strongly with the inner cavity of the cavitand. In some cases, the encapsulation in cucurbit[6]uril leads to substantial stabilisation of dye molecules. For example, Phenol Blue ($-\text{OC}_6\text{H}_4\text{NC}_6\text{H}_4\text{NMe}_2$) decomposes in a 0.1 M HCl solution during 3 min. If this dye is incorporated into cyclodextrin, it decomposes under the same conditions during 7 min. If this dye is

encapsulated in Q6, it is stable for 7 h.²⁸ Higher stabilities of inclusion compounds of dye molecules with cucurbit[6]uril in dilute solutions of formic acid as compared to inclusion compounds with β -cyclodextrin were also confirmed by spectrophotometric measurements.²⁹ The formation of inclusion compounds of cucurbit[6]uril with dyes is used for example, in textile industry for efficient absorption of dissolved, dispersed or emulsified dyes from industrial wastes.^{7, 30}

Cucurbit[6]uril can bind surfactants and polyethylene glycols,³¹ fluorescent compounds,³² and volatile organic compounds from the gas phase.³³ The ¹²⁹Xe and ¹H NMR spectroscopic data provided evidence for the reversible inclusion of xenone into Q6 and the formation of a 1 : 1 complex in an aqueous solution.^{34, 35} In spite of the absence of Coulombic or hydrophobic interactions, the stability of this compound is comparable with the stabilities of Q6 complexes with alkylammonium ions.

3. Synthesis and structures of nanosized rotaxanes

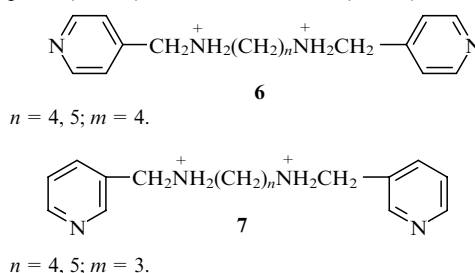
The ability of cucurbit[6]uril (**5**) to form host–guest compounds with alkylidiammonium salts provided the basis for the directed construction of nanosized rotaxanes (coordination polymers), which are not only of interest from the viewpoint of structural chemistry but also possess a series of unique properties due to which they show promise as materials, for example, for molecular electronics.^{12, 13} Rotaxanes are supramolecular compounds in which cyclic molecules (beads) are threaded onto linear molecules containing bulky terminal groups, which keep the beads from sliding off.³⁶ Analogous structures devoid of bulky terminal groups are called pseudorotaxanes. Such macrocycles as cryptands, crown ethers, cyclodextrins and calixarenes are rather widely used in the synthesis of rotaxanes.³⁷ Compounds containing the Q6 molecule as a bead were first prepared and structurally characterised by K. Kim and co-workers.³⁸ Two protonated nitrogen atoms of the $RN^+H_2(CH_2)_4N^+H_2R$ molecule [$R = (CH_2)_3NHC_6H_3(NO_2)_2-2,4$] are fixed at both portals of cucurbit[6]uril thus holding a chain of four polymethylene groups in its cavity, whereas two bulky 2,4-dinitrophenyl groups are located at the ends of the molecule. In addition, a pseudorotaxane compound was prepared in the cited study by the replacement of the 2,4-dinitrophenyl groups with the carbamate groups. In this case, Q6 does not move along the chain due to rather strong interactions between the protonated nitrogen atoms and the carbonyl groups at the portals of cucurbit[6]uril. In crystals, these pseudorotaxanes are linked in chains through hydrogen bonds between the carbamate groups of the adjacent fragments to form one-dimensional polymers.

The formation of pseudorotaxanes in solutions containing diammonium ions and cucurbit[6]uril has been proved by different methods, *viz.*, by IR and NMR spectroscopy and mass spectrometry.^{39–44} It has been demonstrated that pseudorotaxanes can act as molecular switches, *i.e.*, an increase in pH of solutions, as in the case of diamines, leads to deprotonation of the ammonium nitrogen atoms responsible for binding with Q6 and causes the movement of the macrocycle along the chain. In some cases, however, not only an increase in acidity of the medium but also heating are required for the reverse reaction to occur.⁴³ The use of fluorenyltriamine as the guest molecule made it possible to prepare a unique highly sensitive molecular switch in which the reversible movement of Q6 along the chain is accompanied by changes in the colour of the solution and fluorescence intensity.⁴⁴ At pH 1.0, a yellow fluorescent solution of the Q6 complex with the hexanediamine fragment of fluorenyltriamine is formed. As the pH is increased to 7, Q6 moves to the butanediamine fragment of the guest molecule due to deprotonation of the aniline nitrogen atom. This process is accompanied by a change in the colour of the solution to violet and the fluorescence intensity decreases. The use of cucurbit[6]uril as a catalyst for azide–alkyne cyclisation within the cavity made it possible to prepare a polyrotaxane with desired composition⁴⁵ from which the Q6 molecules were removed by increasing the pH of the medium. As a result, oligotriazoles

containing up to nine triazole-linked monomeric units were obtained.⁴⁶

K Kim and co-workers^{12, 13} developed an original approach to the synthesis of cucurbituril-containing polyrotaxanes, which allowed them to prepare first coordination-linked polymers. Initially, Q6 are threaded onto a small organic molecule with the diamine hydrocarbon chain containing suitable terminal functional groups. Then these fragments are linked to form a coordination polymer through bonds between the donor atoms of the terminal groups of the resulting pseudorotaxanes and the metal atoms. The above-described method has particular advantages over the previously known procedures giving rise to polyrotaxanes in which such macrocycles as cyclodextrins or crown ethers are threaded onto organic polymers. First, the resulting polyrotaxanes are characterised by high structural regularity, *i.e.*, cyclic beads are present in each repeated structural unit of the polymer chain. Second, these polyrotaxanes were obtained as single crystals and characterised by X-ray diffraction analysis, whereas single crystals of cyclodextrin-containing polyrotaxanes suitable for X-ray diffraction studies are difficult to prepare because of the existence of numerous isomers with different orientations of the cone-like macrocycle.

Coordination of the donor atoms of the terminal groups of pseudorotaxanes to transition metal atoms [Cu(II), Co(II), Ni(II), Ag(I), Cd(II)] gives rise to one- and two-dimensional polyrotaxanes depending on the coordination number of the metal atom, the structure of pseudorotaxane, the size and the coordination ability of the counterion of the starting metal salt. The products of the reactions of different metal salts with the pseudorotaxanes (PR nm) are shown in Fig. 2. In these compounds, the cucurbit[6]uril molecule accommodates the molecule of dipyridylamines **6** or **7**, which contain chains of n methylene units ($n = 4, 5$) and the *para*- ($m = 4$) or *meta*-substituted ($m = 3$) terminal pyridine rings.



The reactions of pseudorotaxanes of the PR44 ($n = 4, m = 4$) and PR43 ($n = 4, m = 3$) types with aqueous solutions of cobalt(II) nitrates⁴⁷ and nickel(II) nitrates⁴⁸ afforded chain polymers. In these polymers, pseudorotaxanes can be in either the *trans* or *cis* positions at the octahedrally coordinated metal atoms to form linear chains (PR44) (see Fig. 2, structure **A**) and zigzag chains (PR43) (see Fig. 2, structure **B**), respectively. The size of the repeated zigzag fragment in the structure **B** is larger than 23 Å. The reaction of PR44 with $\text{Cu}(\text{NO}_3)_2$ also gave rise to zigzag chains where two pseudorotaxane molecules are coordinated to the copper atom in a square-pyramidal environment.⁴⁹ Silver(I) compounds tend to form linear two-coordinate complexes. The reaction of PR44 with silver tosylate [$\text{Ag}(\text{MeC}_6\text{H}_4\text{SO}_3)$] resulted in the *trans* coordination of two pseudorotaxane molecules to the metal atom giving rise to a virtually linear chain structure.⁵⁰ One-dimensional helical polymers were synthesised by the reactions of AgNO_3 (see Ref. 51) and $\text{Cd}(\text{NO}_3)_2$ (see Ref. 47) with pseudorotaxane PR53 in which the organic molecule encapsulated in cucurbituril contains five methylene groups and the *meta*-substituted terminal pyridine rings. Two silver ions and two pseudorotaxanes coordinated to these ions comprise one turn of the helix (see Fig. 2, structure **C**), the length of one fragment being equal to 17.9 Å. In the compound with cadmium, each turn of the helix (50.5 Å) consists of four pseudorotaxanes PR53 and four metal ions (see Fig. 2, structure **D**). The space between the chains in polyrotaxanes is filled with water molecules and anions linked

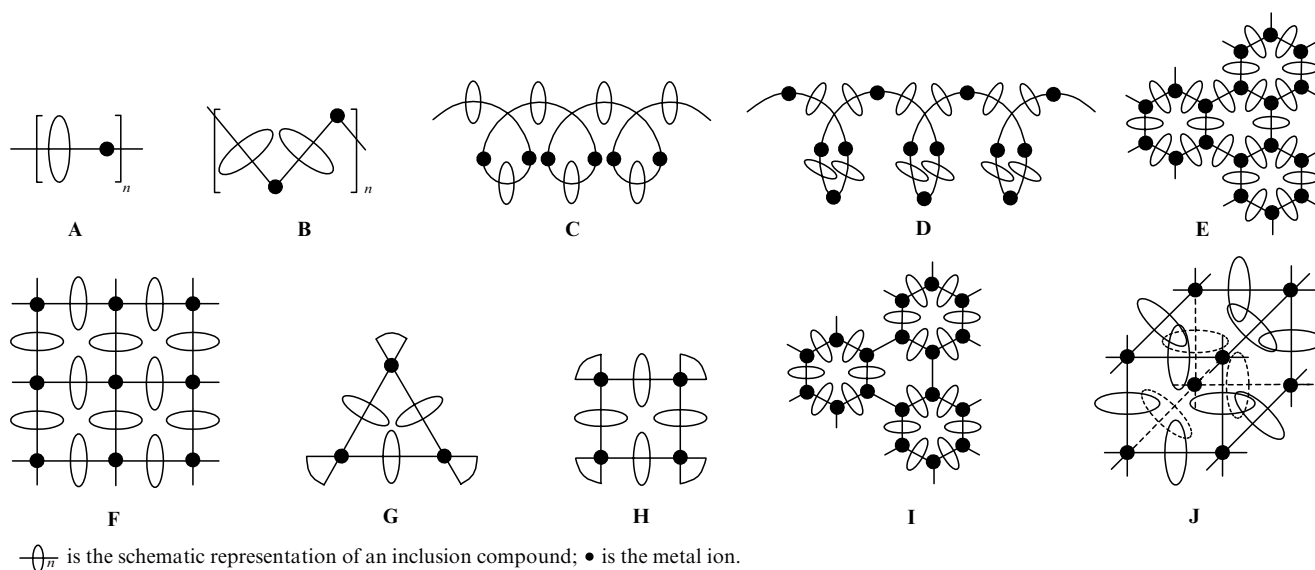


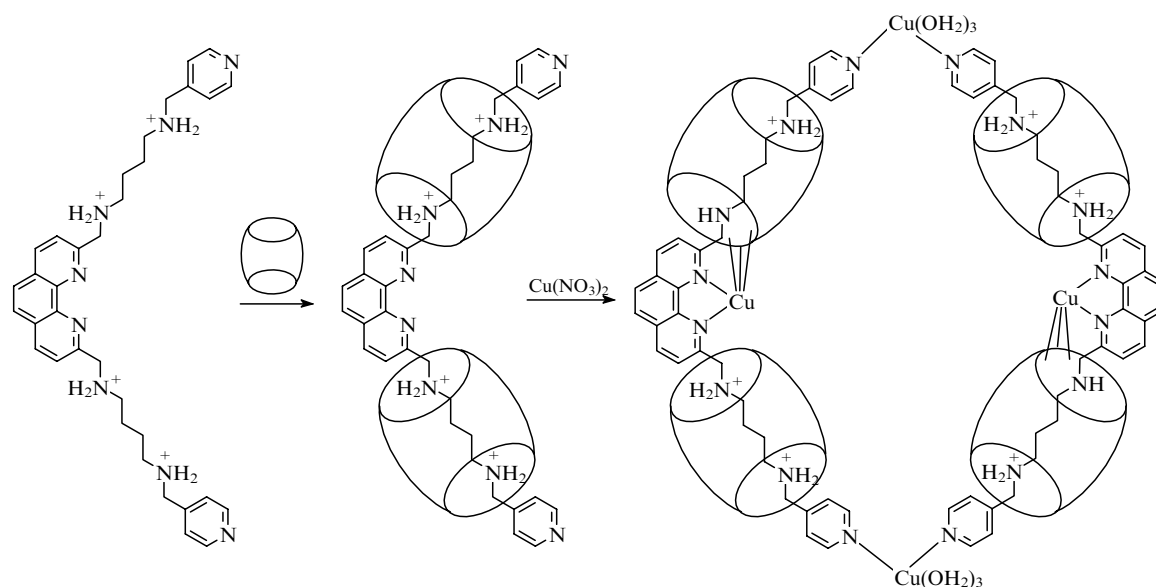
Figure 2. Formation of one-, two- and three-dimensional polyrotaxanes A–J (see the text) in the reactions of pseudorotaxanes with solutions of metal salts.

through an extensive network of hydrogen bonds resulting in additional stabilisation of the structure.

Unlike the above-described reaction with silver tosylate giving rise to a chain structure, the reaction of the pseudorotaxane PR44 with an aqueous solution of silver nitrate afforded a two-dimensional polyrotaxane.⁵⁰ The reaction with the use of another counterion afforded a polymeric structure in which the cucurbituril beads are threaded onto a network of face-sharing chair-shaped hexagons with silver ions occupying each vertex (see Fig. 2, structure E). Each face consists of two silver ions coordinated by two nitrogen atoms of the terminal pyridine rings of the pseudorotaxane. The length of the face is 20.9 Å and the average distance between two opposite angles is 38.0 Å. In the crystal, these two-dimensional polyrotaxane networks form superimposed interpenetrating layers with complete linkage of the hexagons. The resulting compound is the first example of polycatenane–polyrotaxane networks (catenanes are compounds consisting of interpenetrating rings). When the positions of the nitrogen atoms of the terminal pyridine rings of the pseudorotaxane are changed with the simultaneous change of the counterion, the reaction of PR43 with (CF₃SO₃) affords a two-dimensional

polyrotaxane of another type, which can be described as networks consisting of squares with cucurbituril molecules threaded onto all sides of these squares (see Fig. 2, structure F).⁴⁷ The networks are packed in layers (the distance between the layers is 12.7 Å). In this case, the catenane structure is not formed. A compound prepared by the reaction of the pseudorotaxane PR43 with copper nitrate Cu(NO₃)₂ has an analogous layered structure.⁴⁷

The *cis*-coordination of pseudorotaxanes to the metal atoms in a planar-square coordination makes it possible to prepare the so-called molecular necklaces in which several cyclic molecules are threaded onto a larger-size ring. Thus, the coordination of the ethylenediamine ligand in the [Pt(en)(NO₃)₂] complex (en is ethylenediamine) is such that pseudorotaxanes can occupy only *cis* positions on reaction with this complex to give nanocycles with three (PR44) (see Fig. 2, structure G) or four (PR43) (see Fig. 2, structure H) threaded cucurbit[6]uril molecules.⁵² A molecular necklace consisting of four rotaxane fragments was also prepared in the reaction of copper(II) nitrate with a polyrotaxane, whose angular form is dictated by the phenanthroline derivative that links two Q6 molecules.⁵³ The ring is formed upon *cis* coordination of the copper atom by the nitrogen atoms of the terminal



Scheme 1

pyridine groups of two angular pseudorotaxanes. The distance between the metal atoms in these nanocycles is ~ 20 Å (Scheme 1).

The use of molecular necklaces as large building blocks for the design of supramolecular compounds is of obvious interest. The reaction of PR53 with $\text{Cu}(\text{NO}_3)_2$ in the presence of oxalate ions afforded a supramolecular structure in which molecular necklaces consisting of six copper-bound pseudorotaxanes are linked to each other through the coordinated oxalate ions (see Fig. 2, structure I).⁵³ Each planar ring is bound to six other rings giving rise to two types of cavities in the polymer structure. The cavities of one type are located within the hexagons (the diameter is 5 Å), whereas the cavities of another type formed by oxalate ions are located between the hexagons (the diameter is 14 Å). These cavities form channels occupied by the NO_3^- ions and water molecules. The sizes of the channels are sufficiently large and allow NO_3^- ions to be replaced by the PF_6^- and tosylate ions in aqueous solutions. The replacement by bulkier anions, such as tetraphenylborate, does not occur, which is indicative of the rather high selectivity of the polyrotaxane compound in these reactions.

Three-dimensional polyrotaxanes can be prepared upon coordination of the terminal groups of pseudorotaxanes by lanthanide atoms, which typically have large coordination numbers.⁵⁴ Under hydrothermal conditions, the reaction of the pseudorotaxane PR43 containing the terminal 3-carboxyphenyl groups with $\text{Tb}(\text{NO}_3)_3$ afforded a supramolecular compound with a three-dimensional coordination network as the framework. Each lattice node is occupied by two Tb^{3+} cations (see Fig. 2, structure J; one solid circle in each lattice node corresponds to two terbium atoms) coordinated by six pseudorotaxane molecules through the carboxylate groups, with four carboxylate groups serving as bridges between the terbium atoms. As a result of a change in the position of the carboxylate group in the benzene ring, the reaction of $\text{Tb}(\text{NO}_3)_3$ with the pseudorotaxane PR44 yielded a two-dimensional polymer in which each terbium centre is coordinated by three pseudorotaxane fragments. The polycatenane-polyrotaxane structure of this compound is analogous to the structure of the two-dimensional polyrotaxane formed in the reaction of AgNO_3 with a pseudorotaxane containing the terminal pyridine groups (see Fig. 2, structure E).

Cucurbit[6]uril (**5**) has found an interesting application in the chemistry of dendrimers. In the last decade, these three-dimensional organic compounds have attracted the attention of

researchers because of their successful use in various fields of science and technology (medicine, catalysis and agriculture).⁵⁵ In the reaction of Q6 with a dendrimer containing terminal alkyldiammonium groups, the macrocycles are threaded onto these terminal groups to give a dendrimer with terminal pseudorotaxane fragments.

The use of a bulky bead as a component of the terminal groups imparts rigidity to the structure of the dendrimer. The resulting compound has a globular structure and can hold guests within its cavity. If the pH of the solution is increased, Q6 is removed and the dendrimer becomes conformationally flexible and releases the guest molecule. This reversible inclusion of molecules opens up new possibilities for using dendrimers for the transport, for example, of pharmaceuticals.

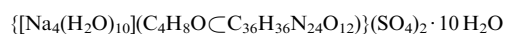
Hence, rotaxanes and pseudorotaxanes based on cucurbit[6]uril (**5**) have proved to be convenient building blocks for the construction of supramolecular compounds. Cucurbit[6]uril is rigidly fixed at the hydrocarbon chain through Coulombic and van der Waals interactions and the resulting rotaxanes and pseudorotaxanes are linked to each other through bonds between the donor atoms of the terminal groups and the metal atoms to form nanosized supramolecular compounds.

III. Supramolecular compounds of cucurbit[6]uril with metal aqua complexes

The ability of cucurbit[6]uril (**5**) to bind metal ions in aqueous solutions was discovered by Behrend and co-workers in 1905.⁵ The presence of more polar oxygen atoms in cucurbit[6]uril as compared to those in crown ethers or cryptands is responsible for the formation of stronger interactions between these oxygen atoms and metal cations. The formation constants of metal complexes with Q6 are much higher than the formation constants of complexes with the above-mentioned organic macrocycles.⁸ Besides, the rigidity of Q6 hinders its conformational changes upon complex formation, in contrast, for example, to metal complexes with crown ethers.⁵⁶ The metal cations are coordinated by the oxygen atoms located in the planes of the portals of cucurbit[6]uril rather than are included into the cavity of the cavitand. Hence, due to the unique structure of cucurbit[6]uril, it can form not only inclusion compounds with organic molecules but also mixed organic–inorganic compounds with metal cations.

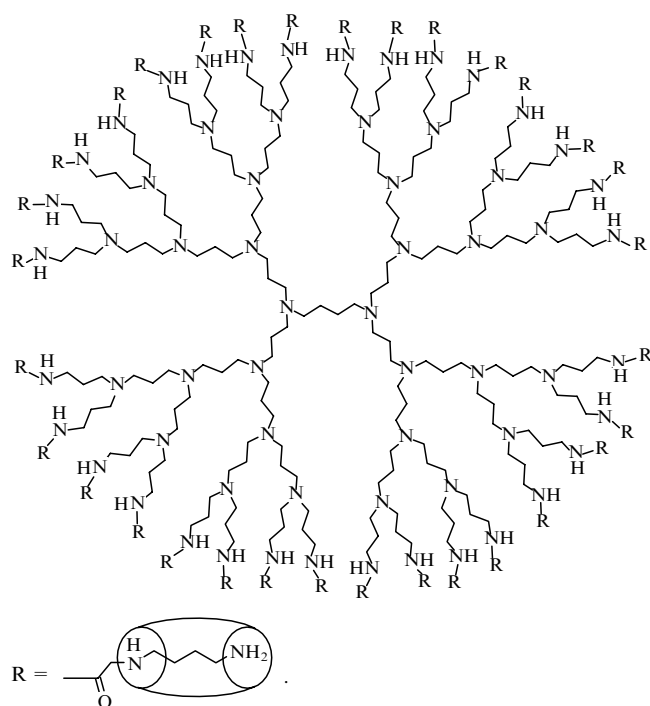
In the late 1990s, interesting supramolecular compounds of Q6 with the sodium, potassium, rubidium and cesium cations were prepared.^{26, 57–59} Cucurbit[6]uril is insoluble in water but its solubility is noticeably increased in the presence of salts of these metals. These compounds were obtained as single crystals by slow diffusion of organic solvents into aqueous solutions and characterised by X-ray diffraction analysis. Metal aqua complexes are bound to the carbonyl oxygen atoms of the Q6 portals to form lids, which efficiently close the cavitand from both sides.

In the compound of cucurbit[6]uril with a sodium aqua complex (**8**), each portal of the macrocycle is coordinated to two metal cations linked to each other through a bridging water molecule (the symbol $\subset$ designates the inclusion into the cavity of the cavitand).²⁶



8

Each sodium atom is bound to two carbonyl oxygen atoms of Q6 and three water molecules. Due to formation of supramolecular compounds of the type 'barrel with two lids', the cavity of the cavitand can include and hold the tetrahydrofuran molecule (Fig. 3). However, an increase in acidity leads to protonation of the carbonyl groups at the Q6 portals, removal of the lids and release of the guest from the cavity of the cavitand. After the addition of Na_2CO_3 , tetrahydrofuran is again included into the cavity because the barrel is again efficiently closed by the lids. According to the ^1H NMR spectroscopic data, other guests, such



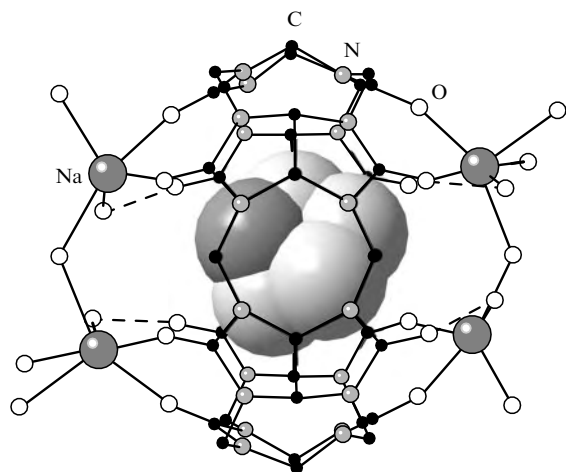
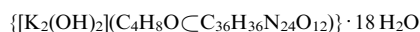


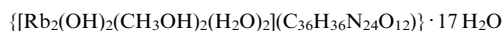
Figure 3. Structure of the supramolecule $\{[\text{Na}_4(\text{H}_2\text{O})_{10}](\text{C}_4\text{H}_8\text{OCC}_{36}\text{H}_{36}\text{N}_{24}\text{O}_{12})\}(\text{SO}_4)_2 \cdot 10 \text{H}_2\text{O}$ (**8**). The cavity of the cavitaund encapsulates the tetrahydrofuran molecule.

as benzene, cyclopentanone and furan, behave analogously. The supramolecular compound of Q6 with the sodium aqua complex is the first example of a molecular container into which guests can be reversibly included through the formation and cleavage of the bonds between the metal aqua complex and macrocycle.

In the compounds with potassium (**9**)⁵⁷ or rubidium (**10**),⁵⁸ the portals of Q6 are also closed by the bridging binuclear aqua complexes serving as the lids.



9



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Each metal atom is coordinated by four oxygen atoms at the portals of two Q6 molecules (two oxygen atoms from each molecule) (Fig. 4). This leads to the formation of hybrid

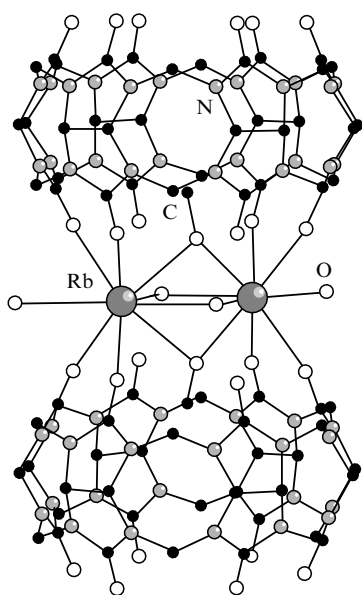


Figure 4. Structure of the supramolecular compound $\{[\text{Rb}_2(\text{OH})_2(\text{CH}_3\text{OH})_2(\text{H}_2\text{O})_2](\text{C}_{36}\text{H}_{36}\text{N}_{24}\text{O}_{12})\} \cdot 17 \text{H}_2\text{O}$ (**10**) (view along the axis *a*).

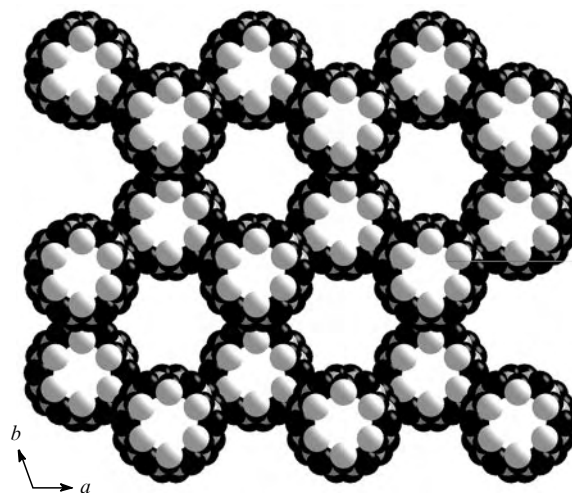


Figure 5. Formation of the honeycomb-like structure in the supramolecule **9** (view along the axis *c*).

organic–inorganic polymers consisting of alternating metal aqua complexes and cucurbit[6]uril. The structures of these compounds are stabilised by van der Waals interactions due to complementarity of the chain folds, *i.e.*, the convexities of one chain match the concavities of the adjacent chains. The polymer chain surrounded by three adjacent chains is shifted by half of the translation along the axis *c* to form a honeycomb-like packing containing large channels (Fig. 5). The resulting compounds are promising for the design of porous materials, which find use in separation processes, supramolecular catalysis and optoelectronics. In the honeycomb-like structure of the compound with the rubidium ion **10**, the diameter of the channels filled with water molecules of solvation is $\sim 10 \text{ \AA}$ and the volume of these chains comprises 23% of the total volume of the structure.⁵⁸ Upon the addition of THF or ethylenediamine, the molecules of these compounds are included only into the cavity of the cavitaund, the channels remaining unoccupied.^{57, 58}

Each portal of cucurbit[6]uril in the supramolecular compound $\{[\text{Cs}_2(\text{H}_2\text{O})_2](\text{H}_2\text{OCC}_{36}\text{H}_{36}\text{N}_{24}\text{O}_{12})\}\text{Cl}_2 \cdot 2 \text{H}_2\text{O}$,⁵⁹ like those in the above-described compounds with sodium (**8**), potassium (**9**) and rubidium (**10**), is coordinated to the metal aqua complexes. However, due to the larger ionic radius of the cesium cation, the barrel can be closed by a mononuclear cesium complex serving as the lid. The cesium atom is bound to four carbonyl oxygen atoms of cucurbituril and three water molecules. The addition of tetrahydrofuran gave rise to the inclusion compound $\{[\text{Cs}(\text{H}_2\text{O})_2\text{Cl}](\text{C}_4\text{H}_8\text{OCC}_{36}\text{H}_{36}\text{N}_{24}\text{O}_{12})\} \cdot 5 \text{H}_2\text{O}$ (**11**) in which the barrel is closed only by one lid, whereas the oxygen atom of the guest THF molecule is coordinated to the cesium ion (Fig. 6). In this case, the inclusion of tetrahydrofuran, as in the case of the sodium complex **8**, is also reversible and depends on the acidity of the medium.

The supramolecular compound of cucurbit[6]uril with the calcium aqua complex $\{[\text{Ca}(\text{HSO}_4)_2]_2(\text{C}_{36}\text{H}_{36}\text{N}_{24}\text{O}_{12})\} \cdot 13 \text{H}_2\text{O}$ is the first example of the structurally characterised cucurbituril compound. The structure of this compound, which was established by Freeman and co-workers⁶ in 1981 and refined by Freeman at a later time,¹⁴ is a polymer consisting of the alternating Q6 molecules linked to the calcium cations through the carbonyl groups. In the presence of methanol, the coordinated CH_3OH molecule is included into the cavity of the cavitaund, the shape and packing of the supramolecules remaining virtually unchanged.⁶⁰ The structure of the fragment of the chain in the $\{[\text{Ca}(\text{H}_2\text{O})_3(\text{HSO}_4)(\text{CH}_3\text{OH})]_2(\text{C}_{36}\text{H}_{36}\text{N}_{24}\text{O}_{12})\}(\text{HSO}_4)_2 \cdot 4 \text{H}_2\text{O}$ complex (**12**) is shown in Fig. 7. Each Q6 molecule is bound to four calcium cations and each calcium cation is bound to two Q6

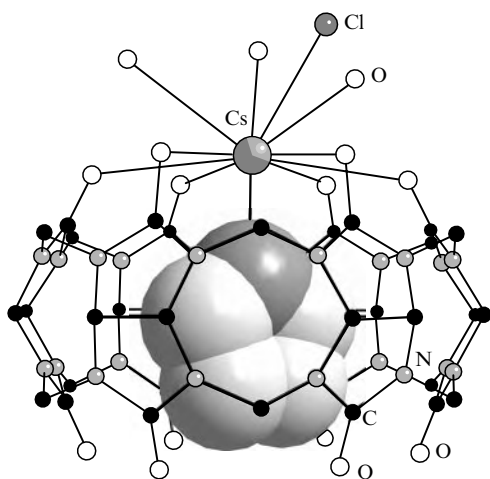


Figure 6. Structure of the supramolecule $\{[\text{Cs}(\text{H}_2\text{O})_2\text{Cl}](\text{C}_4\text{H}_8\text{OCC}_{36}\text{H}_{36}\text{N}_{24}\text{O}_{12})\} \cdot 5 \text{H}_2\text{O}$ (**11**). The cavity of the cavitand encapsulates the tetrahydrofuran molecule.

molecules (one carbonyl group of one molecule and two carbonyl groups of another molecule). In addition to the carbonyl groups of the Q6 molecules, the calcium ions are coordinated by three water molecules, the hydrosulfate anion, and the methanol molecule whose methyl group is located in the hydrophobic cavity of the cavitand.

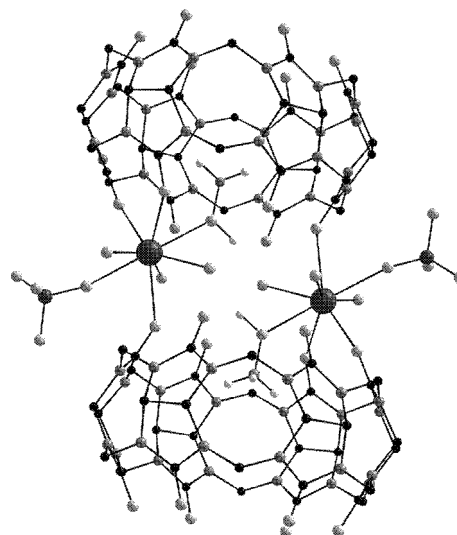


Figure 7. Fragment of the chain of the compound of cucurbit[6]uril with the calcium aqua complex $\{[\text{Ca}(\text{H}_2\text{O})_3(\text{HSO}_4)(\text{CH}_3\text{OH})]_2(\text{C}_{36}\text{H}_{36}\text{N}_{24}\text{O}_{12})\}(\text{HSO}_4)_2 \cdot 4 \text{H}_2\text{O}$ (**12**). The cavity of the cavitand encapsulates the methyl group of MeOH.

In the crystals, the polymer molecules form molecular cylinders linked to each other through hydrogen bonds and the channels are occupied by the water molecules of crystallisation and HSO_4^- anions (Fig. 8).

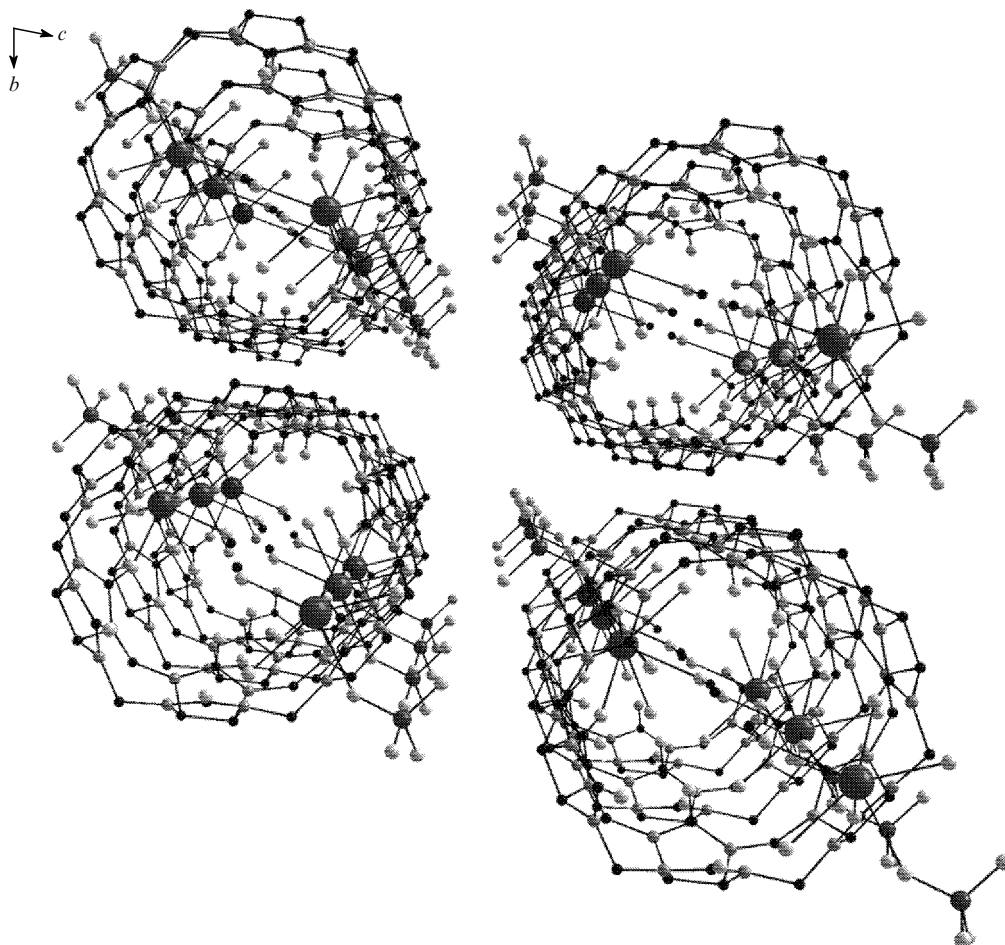


Figure 8. Formation of molecular cylinders (view along the a axis) in the supramolecular compound **12**. Water molecules of crystallisation and sulfate anions are omitted.

Unlike the compounds of cucurbit[6]uril (**5**) with aqua complexes of Groups 1 and 2 metals in which there are direct interactions between the metal atoms and oxygen atoms at the portals of Q6, coordination of Group 13 metals by the macrocycle occurs through hydrogen bonding between the portal oxygen atoms and coordinated water molecules of the aqua complexes. It should be noted that in the latter type of compounds, Q6 acts as an outer-sphere ligand. In supramolecular compounds with cucurbit[6]uril, distortions in the aqua complexes are much smaller than those in the case of insertions of the ligands into the first coordination sphere. Consequently, the structural information for compounds with Q6 corresponds better to the compositions and structures of aqua complexes that are actually present in solution.

In the compounds of cucurbit[6]uril with aqua and chloro aqua complexes of indium and aluminium, the metal complexes are located between the Q6 molecules and are linked to each other through a complex network of hydrogen bonds involving the portal oxygen atoms and water molecules. The complex *trans*-[InCl₂(H₂O)₄]⁺ and *cis*- and *trans*-[InCl₄(H₂O)₂][−] ions were isolated and structurally characterised in the investigation of the reaction of cucurbit[6]uril with indium nitrate in hydrochloric acid solutions.⁶¹ In the compound with composition {[InCl₂(H₂O)₄]₃(Cl⊂C₃₆H₃₆N₂₄O₁₂)}₂Cl·4 H₂O (**13**), the macrocyclic molecules form a hexagonal one-layer packing (Fig. 9), the crystallographic positions occupied by the macrocycles in this structure having the highest symmetry *D*_{6h} possible for cucurbit[6]uril. The cavity of the cavitaund contains the Cl[−] anion disordered over 12 positions. The structure of the (H₃O)₃{[InCl₄(H₂O)₂]₃(C₃₆H₃₆N₂₄O₁₂)₂}·17 H₂O compound is composed of both the *trans* and *cis* isomers of the [InCl₄(H₂O)₂][−]

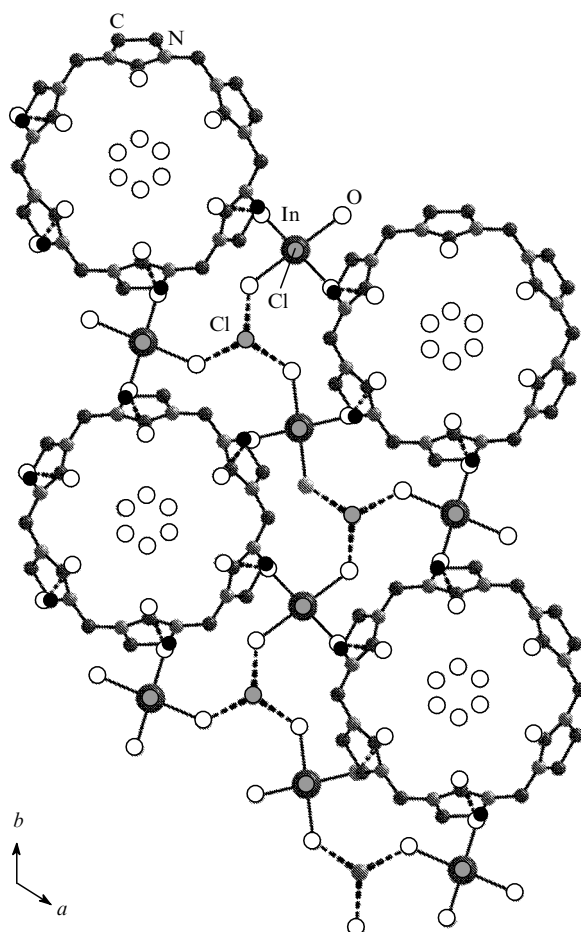
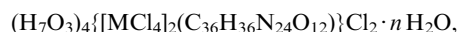


Figure 9. Crystal structure of {[InCl₂(H₂O)₄]₃(Cl⊂C₃₆H₃₆N₂₄O₁₂)}₂Cl·4 H₂O (**13**).

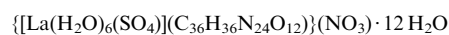
complex. In this crystal structure, the Q6 molecules form a parquet-like packing. The reactions of Q6 with aluminium chloride and indium nitrate in aqueous solutions afforded supramolecular compounds with the aqua complexes [Al(H₂O)₆]³⁺ and [In(H₂O)₆]³⁺ with compositions {[Al(H₂O)₆](C₃₆H₃₆N₂₄O₁₂)Cl₃·18 H₂O and {[In(H₂O)₆](C₃₆H₃₆N₂₄O₁₂)}·(NO₃)₃·9 H₂O, respectively.⁶¹ In the structure of the former compound, the centres of the Q6 molecules follow the body-centered law. In the structure of the latter compound, the molecules of the macrocycle form a parquet-like packing.

In studies of the M³⁺–HCl–Q6 systems, the isostructural compounds with composition

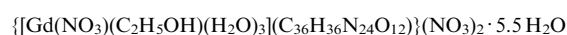


where (M = Ga, *n* = 2;⁶² M = Fe, *n* = 3⁶³), were obtained. In the structures of these complexes, the Q6 molecules alternating with the [MCl₄][−] anions are also linked through a system of hydrogen bonds between the portal oxygen atoms and water molecules.

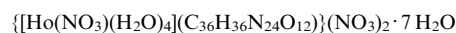
The reactions of lanthanide(III) nitrates and sulfates with Q6 in aqueous solutions afforded supramolecular compounds in which (according to the X-ray diffraction data) the aqua complexes are bound to the macrocycle through both the direct coordination of the metal atom by the oxygen atoms and hydrogen bonding between the coordinated water molecules and portal oxygen atoms of cucurbit[6]uril.⁶⁴ In the resulting compounds, the aqua complex : cucurbit[6]uril ratio is 1 : 1, 2 : 2 or 2 : 3. In complexes **14**–**17** with composition 1 : 1, the metal atom together with its ligand environment forms the lid that closes the Q6 molecule from one side.



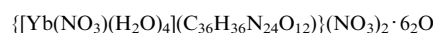
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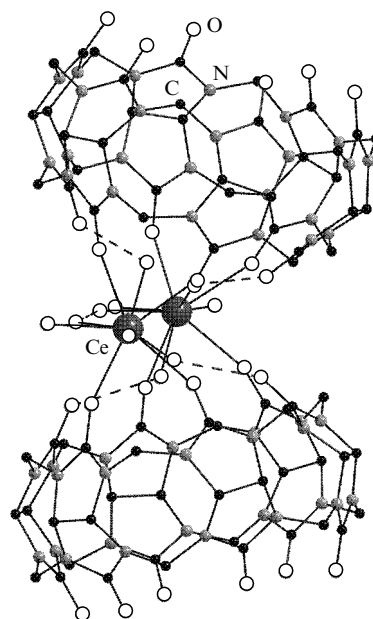


Figure 10. Fragment of the {[Ce(H₂O)₅]₂(C₃₆H₃₆N₂₄O₁₂)₂}Br₆·26 H₂O structure (**18**): formation of the sandwich-type compound.

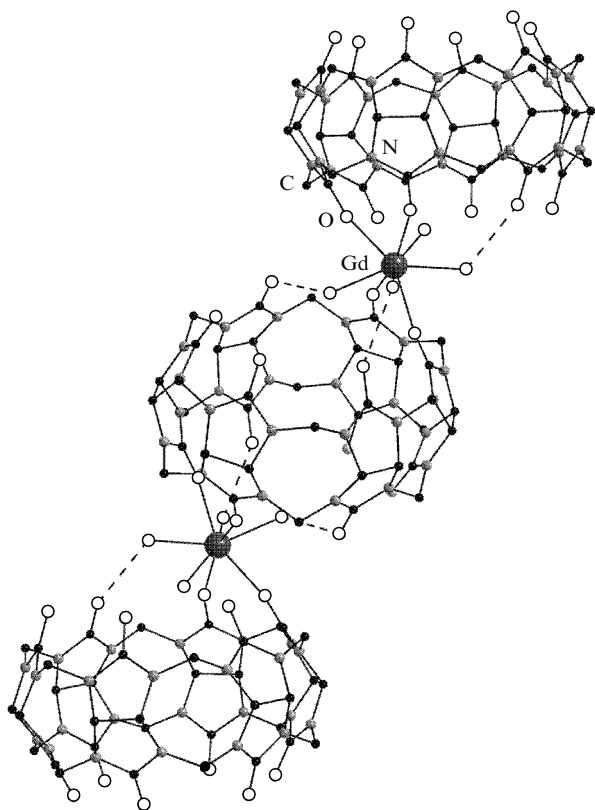
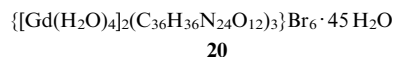
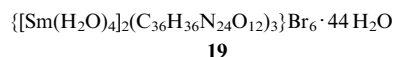


Figure 11. Fragment of the $\{[\text{Gd}(\text{H}_2\text{O})_4]_2(\text{C}_{36}\text{H}_{36}\text{N}_{24}\text{O}_{12})_3\}\text{Br}_6 \cdot 45 \text{H}_2\text{O}$ structure (**20**): the triple-decker sandwich.

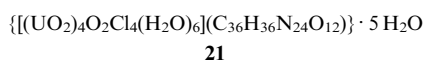
In the $\{[\text{Ce}(\text{H}_2\text{O})_5]_2(\text{C}_{36}\text{H}_{36}\text{N}_{24}\text{O}_{12})_2\}\text{Br}_6 \cdot 26 \text{H}_2\text{O}$ complex (**18**) with composition 2:2, two cerium aqua ions are coordinated by two Q6 molecules to form a sandwich-type compound (Fig. 10).

The crystal structures of compounds **19**⁶⁵ and **20**⁶⁴ with composition 2:3 can be described as packings of nanosized triple-decker sandwiches built from alternating Q6 molecules and metal aqua complexes (Fig. 11).



The shape of this supramolecule can be approximated by a skewed cylinder whose largest van der Waals size is 33 Å. In the crystals of lanthanide(III) compounds, the supramolecules are linked in chains or layers or packed in stacks through hydrogen bonding. In these structures, large channels and cavities are occupied by water molecules of crystallisation and counterions.

The possibility of using Q6 for crystallisation of polynuclear aqua complexes was exemplified by the preparation of the mixed uranium(VI) oxochloride complex.⁶⁶ The supramolecular compound (**21**), which is composed of the tetranuclear uranium aqua complex and cucurbit[6]uril (**5**), is formed through hydrogen bonding between the coordinated uranium atoms, water molecules and carbonyl oxygen atoms of the Q6 portals (Fig. 12).



In the crystals, the Q6 molecules and aqua complexes form alternating layers linked to each other through a system of hydrogen bonds. In the aqua complexes, the uranium atoms of four uranyl groups are virtually in a single plane.

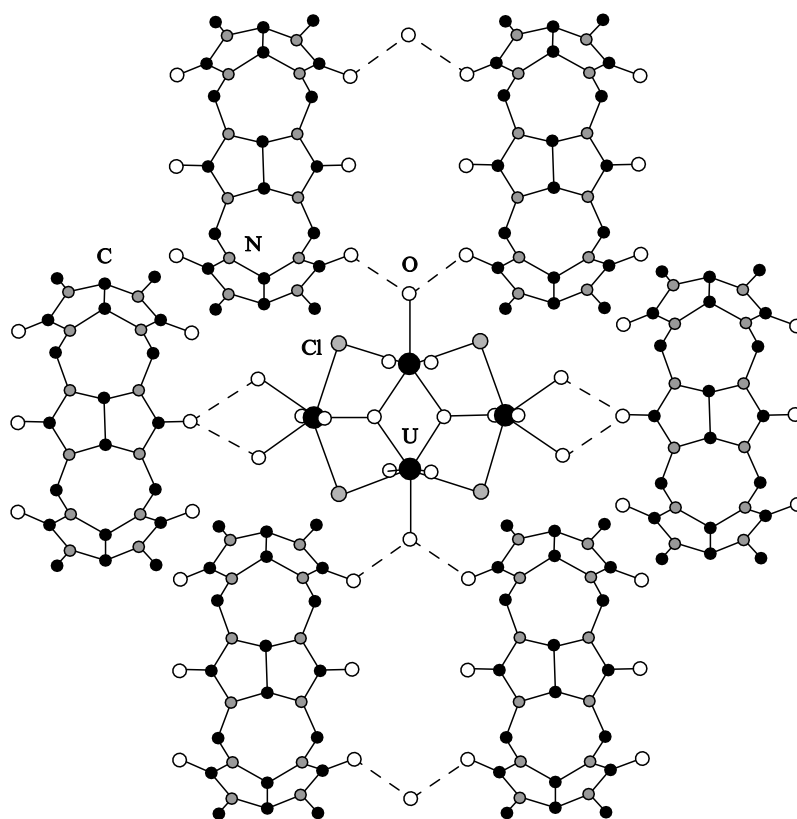
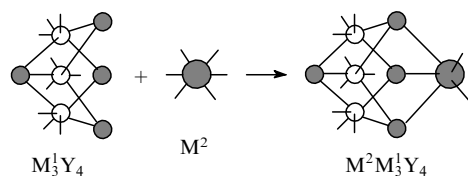


Figure 12. Fragment of the structure of the $\{[(\text{UO}_2)_4\text{O}_2\text{Cl}_4(\text{H}_2\text{O})_6](\text{C}_{36}\text{H}_{36}\text{N}_{24}\text{O}_{12})\} \cdot 5 \text{H}_2\text{O}$ compound (**21**).

By comparing the modes of binding of cucurbit[6]uril (**5**) to different metals, several conclusions can be made. Thus, the carbonyl oxygen atoms of the Q6 portals are directly coordinated to the metal atoms in supramolecular compounds with alkali, alkaline earth and rare-earth metals. These most electropositive metals have rather large ionic radii ($r_{\text{ion}} = 0.97, 1.73, 1.03$ and 1.14 Å for Na^+ , Cs^+ , Ca^{2+} and La^{3+} , respectively⁶⁷) and their binding to the ligands should be considered as Coulombic (ion–dipole) interactions. In these cases, cucurbit[6]uril, which is a weak donor but contains polarised C=O groups, competes with other ligands for site in the coordination sphere about the metal atom. Group 13 metal ions have smaller radii ($r_{\text{ion}} = 0.76$ and 0.50 Å for In^{3+} and Al^{3+} , respectively⁶⁷) and their binding to the ligands is predominantly covalent. The larger charges and smaller sizes of Group 13 metal cations lead to an increase in acidity of the coordinated water molecules of aqua ions. Consequently, the protons of the water molecules coordinated to these metal cations can form much stronger hydrogen bonds with the polarised C=O groups due to which the inclusion of water into the first coordination sphere is more favourable than the inclusion of Q6. If the metal–ligand interaction is predominantly Coulombic, Q6 competes with water for sites in the inner coordination sphere of the metal atom. If this interaction is predominantly covalent, the structure is determined primarily by a system of hydrogen bonds between the aqua ligands and cucurbit[6]uril (**5**) as the outer-sphere ligand.

IV. Supramolecular compounds of cucurbit[6]uril with metal cluster aqua complexes

The use of bulky fragments, which retain their geometry and can form extensive networks of hydrogen bonds due to a large contact surface, is an important condition for the directed construction of nanosized complexes or supramolecular compounds. Molybdenum and tungsten cluster aqua complexes are suitable large molecular building blocks for the construction of supramolecular compounds with cucurbit[6]uril (**5**). Studies of interactions of Q6 with trinuclear thio and seleno complexes of these metals and their heterometallic derivatives led to the discovery of a new class of supramolecular compounds. In aqueous solutions, cluster thio and seleno complexes of molybdenum and tungsten produce the stable trinuclear aqua ions $[\text{M}_3^{\text{I}}\text{Y}_4(\text{H}_2\text{O})_9]^{4+}$ ($\text{M}^{\text{I}} = \text{Mo}$ or W ; $\text{Y} = \text{S}$ or Se) in which the metal atoms are coordinated by one μ_3 -bridging chalcogen atom and three μ_2 -bridging chalcogen atoms.^{68–71} The coordinatively unsaturated μ_2 -bridging chalcogen atoms are readily coordinated to transition and post-transition metal atoms.⁷² In this case, the trinuclear cluster (a cube without one vertex) is transformed into the cubane complex $\text{M}^2\text{M}_3^{\text{I}}\text{Y}_4$ and the μ_2 -bridging chalcogen atoms are transformed into the μ_3 -bridging atoms.



$\text{M}^{\text{I}} = \text{Mo}, \text{W}$; M^2 is the transition or main-group metal atom;
 $\text{Y} = \text{S}, \text{Se}$.

Each M^{I} atom of the cluster core ($\text{M}_3^{\text{I}}\text{Y}_4$ or $\text{M}^2\text{M}_3^{\text{I}}\text{Y}_4$) is coordinated by three water molecules. Six water molecules are in *cis* positions with respect to the μ_3 -bridging chalcogen atom in the trinuclear aqua complexes or with respect to the μ_2 -bridging chalcogen atom, which links only the molybdenum (tungsten) atoms, in the cubane heterometallic complexes. These six aqua ligands are virtually in a single plane and are well suited in size and symmetry to six carbonyl groups at each portal of Q6. In addition, the cluster aqua complexes $[\text{M}_3^{\text{I}}\text{Y}_4(\text{H}_2\text{O})_9]^{4+}$ have rather high positive charges due to which they exhibit pronounced acidic

properties and act as good donors in hydrogen bonding, whereas the oxygen atoms of the polarised carbonyl groups of Q6 are potential acceptors. This geometric and functional (donor–acceptor hydrogen bond) complementarity gives rise to an extensive network of hydrogen bonds between the macrocycles and the triangular (cubane) aqua complexes. In spite of the fact that the energy of each individual hydrogen bond is low, the presence of a system of these bonds facilitates the formation of stable supramolecular compounds.

The use of Q6 for crystallisation of chalcogenide cluster aqua complexes made it possible for the first time to isolate and structurally characterise more than 20 supramolecular compounds. The compounds were crystallised by slow evaporation (in air) of solutions of cluster aqua complexes and Q6 in dilute hydrochloric acid. The resulting crystals are insoluble or weakly soluble in aqueous solutions of hydrochloric acid in which the starting reagents are readily soluble. If the cluster : cucurbit[6]uril ratio in supramolecular compounds is 1 : 1, only one portal of Q6 is closed by the cluster complex (structural type ‘barrel with one lid’). If the cluster : cucurbit[6]uril ratio is 2 : 1, both portals are closed (structural type ‘barrel with two lids’) (Fig. 13). The distances between the carbonyl oxygen atoms of the macrocycle and aqua ligands in both structural types vary in the range of 2.5–3.1 Å. If the lids are coordinated, the cavity of the cavitant

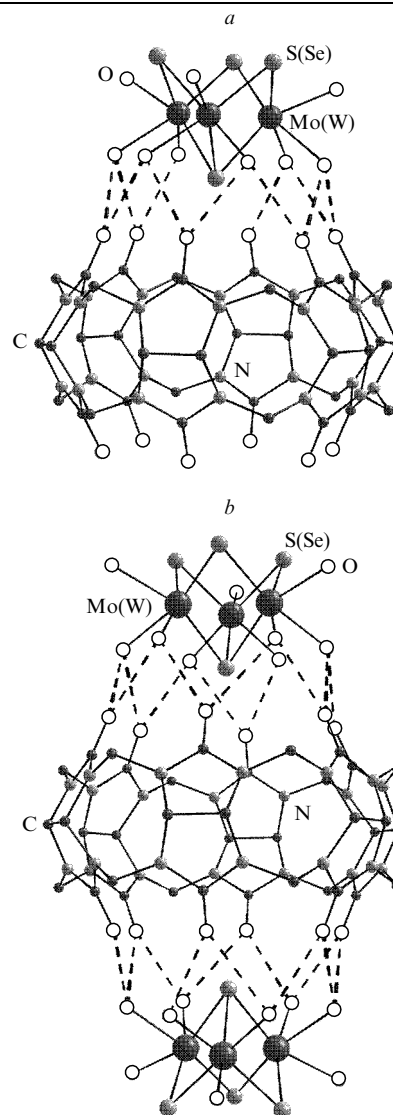


Figure 13. Supramolecular compounds of cucurbit[6]uril with metal cluster aqua complexes: (a) barrel with one lid; (b) barrel with two lids.

becomes isolated and small molecules can be held in the molecular container. The sizes of supramolecules closed by two lids are 25–30 Å.

A wide variety of available supramolecular compounds of Q6 with molybdenum and tungsten cluster aqua complexes is associated with the nature of the chalcogenide cluster, the presence of guests in solution and the concentration of hydrochloric acid in the aqueous solutions in which the reactions proceed.

The reactions of Q6 with the trinuclear tungsten sulfide aqua complex $[\text{W}_3\text{S}_4(\text{H}_2\text{O})_9]^{4+}$ in 2 M HCl afforded products with different compositions and structures depending on the presence of pyridine in the system. The supramolecule $\{[\text{W}_3\text{S}_4(\text{H}_2\text{O})_7\text{Cl}_2](\text{C}_{36}\text{H}_{36}\text{N}_{24}\text{O}_{12})\}\text{Cl}_2 \cdot 10 \text{H}_2\text{O}$ (**22**) belongs to the structural type 'barrel with one lid' in which only one portal of Q6 is closed by the cluster complex through a system of complementary hydrogen bonds between six carbonyl groups and six aqua ligands.⁷³ In the crystal, the supramolecules are linked in zigzag chains through additional hydrogen bonds between the aqua ligands of the cluster and the portal oxygen atoms of Q6 (Fig. 14).

Under the same conditions, the reaction performed in the presence of pyridine led to destruction of the chain structure to form the layered compound $\{[\text{W}_3\text{S}_4(\text{H}_2\text{O})_8\text{Cl}](\text{PyH}\cdot\text{C}_{36}\text{H}_{36}\text{N}_{24}\text{O}_{12})\}\text{Cl}_4 \cdot 10 \text{H}_2\text{O}$.

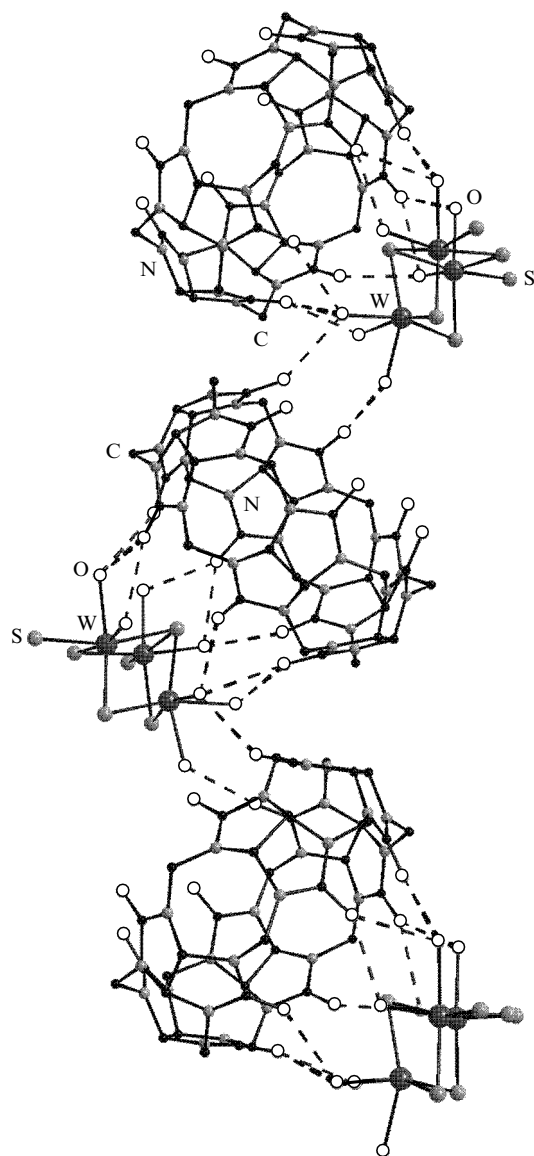
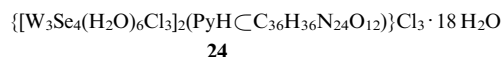
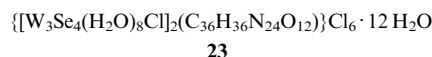


Figure 14. Fragment of the zigzag chain in $\{[\text{W}_3\text{S}_4(\text{H}_2\text{O})_7\text{Cl}_2](\text{C}_{36}\text{H}_{36}\text{N}_{24}\text{O}_{12})\}\text{Cl}_2 \cdot 10 \text{H}_2\text{O}$ (**22**).

$\text{C}_{36}\text{H}_{36}\text{N}_{24}\text{O}_{12})\}\text{Cl}_4 \cdot 10 \text{H}_2\text{O}$.⁷⁴ In this compound, the cavity of the Q6 molecule includes the pyridinium cation and both portals are closed by the trinuclear cluster complexes serving as the lids. In the crystal, these supramolecules are packed in layers. Upon the inclusion of the pyridinium cation into the cavity of Q6, both the guest and host molecules adapt to each other in size resulting in distortions of their structures. Thus, the Q6 molecule becomes slightly extended, whereas the pyridine molecule slightly contracts.

However, the inclusion of a guest does not necessarily lead to such dramatic changes in the structure and packing of supramolecules. The conditions of the preparation of selenium-containing tungsten complexes **23**⁷⁵ and **24**⁷⁶ with cucurbit[6]uril also differ only by the presence of pyridine in the reaction mixture.



Both compounds have chain structures in which the supramolecules of the structural type described as a barrel with two lids are linked to each other through short (compared to the sum of the van der Waals radii of 3.9 Å) nonbonded $\text{Se}\cdots\text{Se}$ interactions (3.59–3.72 Å). The cavity of cucurbit[6]uril in compound **24** contains the pyridinium cation (Fig. 15). The chalcogen–chalcogen

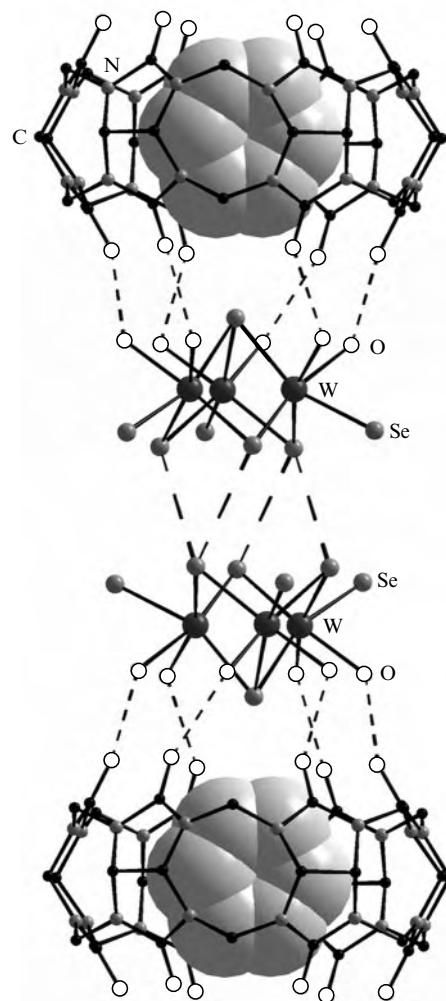


Figure 15. Fragment of the chain structure in $\{[\text{W}_3\text{Se}_4(\text{H}_2\text{O})_6\text{Cl}_3]_2(\text{PyH}\cdot\text{C}_{36}\text{H}_{36}\text{N}_{24}\text{O}_{12})\}\text{Cl}_3 \cdot 18 \text{H}_2\text{O}$ (**24**). The cavity of cucurbit[6]uril accommodates the pyridinium cation.

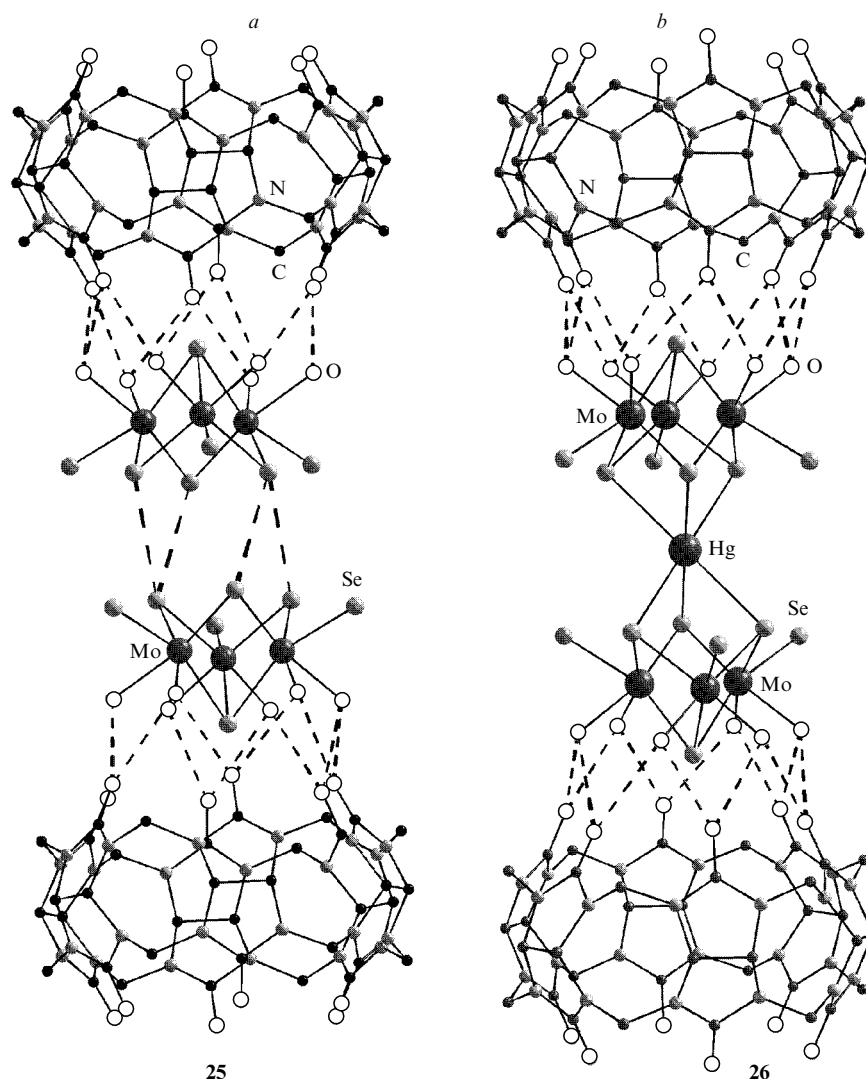
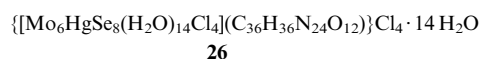
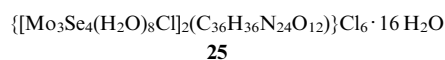


Figure 16. Comparison of the chain structures in $\{[\text{Mo}_3\text{Se}_4(\text{H}_2\text{O})_8\text{Cl}]_2(\text{C}_{36}\text{H}_{36}\text{N}_{24}\text{O}_{12})\}\text{Cl}_6 \cdot 16 \text{H}_2\text{O}$ (**25**) (matrix) and $\{[\text{Mo}_6\text{HgSe}_8(\text{H}_2\text{O})_{14}\text{Cl}_4](\text{C}_{36}\text{H}_{36}\text{N}_{24}\text{O}_{12})\}\text{Cl}_4 \cdot 14 \text{H}_2\text{O}$ (**26**) (intercalate).

gen interactions between adjacent clusters typical of trinuclear chalcogenide clusters of transition metals are of importance in the structure formation of these complexes.⁷⁷ The stronger bonding between the selenide atoms ($\text{Se} \cdots \text{Se}$) as compared to that between the sulfur atoms ($\text{S} \cdots \text{S}$) [according to the structural data available in the Cambridge Structural Database for $\{\text{M}_3\text{Y}_4 \cdots \text{Y}_4\text{M}_3\}$ compounds, where $\text{Y} = \text{Se}$ or S (see Ref. 78)] facilitates the retention of chain structures of the supramolecular compounds of Q6 with selenium-containing tungsten clusters upon the inclusion of a guest molecule. The structures of the selenium-containing complexes differ only by the mode of packing of the chains. In the crystal of compound **23**, the chains are packed to form a hexagonal motif, whereas these chains in the crystal of compound **24** form a distorted square packing.

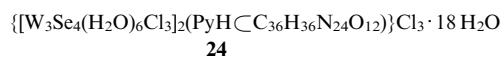
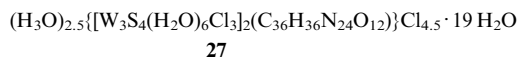
The chalcogen–chalcogen interactions between the adjacent cluster fragments M_3Y_4 of supramolecular compounds are analogous to interactions between the adjacent layers formed by the chalcogen atoms in the layered transition metal dichalcogenides MY_2 ($\text{Y} = \text{S}, \text{Se}$).⁷⁵ An important property of the layered compounds is their ability to incorporate molecules or atoms between the layers giving rise to intercalates. A comparison of the structures of chain supramolecular compounds **25**⁷⁸ and **26**^{75, 79} shows that these compounds are regarded as a matrix and intercalate from the structural viewpoint. Thus, the mercury atom is included between the chalcogenide clusters M_3Y_4 , the

principal parameters of the supramolecules remaining virtually unchanged (Fig. 16).



Therefore, the chemistry of supramolecular compounds of chalcogenide clusters is related to the chemistry of layered compounds more closely than one would expect. In both cases, the nonbonded chalcogen–chalcogen interactions play an important role in the structure formation.

Yet another important factor that has an effect on the formation of supramolecular compounds of Q6 with metal cluster aqua complexes is the concentration of hydrochloric acid in dilute solutions in which these reactions proceed. In solutions of HCl , cluster aqua complexes give different mixed chloro aqua complexes $[\text{M}_3\text{Y}_4(\text{H}_2\text{O})_{9-x}\text{Cl}_x]^{(4-x)+}$ ($\text{Y} = \text{Se}, \text{S}$) whose compositions depend on the nature of the metal and chalcogen atoms. As demonstrated above, six *cis*-aqua ligands of the cluster are involved in complementary binding in the compounds of Q6 with Mo and W aqua complexes, whereas up to three Cl^- anions can be located in *trans* positions (for example, in the supramolecular compounds **27**⁸⁰ and **24**).⁷⁶



An increase in the concentration of hydrochloric acid leads to the replacement of the water molecules in aqua complexes by the halide ligands resulting in a sharp weakening of the cluster–cucurbit[6]uril interaction. First, the cluster complex loses a positive charge, *i.e.*, its acidity and ability to act as a donor in hydrogen bonding are decreased. Second, coordination of more than four Cl^- ligands to the cluster core requires the replacement of the *cis*-aqua ligands responsible for binding of the cluster complex to the portals of the macrocycle. Here, crystallisation of a particular form depends on other factors ($\text{Y} \cdots \text{Y}$ interactions, packing factors, *etc.*). Therefore, cucurbit[6]uril in HCl solutions acts as an outer-sphere ligand with respect to the cluster complex and forms hydrogen bonds only with some of the possible forms of $[\text{M}^3\text{Y}_4(\text{H}_2\text{O})_{9-x}\text{Cl}_x]^{(4-x)+}$.

The latter assumption is exemplified by the data on the structure of the $(\text{H}_3\text{O})_2[\text{Mo}_3\text{Se}_4(\text{H}_2\text{O})_4\text{Cl}_5]_2(\text{C}_{36}\text{H}_{36}\text{N}_{24}\text{O}_{12}) \cdot 15 \text{H}_2\text{O}$ compound (**28**) prepared from a 6 M HCl solution.⁷⁸ This compound contains triangular clusters in the $[\text{Mo}_3\text{Se}_4(\text{H}_2\text{O})_4\text{Cl}_5]^-$ anionic form. Unlike the chain compound **25** (see Fig. 16), which crystallises from a 2 M HCl solution and contains only one chloride ion per trinuclear cluster, the Mo atoms in the compound **28** are coordinated by three or four Cl^- ligands in *cis* positions with respect to μ_3 -Se. As a consequence, the Q6 molecules and the chloro aqua complexes are not involved in a system of complementary hydrogen bonds. The chloro aqua complexes are linked in the dimeric cluster aggregates $\{\text{Mo}_3\text{Se}_4(\text{H}_2\text{O})_4\text{Cl}_5\}_2^{2-}$ through short nonbonded Se $\cdots$ Se interactions. In the crystals, these dimers are packed in layers, which alternate with layers consisting of Q6 molecules.

Analogous dimers are present in the isostructural $(\text{H}_3\text{O})_4\{[\text{M}_3\text{S}_7\text{Cl}_6]_2(\text{C}_{36}\text{H}_{36}\text{N}_{24}\text{O}_{12})\} \cdot 8 \text{H}_2\text{O}$ compounds (**29**, $\text{M} = \text{Mo}$ or W).⁸¹ The $[\text{M}_3\text{S}_7]^{4+}$ cluster core in which the metal atoms are coordinated by the μ_3 -S ligand and three disulfide ligands μ_2 -S₂ exhibits a much higher affinity for halide ions than the $[\text{M}_3\text{S}_4]^{4+}$ core.⁸² In a 3 M HCl solution, each metal atom is coordinated by two chloride ligands due to which hydrogen bonding with Q6 becomes impossible. In this case, the structure formation depends primarily on nonbond S $\cdots$ S interactions between the bridging atoms of the disulfide ligands resulting in dimerisation of the $[\text{M}_3\text{S}_7\text{Cl}_6]^{2-}$ anions. The crystal packing consists of alternating layers of dimeric cluster anions and Q6 molecules.

The heterometallic molybdenum and tungsten aqua complexes $[\text{L}_m\text{M}'\text{M}_3\text{Y}_4(\text{H}_2\text{O})_9]^{n+}$ ($\text{Y} = \text{Se}$ or S) also interact with cucurbit[6]uril to give supramolecular adducts belonging to ‘barrels with one lid’ or ‘barrel with two lids’. In these aqua complexes, the bridging chalcogen atoms are coordinated to the transition and post-transition metal atoms and lose the ability to be involved in nonbonded $\text{Y} \cdots \text{Y}$ interactions. In the crystals, the supramolecules of heterometallic aqua complexes with cucurbit[6]uril are linked either in chains through additional hydrogen bonds, as in compounds **30**⁸³ and **31**⁸⁴ (Fig. 17), or in layers, as in supramolecular compound **32**.⁸⁵

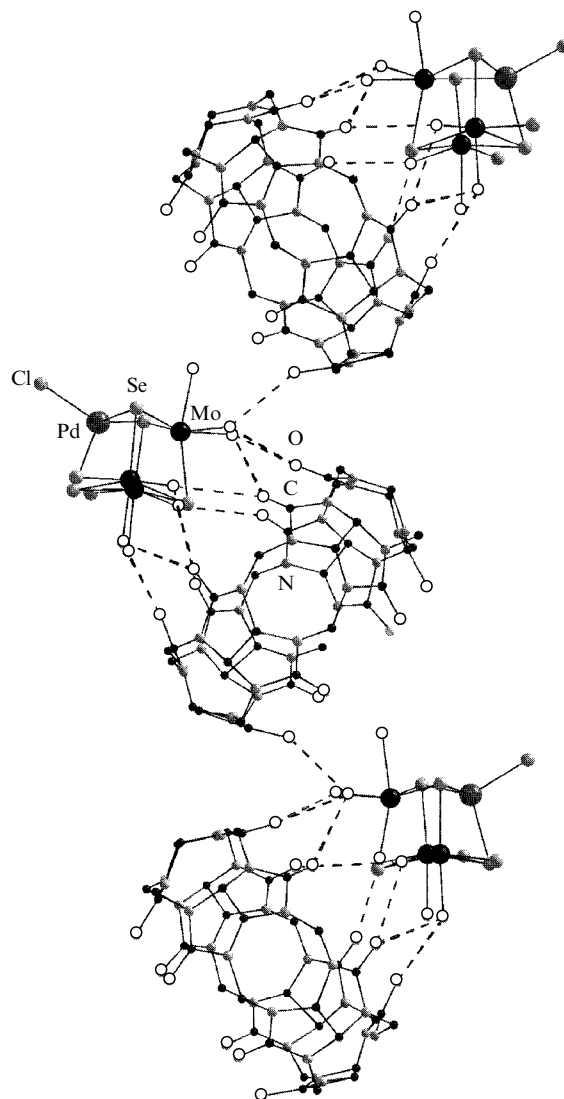
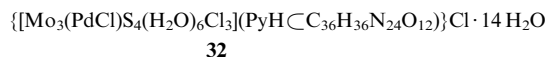
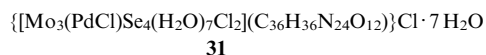


Figure 17. Fragment of the zigzag chain in $\{[\text{Mo}_3(\text{PdCl})\text{Se}_4(\text{H}_2\text{O})_7\text{Cl}_2](\text{C}_{36}\text{H}_{36}\text{N}_{24}\text{O}_{12})\}\text{Cl} \cdot 7 \text{H}_2\text{O}$ (**31**).

From a comparison of compounds **31** and **32** in which only one portal of the macrocycle is closed by the cluster lid, it follows that the inclusion of the pyridinium cation into the cavity of Q6 does not lead to substantial changes in the structures of the supramolecules, *i.e.*, not only the cluster:cucurbit[6]uril ratio but also the total charge (+1) remain unchanged. Only the crystal packing undergoes essential changes. The supramolecules **31** form zigzag chains through hydrogen bonds between the aqua ligands of the cluster and the oxygen atoms at the portals of Q6 of the adjacent adduct, whereas the addition of pyridine gives rise to dimers packed in layers.

The use of Q6 for crystallisation of the reaction products of the palladium complex $[\text{Mo}_3(\text{PdCl})\text{S}_4(\text{H}_2\text{O})_9]^{3+}$ with P(III)- or As(III)-containing *n*-donor ligands made it possible to prepare and structurally characterise the $\{[\text{Mo}_3(\text{PdE}(\text{OH})_3)\text{S}_4(\text{H}_2\text{O})_6\text{Cl}_3]_2 \cdot (\text{C}_{36}\text{H}_{36}\text{N}_{24}\text{O}_{12})\}\text{Cl}_2 \cdot n \text{H}_2\text{O}$ compounds [$\text{E} = \text{P}$, $n = 20$ (**33a**); $\text{E} = \text{As}$, $n = 19$ (**33b**)].⁸⁶ In these compounds, the Q6 molecules are closed by two cluster lids. The palladium atoms of these clusters are coordinated by the inorganic $\text{P}(\text{OH})_3$ or $\text{As}(\text{OH})_3$ ligands (Fig. 18). These are the first examples of the structurally characterised tribasic forms of phosphorous and arsenous acids.

Heterometallic indium- and tin-containing supramolecular compounds of cucurbit[6]uril **34**⁸⁷ and **35**⁷⁸ belong to the structural type described as ‘barrels with two lids’.

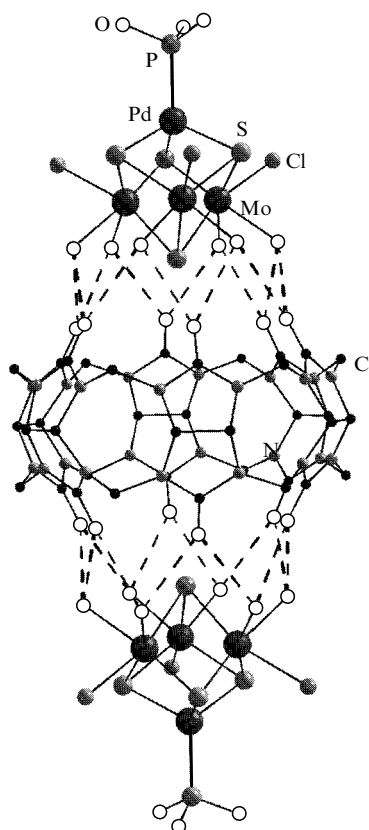
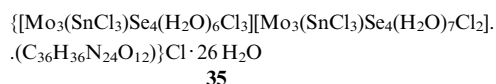
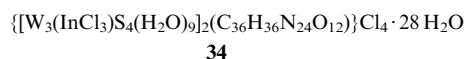


Figure 18. Structure of the supramolecule $\{[\text{Mo}_3(\text{PdP}(\text{OH})_3)\text{S}_4(\text{H}_2\text{O})_6\text{Cl}_3]_2(\text{C}_{36}\text{H}_{36}\text{N}_{24}\text{O}_{12})\}^{2+}$ (**33a**).



Among the characteristic features of the crystal structure of the compound **34**, noteworthy are large channels (~ 7 Å in diameter) occupied by water molecules of solvation and Cl^- counterions. Crystallisation of the tin-containing molybdenum aqua complex with Q6 made it possible for the first time to isolate and structurally characterise the mixed chloro aqua complexes $[\text{Mo}_3(\text{SnCl}_3)\text{Se}_4(\text{H}_2\text{O})_6\text{Cl}_3]$ and $[\text{Mo}_3(\text{SnCl}_3)\text{Se}_4(\text{H}_2\text{O})_7\text{Cl}_2]^+$.

Hence, as a result of the good compatibility of the sizes and symmetry of the carbonyl groups at the portals of Q6 with those of the aqua ligands of the triangular (cubane) molybdenum and tungsten chalcogenide aqua complexes, extensive networks of hydrogen bonds are formed and the macrocycle becomes efficiently closed by the cluster lids.

As in the case of the thio and seleno analogues, the trinuclear molybdenum oxo cluster $[\text{Mo}_3\text{O}_4]^{4+}$ also interacts with Q6 through hydrogen bonds to give the supramolecular compound $\{[\text{Mo}_3\text{O}_4(\text{H}_2\text{O})_6\text{Cl}_3]_2(\text{C}_{36}\text{H}_{36}\text{N}_{24}\text{O}_{12})\}\text{Cl}_2 \cdot 14 \text{H}_2\text{O}$ (**36**). In this compound, the portals are closed by two lids formed by the cluster cations (Fig. 19).⁸⁸ However, unlike the compounds of Q6 with chalcogenide complexes, the plane of the Mo_3 triangle in the supramolecule **36** is tilted to the plane of the portal of the macrocycle (the tilting angle is 18.5°) and the cluster cation is shifted to one end of the portal resulting in the nonequivalence of the hydrogen bonds that are formed. These differences in the structures are attributed to the smaller size of the oxo cluster as compared to the sizes of the chalcogenide clusters and also to the higher acidity of the oxo complex.

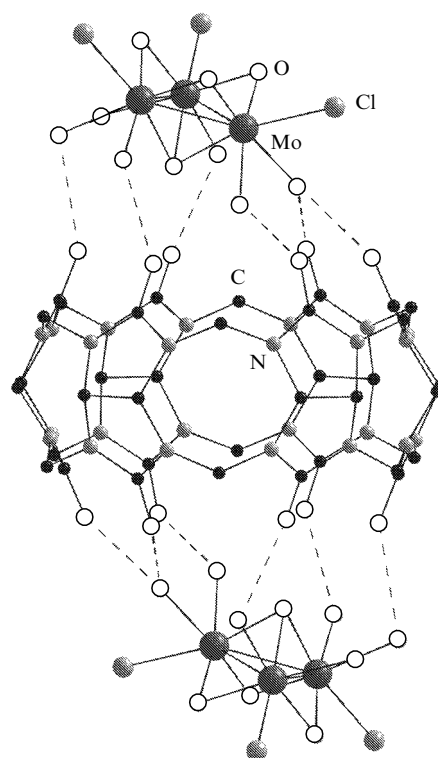


Figure 19. Structure of the supramolecule $\{[\text{Mo}_3\text{O}_4(\text{H}_2\text{O})_6\text{Cl}_3]_2(\text{C}_{36}\text{H}_{36}\text{N}_{24}\text{O}_{12})\}^{2+}$ (**36**).

In the compound of Q6 with the binuclear niobium aqua complex $\{[\text{Nb}_2\text{S}_4(\text{H}_2\text{O})_8](\text{C}_{36}\text{H}_{36}\text{N}_{24}\text{O}_{12})\}\text{Cl}_4 \cdot 15 \text{H}_2\text{O}$ (**37**) (Fig. 20),⁸⁹ the portal of cucurbit[6]uril is incompletely closed by

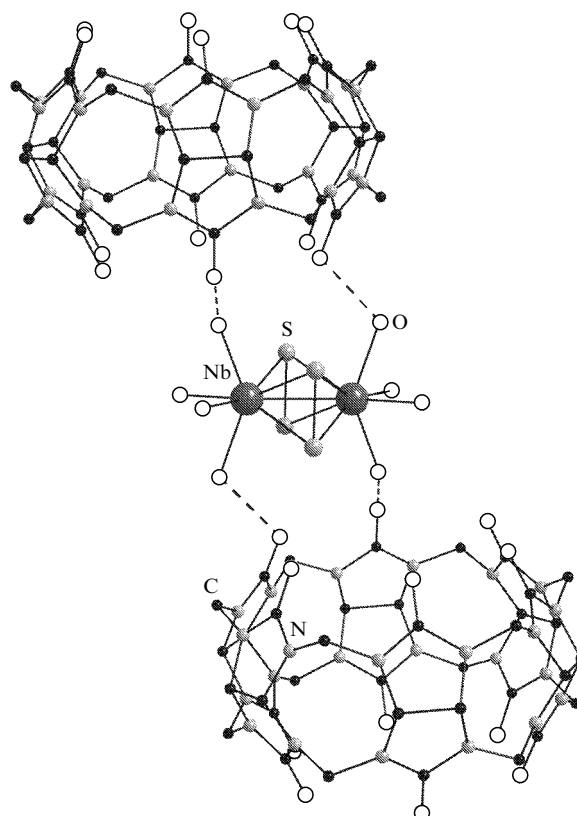


Figure 20. Fragment of the chain structure in $\{[\text{Nb}_2\text{S}_4(\text{H}_2\text{O})_8](\text{C}_{36}\text{H}_{36}\text{N}_{24}\text{O}_{12})\}\text{Cl}_4 \cdot 15 \text{H}_2\text{O}$ (**37**).

the binuclear cluster and the latter is shifted to one end of the portal because of spatial incompatibility. In this case, only two water molecules *trans*-coordinated to the niobium atom are bound directly to the portal oxygen atoms of two Q6 molecules. Several more water molecules present in the hydrophilic region of the portals are involved in additional hydrogen bonds between the aqua complex and macrocycle. In the crystal, the alternating cluster niobium aqua complexes and Q6 molecules are linked in chains.

V. Cucurbit[*n*]urils (*n* = 5, 7–10)

In addition to the above-considered macrocyclic cavitand cucurbit[6]uril (**5**) consisting of six methylene-bound glycoluril fragments, there are also cucurbiturils, which are composed of a smaller or larger number of these fragments and have the shape of barrels with smaller or larger diameters.

Crystals of the cyclic pentamer were first prepared by the reaction of dimethylglycoluril with formaldehyde and structurally characterised in 1992.⁹⁰ The decamethylcucurbit[5]uril has a slightly distorted symmetry D_{5h} and its methyl groups are located at the periphery of the molecule. In the cited study, the nomenclature for cucurbiturils was proposed by analogy with that used for calixarenes. According to this nomenclature, the number of glycoluril (or substituted glycoluril) fragments is denoted by the figure in brackets and the number of substituents is represented by the prefix.

In 2000, K Kim and co-workers⁹¹ performed the reaction of glycoluril with formaldehyde in 9 M sulfuric acid and obtained a mixture of cyclisation products (*n* = 5–11) from which five-, seven- and eight-membered homologues of cucurbituril were isolated in very low yields. These compounds were structurally characterised. A comparison of their structural parameters (Table 1) demonstrates that the diameters of the cavity and portals of cucurbiturils increase as the number of glycoluril fragments in the rings is increased. A twofold increase in the inner diameter of the cavity on going from cucurbit[5]uril to cucurbit[8]uril leads to more than a fivefold increase in the volume of the cavity.

Table 1. Comparison of the structural parameters of cucurbit[*n*]urils.

Cucurbit[<i>n</i>]uril	Portal diameter /Å	Cavity diameter /Å	Cavity volume /Å ³	Molecule height /Å
<i>n</i> = 5	2.4	4.4	82	9.1
<i>n</i> = 6	4.0	5.5	164	9.1
<i>n</i> = 7	5.4	7.3	279	9.1
<i>n</i> = 8	6.9	8.8	479	9.1

Day *et al.*⁹² studied the reactions of glycoluril with formaldehyde in H₂SO₄, HCl or HBF₄ solutions by electrospray mass spectrometry and ¹³C NMR spectroscopy and established the existence of cucurbit[*n*]urils with *n* = 5–16 in solution. Based on the results of investigations into the effects of the nature of acid and its concentration, the concentrations of other reagents and the reaction temperature, a mechanism for the formation of different cucurbit[*n*]urils was proposed and the procedure for their synthesis optimised. Cucurbit[*n*]urils with *n* = 5–10 were isolated in pure form (the yields were 8%, 46%, 24%, 12%, 85% and 5%, respectively). Individual cucurbit[*n*]urils with larger numbers of glycoluril fragments are presently unavailable.

According to the results of theoretical calculations (density functional theory),⁹³ compounds containing six or seven glycoluril fragments are the most stable homologues of cucurbiturils, and decamethylcucurbit[5]uril is the most stable methyl-substituted derivative. These results agree with both the above-described experimental data and the distortions of the NCN

angles at the carbon atoms of the bridging methylene groups that link the glycoluril fragments upon assembly.

As demonstrated above (see Section II), the presence of the hydrophobic cavity along with the polarised carbonyl groups at the portals of cucurbit[6]uril (**5**) are responsible for the formation of numerous inclusion compounds. The smaller cavity in cucurbiturils allows small molecules to be encapsulated and securely held, whereas larger-size molecular containers can accommodate bulkier guest molecules. Besides, an increase in the number of the oxygen atoms at the portals is favourable for the formation of a large number of hydrogen bonds and, correspondingly, more stable supramolecular compounds.

Decamethylcucurbit[5]uril can accommodate a molecule of nitric acid. Due to the fact that the molecular size of nitric acid matches the volume of the cavity, this guest molecule can form rather short contacts and be held in the cavity through both Coulombic interactions with the carbon atoms and hydrogen bonding with the carbonyl oxygen atoms of the macrocycle.⁹⁰ It was proved by electrospray mass spectrometric study of the ammonium acetate–decamethylcucurbit[5]uril system that the N₂, O₂, methanol and acetonitrile molecules can be included into the cavity, held in the cavity through the formation of the NH₄⁺ lids and released upon the removal of these lids. This ability of the rather rigid macrocycle to accommodate small molecules is of interest for purification or separation of gas mixtures.⁹⁴

The cavity volume of cucurbit[5]uril is insufficient for the inclusion of aromatic molecules. However, according to the data from solution ¹H NMR spectroscopy, the reaction with aliphatic hexylamine afforded an inclusion compound.⁹⁵ Hexylamine and 1,6-diaminohexane are not encapsulated into decamethylcucurbit[5]uril. According to the results of X-ray diffraction analysis, the terminal ammonium groups of 1,6-diaminohexane are involved in hydrogen bonds with the portal oxygen atoms of the adjacent macrocycles to form chains.

The water solubility of cucurbit[5]uril and decamethylcucurbit[5]uril as well as the solubility of cucurbit[6]uril are substantially increased upon the addition of salts of ammonium, alkali and alkaline earth metals due to formation of complexes with cations,⁹⁶ decamethylcucurbit[5]uril giving alkali metal complexes with composition 1 : 1.⁹⁷ Cucurbit[5]uril and decamethylcucurbit[5]uril serve as ligands in transition metal complexes (M²⁺ and M³⁺). The formation constants of these complexes were determined by different experimental methods.⁹⁸ It has been also reported that decamethylcucurbit[5]uril in solution exhibits high selectivity toward Pb²⁺ cations.⁹⁷ No compounds of cucurbit[5]urils with metal cations have been structurally characterised.

Due to the larger cavity volumes in cucurbiturils consisting of seven or eight glycoluril fragments, these compounds can encapsulate bulky molecules whose sizes are too large to be included into compounds of Q6. Thus, Q7 forms inclusion compounds with *o*-carborane,⁹⁹ with the 2,3-diazabicyclo[2.2.2]oct-2-ene molecule, whose size matches excellently the cavity size and fills virtually the entire cavity resulting in a stable supramolecular compound.¹⁰⁰

The cavity sizes of cucurbit[*n*]urils (*n* = 8, 10) allows smaller macrocycles to be included giving rise to rather rare compounds. Heating of an aqueous solution of Q8 with 1,4,7,10-tetraazacyclododecane (cyclen) and 1,4,8,10-tetraazacyclotetradecane (cyclam) afforded inclusion compounds, which have been structurally characterised. These compounds are stabilised primarily through van der Waals interactions between the inner macrocycle and the cavity of the outer macrocycle.¹⁰¹ The small and large macrocycles are inclined to one another (the angle between the equatorial planes is ~38°). The ability of tetraazamacrocycles to coordinate transition metal ions (these complexes are known as catalysts, for example, of epoxidation or DNA hydrolysis) was used in the reactions of the resulting inclusion compounds with Cu²⁺ and Zn²⁺ salts. The compound containing [Cu(cyclen). (H₂O)]²⁺ in the cavity of Q8 was studied by X-ray diffraction analysis. In this compound, the macrocycles are virtually parallel to each other (Fig. 21) and the copper atom present in the inner

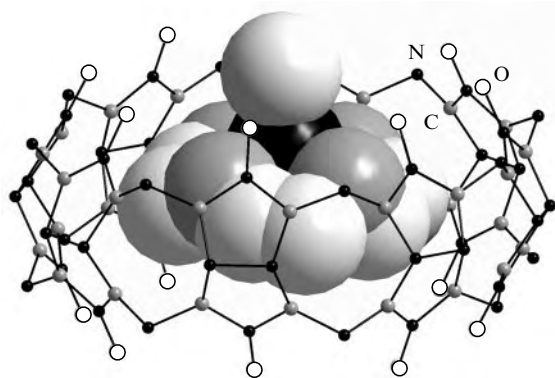


Figure 21. Structure of the compound containing $[\text{Cu}(\text{cyclen})(\text{H}_2\text{O})]^{2+}$ in the cavity of cucurbit[8]uril. The copper atom is represented by a large solid circle.

macrocycle additionally coordinates the water molecule, which is located in the plane of the portal of Q8 and can be replaced by other ligands. It should be noted that the cyclen coordinated by the metal atom is not encapsulated into cucurbit[8]uril because the formation of the complex with the metal atom enhances its conformational rigidity and hinders its inclusion into the cavity of Q8.

Recently, the unique compound of cucurbit[5]uril encapsulated into cucurbit[10]uril was prepared and characterised by X-ray diffraction analysis (Fig. 22).¹⁰² The molecules of the macrocycles are inclined to each other (the angle between their equatorial planes is 64°). This fact along with the ^1H and ^{13}C NMR spectroscopic data provide evidence that the macrocycles in solution undergo free rotation with respect to each other (molecular analogue of a gyroscope). The cavity of Q5 contains the chloride anion and there is a system of hydrogen bonds between the portal oxygen atoms of both macrocycles and water molecules serving as the lids of the inner pentamer (see Fig. 22). It is believed that Q5 serves as a template for the assembly of larger-size cucurbiturils. Cucurbituril Q10 is as yet unavailable as an individual compound.

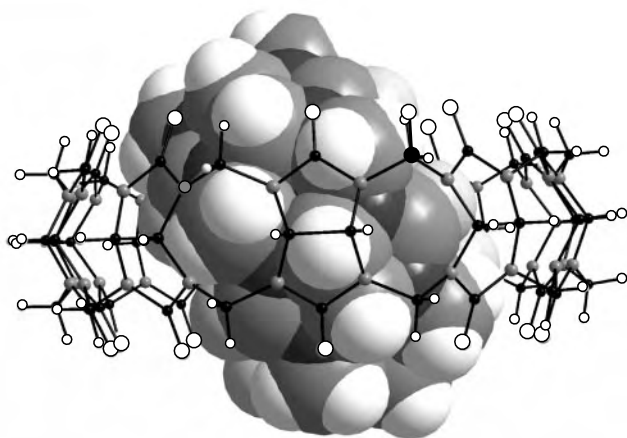


Figure 22. Structure of the inclusion compound of cucurbit[5]uril in cucurbit[10]uril.

A compound of cucurbit[7]uril was prepared in which the inorganic *cis*- $[\text{SnCl}_4(\text{OH}_2)_2]$ complex is completely encapsulated in the cavity of the macrocycle.^{103, 104} A compound of Q7 with the trinuclear anionic chromium complex $[\text{Cr}_3\text{O}_{10}]^{2-}$ has been synthesised. In this compound, the molecules of the macrocycle are linked in hexagons to form large pores with a diameter of $\sim 17 \text{ \AA}$. The Q7 molecules, trinuclear anions and coordinated water

molecules are linked through an extensive network of hydrogen bonds.¹⁰⁴

Like cucurbit[6]uril, larger macrocycles form stable inclusion compounds with organic molecules whose protonated nitrogen atoms are linked to the polarised oxygen atoms at the portals through Coulombic interactions. Due to the larger sizes of the cavities, such bulky molecules as 2,6-bis(4,5-dihydro-1*H*-imidazol-2-yl)naphthalene can be accommodated in these macrocycles. Inclusion compounds with compositions 1:1 and 2:1 were prepared with cucurbit[7]uril and cucurbit[8]uril, respectively.⁹¹ The results of quantum-chemical calculations (density functional theory) of the former compound demonstrated that not only van der Waals interactions and the hydrophobic effect but also hydrogen bonding between the protonated dihydroimidazole substituents and the portal oxygen atoms of Q7 play an important role in the formation of inclusion compounds.¹⁰⁵ Two such bulky molecules are located in an even larger inner cavity of Q8. According to the X-ray diffraction data, the imidazole substituents are located outside and are bound to the portals of Q8. Two naphthalene rings within the cavity are located parallel to each other at a distance of $\sim 3.4 \text{ \AA}$, which is indicative of π - π interactions between these rings (Fig. 23).⁹¹

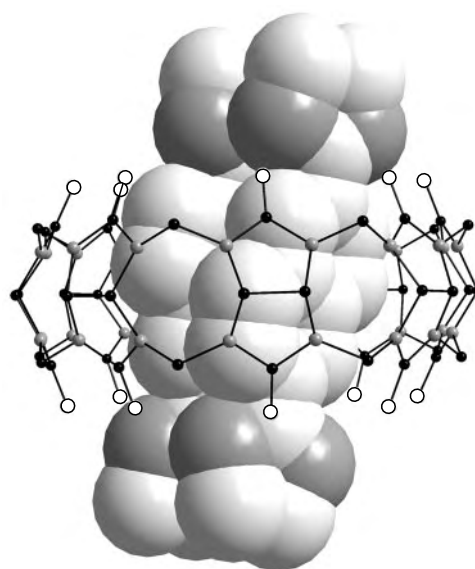
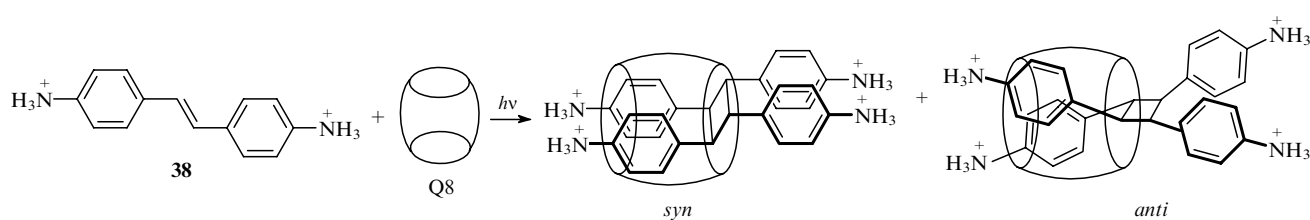


Figure 23. Structure of the inclusion compound of two 2,6-bis(4,5-dihydro-1*H*-imidazol-2-yl)naphthalene molecules in cucurbit[8]uril.

The encapsulation of two or more guest molecules into the cavity of the macromolecule is of great interest in view of the unique possibility of studying new types of stereoisomerism, bimolecular reactions and the behaviour of the molecules in the microenvironment. The Q8 molecule possessing a very large cavity provides rich possibilities for investigating such interactions.

K Kim and co-workers¹⁰⁶ were the first to study the selective encapsulation of two different guests into the cavity of one host. Interactions between two guests are the driving forces for the formation of supramolecular compounds. Two organic molecules, *viz.*, the electron-deficient molecule **A** and molecule **B** acting as the electron donor, are accommodated in the cavity of Q8 [**A** is the *N,N'*-dimethyl-4,4'-bipyridinium cation (methylviologen $\text{MeN}^+\text{C}_{10}\text{H}_8\text{N}^+\text{Me}$) and **B** is 2,6-dihydroxynaphthalene or 1,4-dihydroxybenzene]. It should be noted that inclusion compounds with only either molecules **A** or molecules **B** were not obtained. The data from ^1H NMR, emission and UV spectroscopy are unambiguously indicative of strong charge-transfer interactions between the guest molecules due to their tight contact within the cavity. This interaction is much stronger than the interaction

Scheme 2



between these guest molecules if they are not encapsulated in the cavity of the cavitand. The resulting inclusion compounds are rather stable, which enables one to isolate and structurally characterise these compounds. For instance, the structure of the compound of Q8 with the unsymmetrical guest, *viz.*, the cation of carboxybenzylviologen $\text{CH}_3\text{N}^+\text{C}_{10}\text{H}_8\text{N}^+\text{CH}_2\text{C}_6\text{H}_4\text{CO}_2\text{H}$, was established by X-ray diffraction analysis (Fig. 24). The methylpyridine fragment of this cation and the naphthalene ring of 2,6-dihydroxynaphthalene serving as the electron donor are located in the cavity virtually parallel to each other at a distance of 3.4 Å. This confirms the occurrence of a strong interaction, which was found by spectroscopic methods.

The ability of cucurbit[8]uril to accommodate two closely spaced guests located in particular orientations allows one to use this compound as the synthetic molecular container in which bimolecular reactions between specially selected guests can proceed with high regio- and stereoselectivity. Thus, photodimerisation between two molecules of 4,4'-diammonio-1,1'-stilbene dichloride (**38**) encapsulated into the cavity of Q8 proceeded with a much higher rate and high stereoselectivity (0.5 h, the ratio *syn* : *anti* > 95 : 5) as compared, for example, with this reaction in the presence of γ -cyclodextrin (72 h, the ratio *syn* : *anti* ~ 4 : 1).¹⁰⁷ According to the ¹H NMR spectroscopic data, Q8 forms a stable inclusion compound with two molecules **38** in solution even if the starting reagents are taken in a ratio of 1 : 1. In this case, the guests can occupy only particular positions, *viz.*, with the parallel orientation of the alkene groups involved in photodimerisation (Scheme 2).

Owing to rather rigid structures and the ability to include various molecules and ions, cucurbiturils are very attractive compounds both as synthetic receptors and convenient building

blocks for the construction of supramolecular materials. The detailed study of supramolecular compounds based on the known cucurbiturils is hindered, in particular, by their very low solubilities in water and organic solvents. Because of this, the most promising line of investigation of the chemistry of these compounds is the development of procedures for the preparation of soluble derivatives by the insertion of substituents containing different functional groups. One approach to the solution of this problem involves the synthesis of cucurbiturils by condensation of substituted glycolurils whose bridging CH groups contain either alkyl or aryl substituents instead of hydrogen atoms. However, decamethylcucurbit[5]uril containing peripheral methyl groups, which was synthesised from dimethylglycoluril,⁹⁰ also appeared to be a poorly soluble compound. The synthesis of cucurbiturils consisting of five or six cyclohexanoglycoluril fragments¹⁰⁸ is the first success after years of failed attempts. The resulting compounds were reliably characterised by different methods, among them X-ray diffraction analysis. The cyclohexane fragments formed by two carbon atoms of glycoluril and four methylene units are located at the periphery of cucurbiturils. The sizes of the cavities and portals are only slightly different from those in the unsubstituted analogues. These compounds are readily soluble in water, methanol and DMSO and moderately soluble in ethanol, DMF and acetonitrile. Good solubility in organic solvents enables one to use cyclohexanocucurbit[*n*]urils (*n* = 5, 6) as membrane ion-selective electrodes. Cyclohexanocucurbit[6]uril dissolved in water can be used for highly selective isolation of acetylcholine (neurotransmitter).¹⁰⁸

* * *

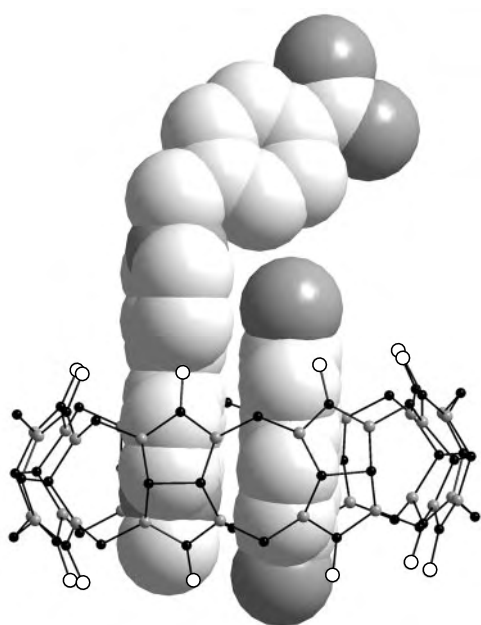


Figure 24. Encapsulation of 'heteroguests', *viz.*, electron-deficient (carboxybenzylmethylviologen) and electron-donating (2,6-dihydroxynaphthalene) molecules in cucurbit[8]uril.

To summarise, the recent advances in the chemistry of cucurbiturils surveyed in the present review provide evidence that these macrocyclic organic molecules can be considered as molecular building blocks for the directed construction of nanosized highly ordered supramolecular compounds. The advantages of cucurbiturils over other macrocyclic cavitands are the presence of a rather rigid hydrophobic inner cavity along with hydrophilic portals, which can form supramolecular compounds with metal aqua complexes through systems of hydrogen bonds. Large cucurbit[*n*]urils (*n* = 7–10), which became readily available in recent years, show considerable promise. Thus, large molecular containers can encapsulate bulkier guests, and the inclusion of two or more molecules provides a unique possibility for studying new types of stereoisomerism, bimolecular reactions and molecular behaviour in a microenvironment. This review will hopefully be found interesting and useful and contribute to the progress of the chemistry of cucurbiturils.

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Proton-conducting electrolyte membranes based on aromatic condensation polymers

A L Rusanov, D Yu Likhatchev, K Müllen

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Abstract. The results of investigations in the field of development and applications of proton-conducting electrolyte membranes based on aromatic condensation polymers are analysed and summarised. Primary attention is paid to the properties of the starting polymers, such as the thermal stability, water uptake and proton conductivity. General approaches to the preparation of aromatic condensation polymers with high proton conductivity are considered, including sulfonation, synthesis from monomers containing sulfonic acid groups, incorporation of alkylsulfonated substituents and formation of acid–base polymer complexes. The bibliography includes 115 references.

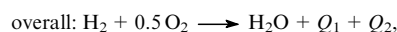
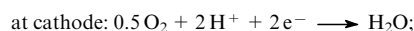
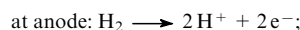
I. Introduction

Advanced technologies of the 21st century are thought to be associated with wide use of fuel cells that allow fuels to be utilised in the fuel cell based engines with much higher efficiency compared to internal combustion engines.¹ Currently, fuel cells are used as power sources in both stationary and mobile (motor vehicles, buses, locomotives, *etc.*) engines. The most important components of fuel cells are proton-conducting, ion-containing membranes which can operate under severe conditions. The operating conditions include, first, high operating temperatures (sometimes, they exceed 100 °C) and, second, the medium that can be chemically active towards the material the membranes are made of due to the use of aggressive fuels (*e.g.*, methanol and products of its partial oxidation), oxidants (*e.g.*, oxygen) and catalysts, and due to the generation of active radicals at electrodes (especially, at cathode).¹

Of particular interest are new proton-conducting ion-exchange membranes based on solid polymer electrolytes.^{2,3}

The idea of using organic cation-exchange membranes as solid electrolytes in electrochemical cells was first materialised in 1959.⁴ Currently, the solid polymer electrolyte fuel cells (SPEFCs) are considered to be the most promising candidate systems out of all types of fuel cells.^{5–8} These devices are frequently called also as polymer electrolyte membrane or proton exchange membrane fuel cells (PEMFCs). The structure of a PEMFC is schematically shown in Fig. 1. A polymer electrolyte membrane is sandwiched between two noncorrosive porous electrodes. Electrochemical stacks can be fabricated by mechanically compressing individual assemblies across electrically conducting separators.

Generally, PEMFCs require humidified gases, *viz.*, hydrogen and oxygen (or air) as fuels for their operation. The electrochemical reactions occurring at electrodes are as follows:



where Q_1 is the electrical energy and Q_2 is the heat energy.

Membranes for PEMFCs⁹ must possess some specific properties, such as:

- low permeability with respect to oxygen and hydrogen (to prevent membrane breakdown);
- high swelling (to provide efficient dissociation of acids and to form a hydrated ionic phase within the thickness of the membrane);
- good water uptakes at temperatures above 100 °C;

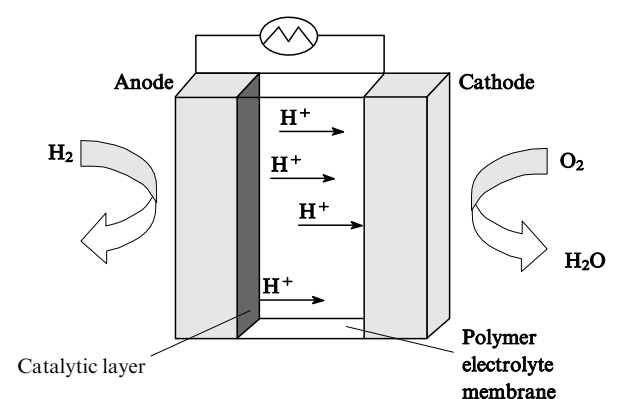


Figure 1. A scheme of a PEMFC.

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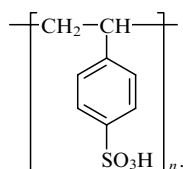
Uspekhi Khimii 71 (9) 862–877 (2002); translated by A M Raevsky

- high ion-exchange capacity sufficient to provide a conductivity of the order of $10^{-1} \text{ S cm}^{-1}$ at temperatures near 50°C ;
- high proton conductivity at temperatures above 100 and below 0°C ;
- high chemical and mechanical stability for long-term operation under severe conditions (over 2000 h for electric vehicle applications).[†]

In addition, ion-conducting films must be coated onto catalyst particles with ease. And of course, such membranes have to meet all requirements placed upon commercial products in the fuel cell market.

As a rule, proton-conducting polymers are prepared using polymer electrolytes containing negatively charged groups. The polymer electrolytes with sulfate and phosphate groups are most widely used. In dry state, they are rigid-chain, proton-conducting systems. As the content of water increases, the proton conductivity of hydrated polymer electrolytes substantially increases and can be as high as $10^{-2} - 10^{-1} \text{ S cm}^{-1}$.

The first PEMFC (a 1 kW power plant) used in an operational system was built at General Electric Co. (USA).¹⁰ The polymer membrane was made of poly(styrenesulfonic acid) (PSSA)



This type of PEMFC was used for primary power sources for the Gemini (USA) spacecrafts in the mid-1960s.

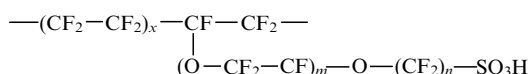
The lifetime of these PEMFCs was limited due to the degradation of the PSSA membrane under the action of $\text{HO}_2^\cdot$ radicals.

Research on fluorinated polymers^{11–14} led to considerable advances in the development of polymer electrolytes. The most widely used fluorinated polymers are prepared by copolymerisation of tetrafluoroethylene and perfluorinated vinyl ethers of the type



accompanied by hydrolysis of fluorosulfonic acid groups. The basic perfluorinated chains of such polymers determine high chemical and thermal stability, while the side chains possess the properties of strong acids.

Perfluorinated electrolyte membranes with the general formula



are also widely used.

Membrane	<i>x</i>	<i>m</i>	<i>n</i>
Nafion	6–10	1	2
Flemion	3–10	0.1	1–5
Aciplex-S	1.5–14	0.3	2–5
Dow membrane	3–10	0	2

An improved PEMFC for the Gemini spacecrafts was based on a perfluorinated Nafion membrane. This membrane possesses substantially improved characteristics compared to the PSSA membranes; particular types of Nafion membranes are characterised by lifetimes of 50 000 h. Different types of Nafion membranes have different equivalent masses (grammes of polymer per mole H^+), namely, 1200 (Nafion 120), 1100 (Nafion 117 and Nafion 115) and 1000 (Nafion 105).

[†] Optimum durability is ten years.

Perfluorinated membranes (Dowmembrane) were developed at Dow Chemical Co. (USA). They have equivalent masses of 800–850 and a dry state thickness of $\sim 5 \mu\text{m}$.

The Flemion membranes with equivalent masses ~ 1000 were developed at Asahi Glass Co. (Japan).⁵

Aciplex-S membranes developed at Asahi Chemical Industry (Japan) are characterised by equivalent masses of 1000–1200.

All the membranes mentioned above, as well as the Neosepta-F (Tokuyama, Japan) and Gore-Select (W L Gore and Associates, Inc., USA) membranes possess high proton conductivity ($10^{-2} - 10^{-1} \text{ S cm}^{-1}$) at water uptakes up to 15 H_2O molecules per SO_3H group and are characterised by good thermal, chemical and mechanical properties. On the other hand, these membranes are poor ionic conductors at reduced humidity and/or elevated temperatures. For instance, the conductivity of fully hydrated Nafion membranes at room temperature reaches $10^{-2} \text{ S cm}^{-1}$; however, it dramatically decreases at 100°C because of the loss of absorbed water in the membranes. In addition, such membranes tend to undergo chemical degradation at elevated temperatures. Finally, their fabrication is rather expensive. Therefore, the development of new solid polymer electrolytes, which combine sufficient electrochemical characteristics and low cost, is of current interest. A promising way of attacking this problem involves preparation of membranes based on aromatic condensation polymers (ACPs). The chemistry of ACPs was characterised by considerable progress in the 1960–1990s.^{15–26}

ACPs have some advantages that make them practically attractive:

- ACPs are cheaper than perfluorinated polymers, and some of them are commercially available;
- ACPs containing polar groups have high water uptakes over a wide temperature range;
- decomposition of ACPs can be to a great extent suppressed by proper molecular design;
- ACPs are easily recycled by conventional methods.

A number of reviews concerning the development of proton-conducting membranes based on polymer electrolytes are available.^{1, 7, 8, 27–30} They contain information on the advanced materials, their electrochemical properties, water uptakes and thermal stabilities. However, rapid accumulation of newly obtained results gives an impetus to further generalisation of information in this field.

In the last decade, research into PEMFCs has been most intensively carried out in the following avenues:

- development of sulfonated aromatic condensation polymers (ACPs) and membranes based on them;
- development of alkylsulfonated ACPs and membranes based on them and
- development of acid–basic polymer complexes and membranes based on them.

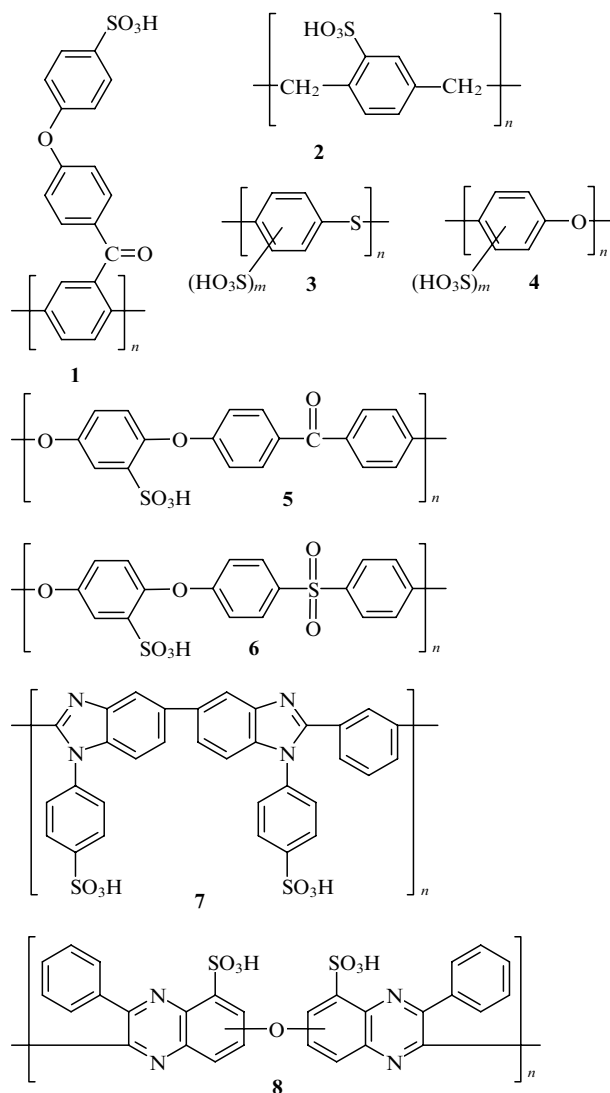
II. Sulfonated aromatic condensation polymers and membranes based on them

Aromatic polymers containing sulfonic acid groups can be prepared by sulfonation of high-molecular-mass ACPs or their fragments and by condensation of monomers containing sulfonic acid groups.

1. Sulfonation of high-molecular-mass aromatic condensation polymers

The simplest and most widely used method for the synthesis of sulfonated ACPs involves sulfonation of different classes of polymers, such as poly(1,4-phenylenes),^{31–33} poly(*p*-xylylene),^{34, 35} poly(1,4-oxyphenylenes),³⁶ poly(ether ether ketones) (PEEK),^{37–44} poly(arylene ether sulfones),^{3, 45–52} poly(phenylene sulfides),⁵³ poly(phenylquinoxalines),^{54–56} poly(benzimidazoles)⁵⁷ and some other ACPs. The chemical structures of sulfonated poly(4-phenoxybenzoyl-1,4-phenylene) (S-PPBP) (1), poly(*p*-xylylene) (S-PPX) (2), poly(phenylene sulfide) (S-PPS) (3),

poly(phenylene oxide) (S-PPO) (4), poly(ether ether ketone) (S-PEEK) (5), poly(ether ether sulfone) (S-PEES) (6), arylsulfonated poly(benzimidazole) (S-PBI) (7) and sulfonated poly(phenylquinoxaline) (S-PPQ) (8) are shown below.



ACPs are sulfonated using known sulfonating agents.^{58–60} In particular, PEEK can be sulfonated with concentrated sulfuric acid,⁶¹ chlorosulfonic acid,⁶² SO_3 (either pure or taken in a mixture),^{42, 48, 62, 63} a mixture of methanesulfonic acid with concentrated sulfuric acid⁶⁴ and acetyl sulfate.^{65, 66}

Sulfonation of ACPs was systematically studied taking a number of polymers (first of all, PEEK and PPBP) as examples.⁷ It was shown that sulfonation with chlorosulfonic or fuming sulfuric acid is sometimes accompanied by degradation of these polymers. The sulfonation rate of ACPs in sulfuric acid can be controlled by varying the reaction time and the acid concentration.⁶⁷ This technique allows preparation of target ACPs with sulfonation degrees ranging from 30% to 100% without chemical degradation or cross-linking of the polymers.⁶⁸ However, it should be noted that direct sulfonation reactions cannot be used for preparation of random sulfonated copolymers and sulfonation levels of less than 30%, since sulfonation in sulfuric acid occurs under heterogeneous conditions due to high viscosity of the reaction solutions.^{40, 61} For this reason, preparation of random copolymers requires the duration of the dissolution process to be shortened to 1 h. The dependences of the degree of sulfonation of PEEK and PPBP²³ on the reaction time at room temperature are shown in Fig. 2.

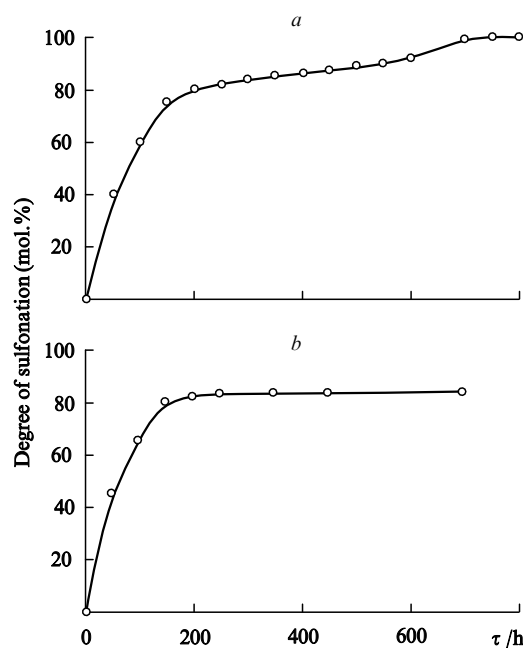


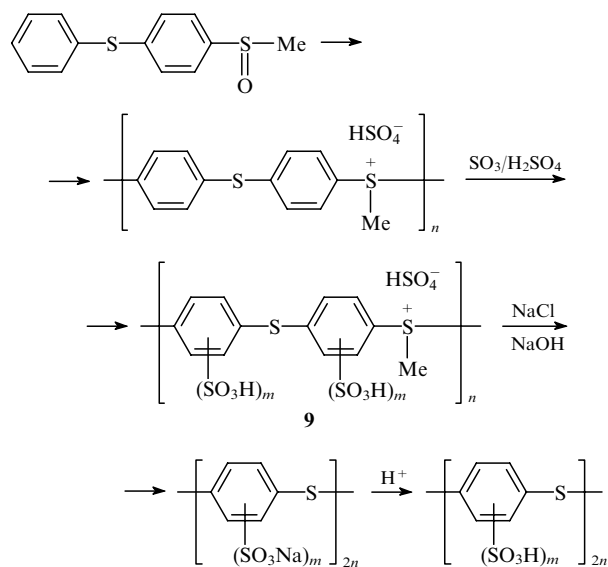
Figure 2. Degree of sulfonation of PEEK (a) and PPBP (b) as a function of reaction time at room temperature.⁷

Sulfonation is a kind of electrophilic substitution reaction; therefore, it strongly depends on the nature of substituents in the rings, namely, electron-donor substituents favour the reaction, whereas electron-acceptor substituents do not. For instance, in the case of PPBP the terminal phenyl ring of the side chain can be sulfonated under mild conditions that are comparable with the sulfonation conditions of PEEK. In contrast to this, the phenyl ring of the substituent in poly(4-benzoyl)-1,4-phenylene (PBP), which contains an electron-acceptor carbonyl group, cannot be sulfonated under these conditions.⁷ The sulfonation level of PPBP and PEEK reaches nearly 80% within 100 h. The degree of sulfonation of PPBP is saturated at 85%, whereas that of PEEK can be as high as 100%. This is thought to be due to steric hindrances to further sulfonation of PPBP in a viscous sulfuric acid solution.

The solubility of polymers changes as the degree of sulfonation increases. For instance, S-PEEK containing 30 mol.% sulfonic acid groups can be dissolved in DMF, DMSO and *N*-methyl-2-pyrrolidone (*N*-MP); at 70% sulfonation, the polymer is soluble in methanol and at 100%, in water. Non-sulfonated PPBP is soluble in conventional chlorinated solvents (*e.g.*, chloroform and dichloromethane), whereas S-PPBP with 30% sulfonation is insoluble in these solvents; however, the polymer can be dissolved in DMF, DMSO and *N*-MP. At sulfonation levels above 65%, S-PPBP swells in methanol and water.

Sulfonation of PEEK in concentrated sulfuric acid at room temperature is accompanied by incorporation of no more than one sulfonic acid group into each repeating unit of the polymer.^{62, 65, 69} From the results of FT-IR spectroscopy studies it follows that PEEK is sulfonated at the phenylene ring between the ether groups. Sulfonation of PPBP occurs at the *p*-position of the terminal phenoxy group.

Tsuchida *et al.*^{70, 71} reported the synthesis of poly(thiophenylsulfonic acid) containing up to two sulfonic acid groups per repeating unit. Polymerisation of 4-(methylsulfinyl)diphenyl sulfide in sulfuric acid upon heating or in the presence of SO_3 resulted in a sulfonated poly(sulfonium cation), which was then converted into the corresponding sulfonated poly(phenylene sulfide).



$m = 1-2$.

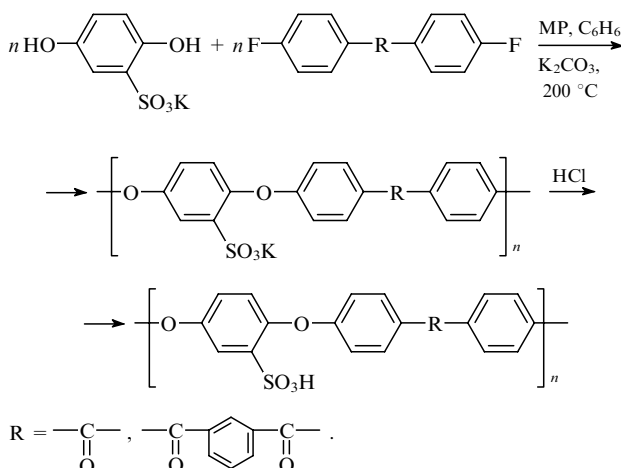
The course of sulfonation was controlled by varying the reaction time, the temperature and/or by adding SO_3 . Polymer electrolytes thus obtained are soluble in water and methanol and can form transparent films.

Novel polymer electrolytes exhibiting high proton conductivity (higher than $10^{-2} \text{ S cm}^{-1}$) were prepared by sulfonation of poly(ether sulfone) (PES).^{72, 73} In these polymers the protons of the sulfonic acid groups are partially replaced by metal ions (Mg, Ti, Al, Ln), which leads to extension of the durability of the electrolytes.

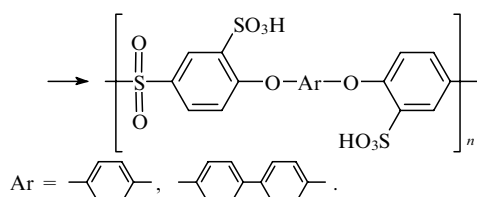
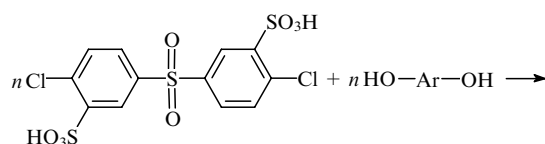
2. Synthesis of aromatic condensation polymers based on sulfonated monomers

Sulfonated ACPs are prepared both by direct sulfonation and by the polycondensation and polycyclocondensation of sulfonated compounds.

In particular, sulfonated PEEK were prepared by the reactions of sulfonated hydroquinone with difluoro-substituted aromatic compounds containing carbonyl groups:⁷⁴



An analogous procedure was employed in recent studies^{75, 76} on the synthesis of poly(arylene ether sulfones) in the reactions of sulfonated 4,4'-dichlorodiphenyl sulfone with various bisphenols.



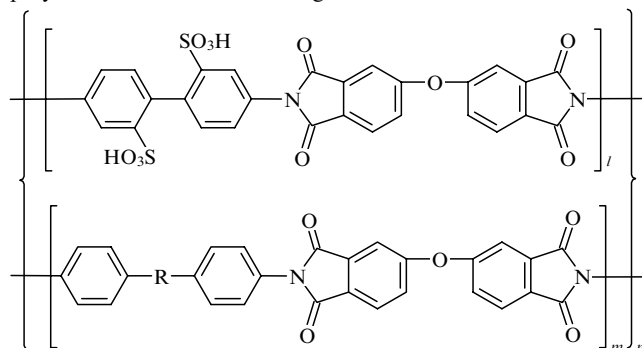
The use of *m*-aminophenol as an additive along with bisphenols allowed the preparation of poly(arylene ether sulfones) with terminal amino groups.⁷⁷

Sulfonated poly(thiophenylene sulfones) were prepared by the interaction of sulfonated 4,4'-difluorodiphenyl sulfone with 4,4'-dimercaptobenzophenone.⁷⁸ Not only homopolymers, but also copolymers were obtained (in the latter case, a fraction of sulfonated 4,4'-difluorodiphenyl sulfone was replaced by non-sulfonated monomer) (Scheme 1).

Using this approach, one can not only prepare polymers with regular arrangement of sulfonic acid groups, but sometimes introduce a larger number of sulfonic acid groups into the ACP macromolecules compared to the sulfonation of ACPs in the last stage of the synthesis.

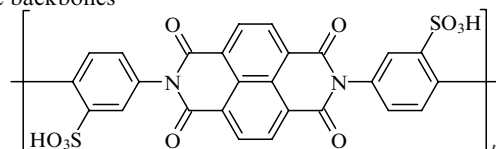
Sulfonated monomers were also used for the synthesis of sulfonated polyimides.^{79, 80} In particular, a sodium salt of sulfonated bis-4-[(3-aminophenoxy)phenyl]phenylphosphine oxide was used for the preparation of sulfonated polyimides (Scheme 2).⁷⁹

Of considerable interest is the use of 4,4'-diamino-2,2'-diphenylsulfonic acid^{80–82} produced on a semi-industrial scale as a sulfonated monomer for the preparation of polyimides. The reactions of a mixture of this monomer and 4,4'-diaminodiphenylmethane and 4,4'-diaminodiphenyloxide with diphenyloxido-3,3',4,4'-tetracarboxylic acid dianhydride resulted in sulfonated polyimides⁸⁰ with the following formulae:



$R = \text{O}, \text{CH}_2.$

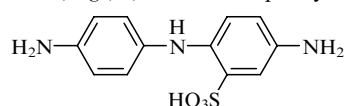
Poly(naphthylimides) containing six-membered imide rings in the backbones^{80–86}

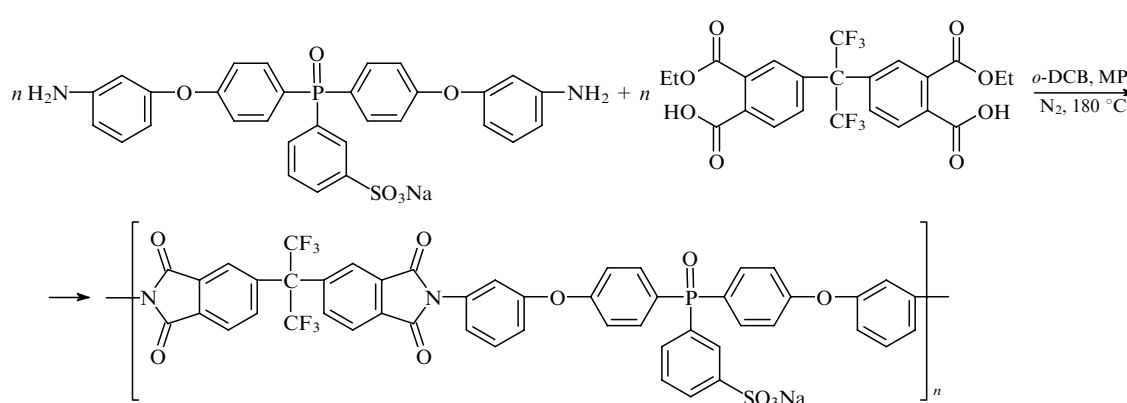
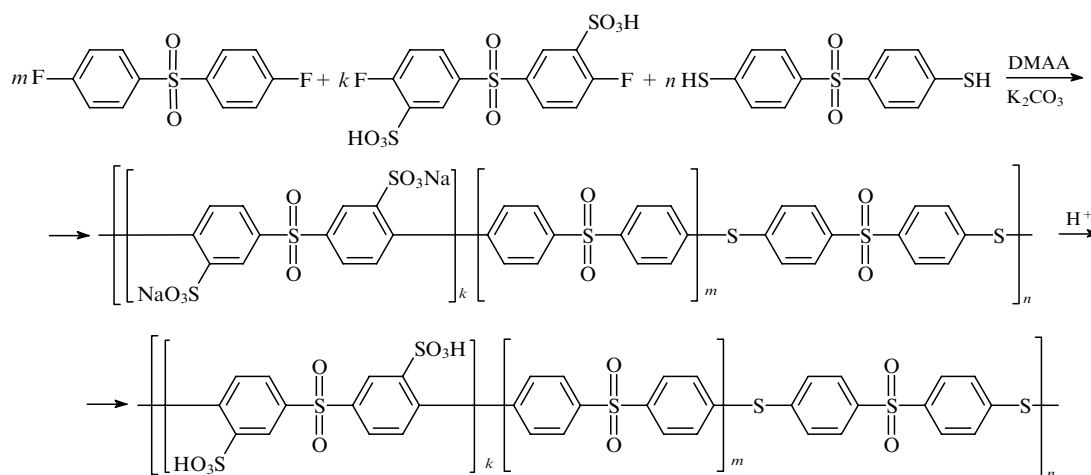


are characterised by substantially improved chemical resistance compared to analogous poly(phthalimides).^{87–89}

Almost all studies on the synthesis of poly(naphthylimides) based on 4,4'-diamino-2,2'-diphenylsulfonic acid were aimed at preparing copolymers with controlled properties that can be varied over a wide range.

Poly(naphthylimides) can be synthesised from sulfonated diamines, e.g., 4,4'-diaminodiphenylamino-2-sulfonic acid.⁹⁰





3. Properties of sulfonated aromatic condensation polymers

The most important properties of sulfonated ACPs are their thermal stability, water uptake and proton conductivity.

PEMFCs and other electrochemical devices operating in the temperature range 100–200 °C require polymer electrolyte membranes characterised by fast proton transfer.

Operation of PEMFCs at elevated temperatures has a number of advantages. It causes an increase in the rates of the fuel cell reactions and reduces catalyst poisoning with absorbed carbon monoxide, thus reducing the demand for catalysts.

Thermal stability of proton-conducting polymer electrolyte membranes is an important characteristic, which determines the possibility of their use for fuel cell applications.

The thermal stability of polymer membranes based on S-PPBP was studied⁷ by heating the samples followed by elemental analysis (thermogravimetric analysis, or TGA, at a heating rate of 10 deg min⁻¹ in nitrogen atmosphere) (Fig. 3).

According to the results of TGA studies, S-PPBP showed a mass loss of nearly ~20% in the temperature range between 250 and 400 °C, which corresponds to the decomposition of sulfonic acid groups.

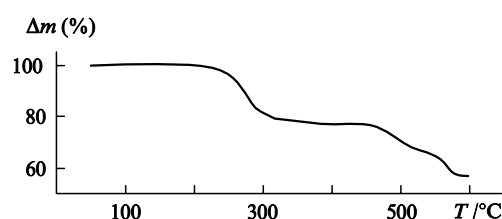


Figure 3. TGA curve of S-PPBP with 80 mol.% sulfonation level.⁷

The dependence of the degradation temperature, T_d , of S-PPBP and S-PEEK on the degree of sulfonation is presented in Fig. 4.

Degradation of sulfonated polymers was observed between 250 and 350 °C, *i.e.*, at temperatures that are much lower than the decomposition temperatures of non-sulfonated PPBP and PEEK.

As the degree of sulfonation increased, the degradation temperatures decreased from 500 down to 300 °C for S-PEEK and from 500 down to 250 °C for S-PPBP. The results of elemental analysis of the residues indicated a dramatic (nearly tenfold) decrease in the sulfur content in the polymers after heating at temperatures above 400 °C. These data confirm that thermal decomposition occurs by desulfonation mechanism.

No thermal decomposition of sulfonated polymers was observed at temperatures below 200 °C. This means that the thermal stabilities of the polymers are sufficient for fuel cell applications even at high sulfonation levels.⁷

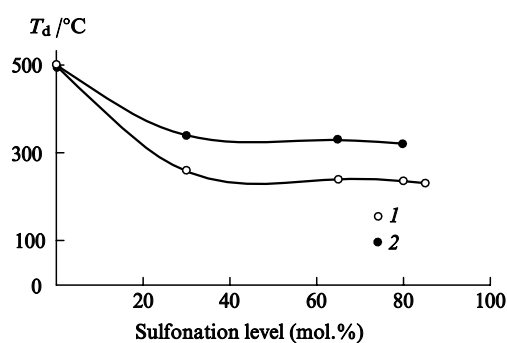


Figure 4. Degradation temperature of S-PPBP (1) and S-PEEK (2) as function of sulfonation level.⁷

Other proton-conducting polymer electrolytes based on sulfonated aromatic polymers also show the onset of thermal degradation at temperatures between 200 and 400 °C. Desulfonation of arylsulfonic acids occurs with ease on heating their aqueous solutions to 100–175 °C. Therefore, desulfonation imposes limitations on the thermal stability of sulfonated aromatic polymer electrolytes. Mention may be made that the presence of bulky substituents attached to the phenyl rings can to some extent favour an increase in the temperature of the onset of thermal degradation.

According to Tsuchida *et al.*,⁷⁰ highly sulfonated poly(phenylene sulfide) exhibits higher thermal stability compared to other sulfonated aromatic polymer electrolytes. This conclusion was based on the results of a TGA study of the thermal stability of poly(thiophenylenesulfonic acid) with different degrees of sulfonation. The degradation temperature of a highly sulfonated polymer (degree of sulfonation $m = 2.0$) is 265 °C, which is 125 °C higher than that of the low sulfonated polymer ($m = 0.6$). The C–S bond in the highly sulfonated polymer is stronger due to the presence of two electron-acceptor sulfonic acid substituents attached to each benzene ring. The initial mass loss of this polymer at 265–380 °C is only 13%, which corresponds to the loss of two water molecules per repeating unit. Therefore, the desulfonation reaction in this polymer slows down upon introduction of electron-acceptor.

Water is carried out in the fuel cells *via* humidified gas streams (H_2 , O_2) and enters electrodes as a result of gas diffusion. A mixture of liquid water and water vapours passes through each electrode towards the electrode/electrolyte interface and crosses it, thus assisting the hydration of the electrolyte membranes. Oxygen reduction at the cathode provides an additional source of water in the electrolyte.

Water transport in the membrane occurs in two ways, *viz.*, due to electro-osmotic drag of water by proton transfer from anode to cathode and due to diffusion of water molecules down concentration gradients that build up.

Optimum hydration level of electrolyte membranes is a key factor for normal fuel cell operation: if the electrolyte membrane is too dry, its conductivity decreases, whereas an excess of water in the membrane can lead to cathode flooding. In both cases the fuel cell performance reduces.

Absorption of water vapour by polymer films prepared from S-PEEK and S-PPBP was studied by placing the films in atmospheres with different humidities and measuring the equilibrium water content. The results obtained were found to be close to those reported in an analogous study of Nafion membranes.¹⁰ The dependence of the water uptakes of the S-PEEK and S-PPBP films on the relative humidity at room temperature is shown in Fig. 5.

Assuming that water activity and water content in the membrane obey the Raoult law, the activity coefficient of water in the

polymer is larger than unity at relative humidities exceeding a particular value. The equilibrium content of water in S-PEEK and S-PPBP increases as the sulfonation level increases. At relative humidities in the range from 0% to 50% (first region), a relatively small increase in the water uptake is observed, whereas an increase in the relative humidity from 50% to 100% (second region) leads to a much greater increase in the water uptake. The first region corresponds to water uptake due to solvation of the proton and sulfonate ions. During solvation, water is involved in the interaction with ionic components of the polymer. These interactions overcome the tendency of the polymer to exclude water due to its hydrophobic nature and resistance to swelling.⁷ The second region corresponds to the uptake of water involved in polymer swelling.

The content of water in S-PPBP (65 mol.% sulfonation) is larger than in S-PEEK with the same sulfonation level. At a relative humidity of 100% and room temperature, the content of water in S-PPBP and S-PEEK is 8.7 and 2.5 molecules per sulfonic acid group, respectively.

Picnometric measurements showed that the densities of the polymers with a sulfonation level of 65 mol.% were 1.338 (S-PEEK) and 1.373 g cm⁻³ (S-PPBP). According to the results obtained by scanning electron microscopy, both polymers exhibited very close characteristics of their surfaces and fracture surfaces.

The difference in water uptake between S-PEEK and S-PPBP can be explained by the flexibility of the phenoxybenzoyl group in the side chain of S-PPBP, which favours water permeation into the polymer and water absorption in the terminal sulfonic acid groups. The water uptake of S-PPBP is comparable with that of Nafion membranes.

DTA studies revealed a rather strong interaction between the water molecules in sulfonated hydrocarbon polymers and their sulfonic acid groups, which leads to high proton conductivities at high temperatures and low humidities.

The proton conductivity of sulfonated poly(phenylene sulfide) is 10^{-5} S cm⁻¹ at room temperature and a relative humidity of 30%. It exponentially increases as the relative humidity increases and reaches a value of 2×10^{-2} S cm⁻¹ at 94% humidity (Fig. 6). In this case, the content of water in the polymer is 10.3 molecules per sulfonic acid group. The maximum conductivity of sulfonated poly(phenylene sulfide) ($m = 2.0$) at 80 °C was 4.5×10^{-2} S cm⁻¹.

Experiments⁷ on water absorption in the S-PEEK and S-PPBP films showed that the proton conductivities of the films containing equilibrium amounts of absorbed water depend on the relative humidity. Figure 7 presents the plots of the proton conductivities of S-PPBP and S-PEEK with different sulfonation levels as a function of the relative humidity. As can be seen, the proton conductivities of the films increase with the relative

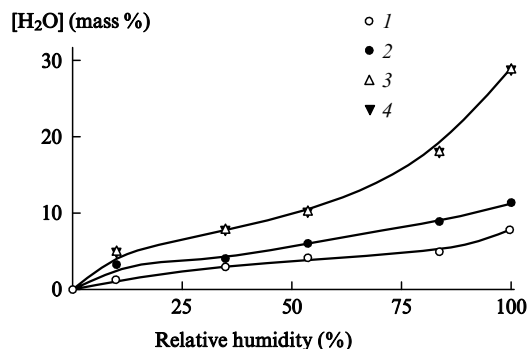


Figure 5. Water uptake of S-PPBP (1–3) and S-PEEK (4) at room temperature as function of relative humidity.⁷ Concentration of SO_3H groups in the polymer (mol.%): 30 (1), 65 (2), 80 (3) and 65 (4).

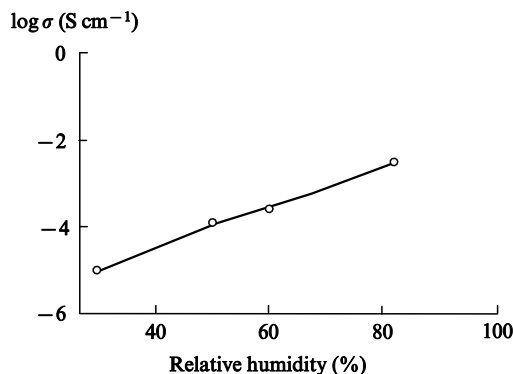


Figure 6. Proton conductivity of compound 9 ($m = 2.0$) at room temperature as function of relative humidity.⁷⁰

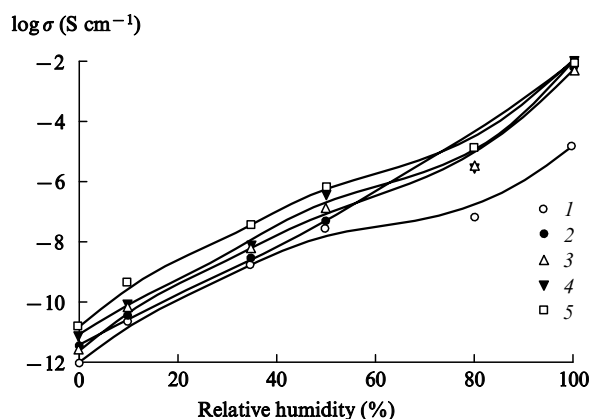


Figure 7. Proton conductivity of S-PEEK (1) and S-PPBP (2–5) with different sulfonation levels as a function of relative humidity at room temperature.⁷ Sulfonation level (mol.%): 65 (1), 30 (2), 65 (3), 80 (4) and 85 (5).

humidity and water uptake and can be as high as 10^{-5} S cm⁻¹ (for S-PEEK).

The proton conductivities of S-PEEK and S-PPBP with equal degrees of sulfonation (65 mol.%) at a 100% relative humidity can be compared using the plots shown in Fig. 8. As can be seen, the proton conductivity and water uptake of S-PPBP are much higher than those of S-PEEK. Moreover, the proton conductivity of S-PEEK dramatically decreases at temperatures above 100 °C, whereas that of S-PPBP is much less temperature dependent.

Sulfonated poly(phenylene sulfide) and S-PPBP exhibit stable proton conductivities at elevated temperatures. For this reason, they are considered as promising polymers for creation of proton-conducting electrolyte membranes to be used at elevated temperatures and low humidities.

On the contrary, the conductivity of perfluorinated polymer electrolytes usually appreciably decreases with increasing temperature, that is, the conductivity of such electrolytes at 80 °C is by an order of magnitude lower than at 60 °C. Perfluorinated polymer membranes become less conducting at high temperatures, since the loss of water causes the channels to collapse, thus making proton transport more difficult.

In particular, the proton conductivity of Nafion membranes at temperatures above 100 °C dramatically decreases due to their dehydration.

In Fig. 9, we present the temperature dependences of the proton conductivity of S-PEEK with a sulfonation degree of 85 mol.% at different relative humidity values.

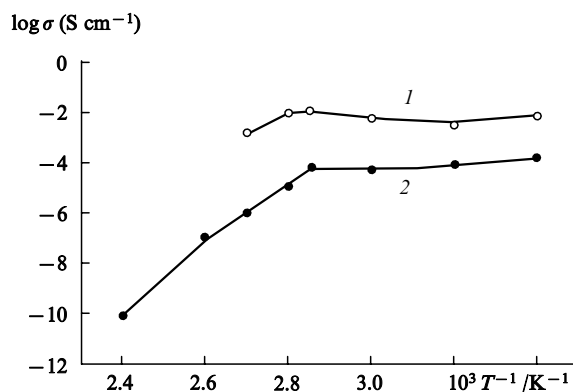


Figure 8. Temperature dependences of proton conductivity of S-PPBP (1) and S-PEEK (2) with the same degrees of sulfonation (65 mol.%) at a relative humidity of 100%.⁷

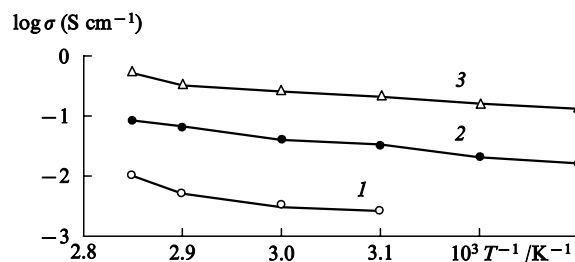


Figure 9. Temperature dependence of proton conductivity of an S-PEEK membrane with sulfonation level of 85% at a relative humidity of 50% (1), 70% (2) and 90% (3).⁷

Similarly to Nafion membranes, the proton conductivity of S-PEEK substantially decreases as the humidity decreases.⁷⁴ The dependence of proton conductivity on humidity reflects a tendency of S-PEEK to absorb water vapours. This can be attributed to the 'liquid' proton conductivity mechanism when protons are transported in the form of hydronium ions through water-filled pores in the membrane.³⁰

S-PEEK samples exhibited a slight increase in conductivity with increasing temperature at all relative humidities (50%, 70% and 90%). This can be due to the strong interaction between the sulfonic acid groups and the absorbed water molecules.

Proton-conducting polymer electrolyte membranes based on ACPs such as S-PPBP and sulfonated poly(phenylene sulfide) contain rather large amounts of bound water. This seems to be the reason for such a salient feature of these membranes as an increased proton conductivity at high temperatures and/or low humidities. This conclusion was confirmed by the results of differential scanning calorimetry (DSC) studies of these systems.⁷

III. Alkylsulfonated aromatic condensation polymers and proton-conducting electrolyte membranes based on them

The major drawback of sulfonated proton-conducting polymer electrolytes is their degradation at 200–400 °C due to desulfonation.

By introducing alkylsulfonated substituents into the macromolecules of aromatic polymers one can prepare thermostable proton-conducting polymers. Their electrochemical properties can be controlled by varying the number of substituents and the length of alkyl chains. The water uptake and proton conductivity of alkylsulfonated polymers are close to those of sulfonated electrolytes that exhibit high thermal and chemical stability and mechanical strength.

Poly(*p*-phenyleneterephthalamido-*N*-propylsulfonate) and poly(*p*-phenyleneterephthalamido-*N*-benzylsulfonate) were synthesised based on related polyamides containing reactive NH groups.⁹¹ The polyamides were modified by treating with NaH and DMSO^{91,92} and the polyanion obtained was introduced in the reaction with 1,3-propane sultone (Scheme 3).

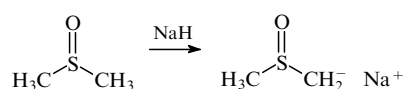
An analogous approach was employed in the modification of poly(benzimidazoles) (PBI).^{93–100}

Yet another synthetic route to sulfonated PBI involves treatment of the above-mentioned polyanion with 4-bromobenzylsulfonate resulting in poly[2,2'-*m*-phenylene-bi(*N*-benzylsulfonato)benzoimidazolo-5,5'-diyl] (Scheme 4).

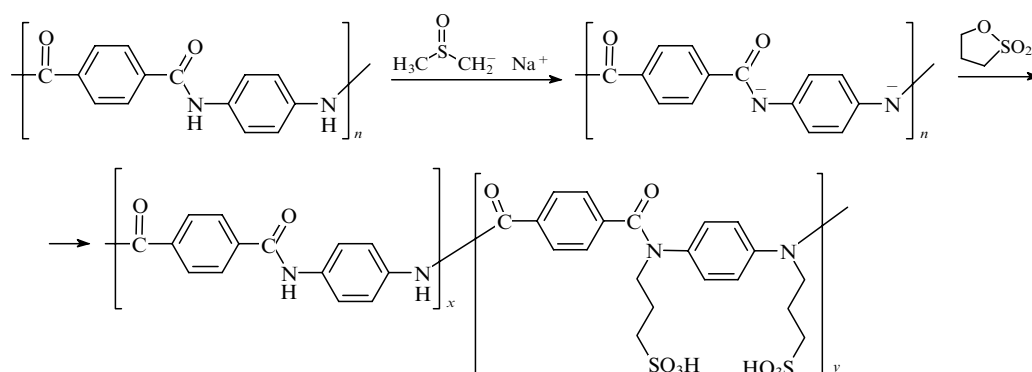
Compared to the starting polymers, alkylsulfonated PBI are more soluble in polar organic solvents (DMAA or DMSO). The solubility depends on the degree of alkylsulfonation.

The degree of alkylsulfonation as a function of the 1,3-propane sultone:PBI ratio is plotted in Fig. 10.

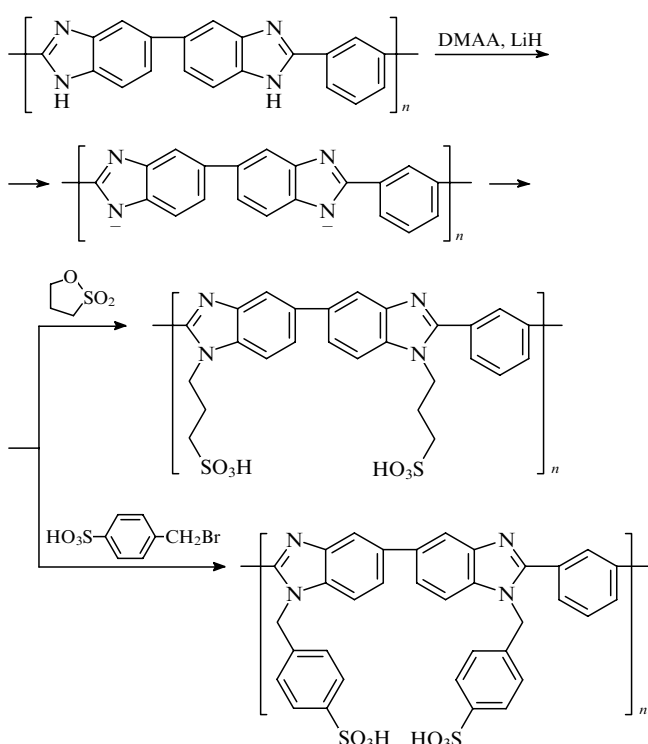
The degree of alkylsulfonation of NH groups in PBI was estimated based on the results of ¹H NMR study and elemental analysis. This parameter can be controlled with ease by varying



Scheme 3



Scheme 4



the 1,3-propane sultone:PBI ratio. For instance, the alkylsulfonation level can be as high as 60 mol.% at a 1,3-propane sultone:PBI ratio of 5.0.

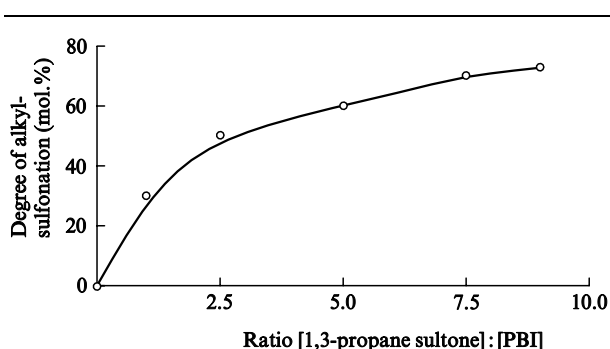


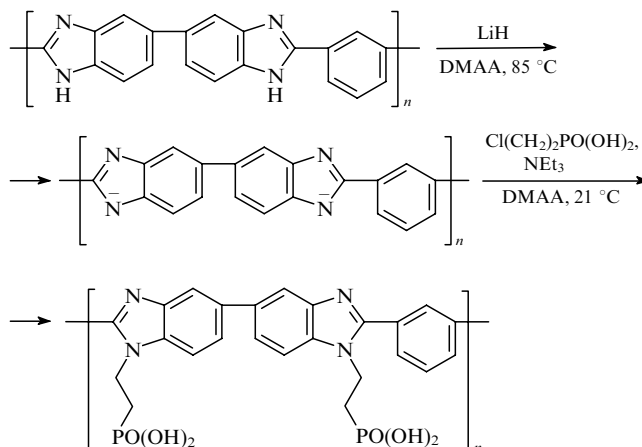
Figure 10. Degree of alkylsulfonation of PBI as function of 1,3-propane sultone:PBI ratio.⁷

An attempt to synthesise ethylphosphorylated PBI using the above-mentioned treatment of PBI at NH groups (Scheme 5) was reported.⁷ The substitution reaction at the NH sites of benzimidazole rings was performed successfully, but the resulting polymer was insoluble in organic solvents. The reason can be aggregation of phosphoric acid groups during the substitution reaction. Ethylphosphorylated PBI exhibited high proton conductivity ($10^{-3} \text{ S cm}^{-1}$) even in the pellet form. According to the results obtained, the presence of polar phosphoric acid groups enhances the proton conductivity of the polymer electrolytes.

Alkylsulfonation and arylsulfonation of the starting aromatic polymers was aimed at increasing their water uptakes and proton conductivities while retaining high thermal stabilities. The polymers obtained were studied by TGA in inert and oxidative atmospheres.⁹⁶ The parent PBI exhibits a very high thermal stability. In an inert atmosphere, the onset of its degradation occurs at 650 °C, a 5% mass loss is observed at 700 °C, while more than 80% of the initial mass is retained at 800 °C. Introduction of substituents that are not conjugated with the polymer backbones reduces the degradation temperature in an inert medium, which is consistent with the expectations. The degradation of poly[2,2'-*m*-phenylene-bis(*N*-benzylsulfonato)benzimidazolo-5,5'-diyl] with 22% substitution begins at 480 °C while the onset of mass loss process of poly-{2,2'-*m*-phenylene-bis[*N*-(3-propylsulfo)benzimidazolo-5,5'-diyl]} with a substitution level of 54% is observed at 450 °C. After removal of the substituents the degradation slows down so nearly 50%–60% of the initial mass is retained at 800 °C.

The degradation of PBI in an oxidative atmosphere (dry air) begins at 520 °C, which is nearly 100 °C lower than the degradation temperature of this polymer in inert medium.

Scheme 5



The degradation temperatures of substituted PBI in oxidative media are close. For all polymers, the mass loss in air is much larger than in nitrogen and the amount of the residual char is much smaller. This is first of all due to the lower stability of the starting PBI in dry air and to some extent to the introduction of substituents.

In an inert atmosphere, poly(*p*-phenylene terephthalamide) (PPTA) is stable below 550 °C. Rapid mass loss of the polymer (up to 50% of the initial mass) begins at 600 °C. After modification with propylsulfonate side groups (a 66% substitution) the polymer is stable below 400 °C; only 40% of the initial mass is retained at 800 °C. The benzyisulfonated derivative of PPTA with 66% substitution level is more thermally stable compared to the propylsulfonated derivative; its degradation begins at 470 °C. A decrease in mass of the sample down to 50% of initial mass is observed at 800 °C. The degradation temperature of PPTA in a dry air atmosphere is 70 °C lower than in nitrogen atmosphere.⁹⁶ Comparison of degradation processes of benzyisulfonated PPTA with a 66% substitution in air and in nitrogen showed that the degradation in air begins at a lower temperature. The major difference in behaviour is that the mass loss is larger while after the initial mass loss it is much smaller at high temperatures, which is due to oxidative degradation of the polymer chains. Introduction of substituents into aromatic polymers reduces their thermal stability irrespective of the medium in which degradation occurs. This is the expected manner of changes in properties, since the side groups, especially sulfonic acid groups, are not stabilised by conjugation with the polymer backbones.

Gieselmann and Reynolds concluded⁹⁶ that the benzyisulfonate side group is more stable than the propylsulfonate group irrespective of the structure of the polymer backbone. This suggests that the side group cleavage point is not only at the N—C bond. A TGA study of benzyisulfonated PBI with 75% degree of sulfonation in air at a heating rate of 1 deg min⁻¹ showed⁹⁷ that introduction of benzyisulfonate groups into the polymer reduces its thermal stability. In this case, thermal degradation begins at 370 °C while the mass loss in the temperature range 370–420 °C is attributed to the degradation of the sulfonic acid groups. The degradation mechanism of these polymer electrolytes seems to be very complex, since the results of TGA studies are affected by the residual water, impurities, sulfonation level and measurement conditions.

In air, arylsulfonated PBI is stable up to 350 °C (see Ref. 97), while benzyisulfonated PBI is stable up to 500 °C (see Ref. 96). These results are hard to compare because of different degrees of sulfonation of the PBI samples under study. One can assume that benzyisulfonated PBI is less stable than propylsulfonated PBI due to the presence of weak aryl—S bond. In fact, the degradation temperature of benzyisulfonated PBI is comparable with those of polymer electrolytes obtained by sulfonation with sulfuric acid.

The thermal stability of anhydrous propylsulfonated PBI (PBI-PS) in a nitrogen atmosphere was studied⁷ by TGA at a heating rate of 5 deg min⁻¹. Prior to analysis, all samples were vacuum oven dried at 60 °C for 48 h. However, this polymer is hygroscopic and again rapidly absorbs water after vacuum oven drying. Because of this, it was dried *in situ* and then differential thermal analysis was immediately performed.

In contrast to PBI, degradation of PBI-PS was observed in the temperature range 400–450 °C. The decomposition temperature of PBI-PS decreases as the degree of alkylsulfonation increases to 400 °C (Fig. 11); however, it is higher than the degradation temperature of perfluorinated polymer electrolytes (nearly 280 °C).

Degradation of PBI-PS was studied by elemental analysis and FT-IR spectroscopy. It was found that the intensities of SO stretching vibrations decreased after heating the PBI-PS samples above 400 °C for 1 h. These results are close to those reported by Gieselmann and Reynolds⁹⁶ who found that the degradation of PBI-PS occurs due to desulfonation. Hence, alkylsulfonated PBI is more thermally stable than sulfonated aromatic polymer

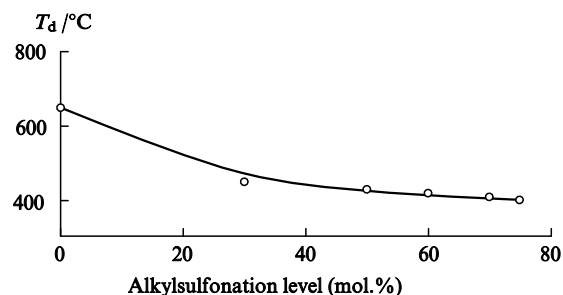


Figure 11. Decomposition temperature of PBI-PS as function of alkylsulfonation level.⁷

electrolytes characterised by degradation temperatures lying between 200 and 350 °C. The thermal stability of alkylsulfonated polymer electrolytes can be attributed to strong chemical bond between the alkyl and the sulfonic acid groups. The introduction of alkylsulfonic acid groups into thermostable polymers involving alkane sultone is one of the most important approaches to the preparation of thermostable proton-conducting polymer electrolytes.

Introduction of arylsulfonic and alkylsulfonic acid groups into aromatic polymers induces water absorption and makes them more hygroscopic. The water uptake of PBI-PS was determined⁷ by measuring the mass of the polymer before and after hydration. In Fig. 12, we present the dependence of the water uptake of PBI-PS on the relative humidity. As can be seen, the water uptake changes with the relative humidity. The equilibrium water uptake of PBI-PS increases as the relative humidity and degree of alkylsulfonation increases. The water uptake of PBI-PS with an alkylsulfonation level of 73.1 mol.% is 11.3 H₂O molecules per SO₃H group at room temperature and a relative humidity of 90% (*cf.* 11.0 H₂O molecules per SO₃H group for Nafion 117 membranes under the same conditions).

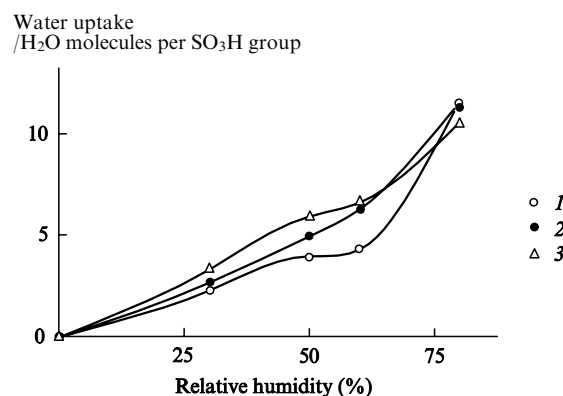


Figure 12. Water uptake of PBI-PS as a function of relative humidity at alkylsulfonation levels of 49.3 mol.% (1), 61.5 mol.% (2) and 73.1 mol.% (3).⁷

This procedure was also employed for the synthesis of butylsulfonated and (methyl)propylsulfonated PBI (PBI-BS and PBI-MPS, respectively) *via* butane sultone and methylpropane sultone. The water uptakes of these polymers differ from that of PBI-PS and are 19.5 (PBI-BS) and 27.5 (PBI-MPS) H₂O molecules per SO₃H group at a relative humidity of 90%. The water uptakes of alkylsulfonated PBI depend on the length of alkyl chains and on the degree of chain branching, that is, as the chain length and the degree of alkyl chain branching increase, the water uptake also increases. This is thought to be associated with the

greater flexibility of long alkyl chains and with larger amount of water absorbed in the cavities between the branched chains.

The specific role of the absorbed water in polymer electrolytes and the physical state of the water absorbed by polymer electrolytes were studied by IR¹⁰¹ and ¹H NMR spectroscopy (low-temperature relaxation time measurements)¹⁰² and DSC.⁷ The DSC curve of a hydrated PBI-PS film (73.1 mol.%) containing 11.3 H₂O molecules per SO₃H group is shown in Fig. 13.

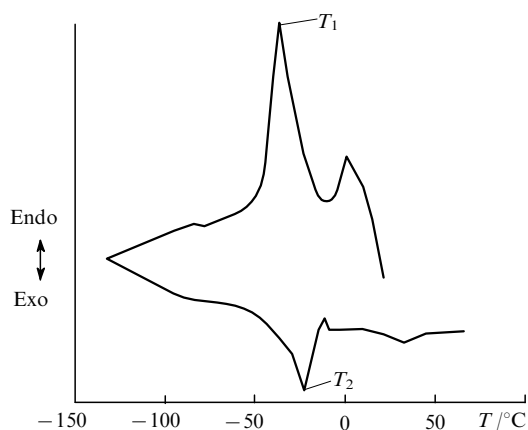


Figure 13. DSC curve of hydrous PBI-PS (73.1 mol.%) film containing 11.3 H₂O molecules per sulfonic acid group.⁷ T_1 is the freezing temperature (-36.6 °C) and T_2 is the melting temperature (-21.6 °C).

The DSC curve of anhydrous PBI-PS exhibited no peaks, whereas the DSC curve of hydrated PBI-PS exhibited two peaks corresponding to phase transitions of absorbed water at -36.6 and -21.6 °C that were attributed to the freezing and melting temperatures of the absorbed water, respectively.

A study of hydrated Nafion membranes under the same conditions revealed a phase transition at 0 °C. These results indicate that the adsorbed water in the Nafion membrane is bound to a lesser extent compared to PBI-PS which can exist in the hydrated state even at elevated temperatures.

Wet PBI-PS films possess no electron conduction despite the fact that the main polymer chains are conjugated. To elucidate the nature of charge carriers in PBI-PS, the conductivity of PBI-PS films containing H₂O and D₂O was measured.⁷ The results of measurements are presented in Fig. 14. As can be seen, the conductivity of the films containing water increased with increasing water uptake and was higher than that of the PBI-PS films containing D₂O in the same temperature range. This points that the charge carrier in hydrated PBI-PS is a proton (hydronium ion).

The temperature dependence of proton conductivity of PBI-PS containing the equilibrium amount of water is shown in

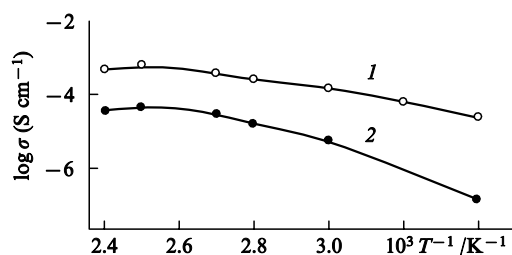


Figure 14. Temperature dependence of proton conductivity of PBI-PS (61.5 mol.%) films containing H₂O (1) and D₂O (2).⁷

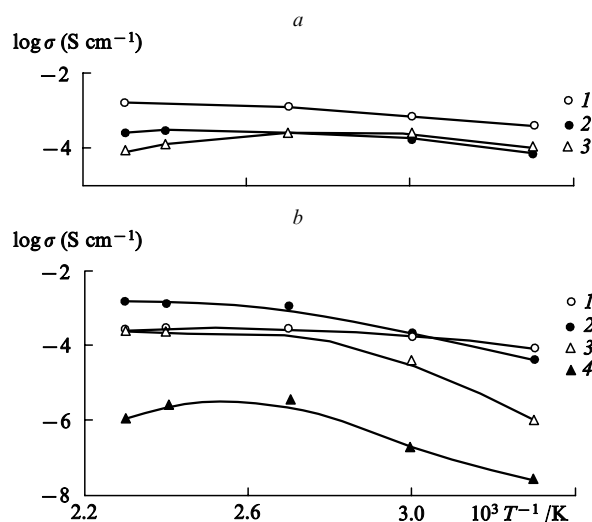


Figure 15. Temperature dependences of proton conductivity of PBI-PS films with the same water uptake (48%) and different degrees of sulfonation (a) and with the same degree of sulfonation (73.1%) and different water uptakes (b).⁷ (a): degree of sulfonation (mol.%): 49.3 (1), 61.5 (2) and 73.1 (3); (b): water uptake: 11.2 (1), 25.0 (2), 29.0 (3) and 48.0 (4).

Fig. 15. Hydrated PBI-PS exhibits a high proton conductivity at room temperature. The conductivity of a PBI-PS sample containing 3.1 H₂O molecules per SO₃H group reached 10^{-5} S cm⁻¹ at 80 °C and decreased slightly at higher temperatures due to a small loss of water (~ 10 mass %). The conductivity of a PBI-PS film containing more than 5.2 H₂O molecules per SO₃H group increased as the temperature increased and was as high as 10^{-3} S cm⁻¹ at temperatures above 100 °C. The proton conductivity of a PBI-PS film containing 11.3 H₂O molecules per SO₃H group was $\sim 10^{-3}$ S cm⁻¹.

The water uptake of PBI-PS films placed in an atmosphere with a relative humidity of 90% was comparable with that of Nafion membranes. The proton conductivity of Nafion membranes was as high as 10^{-3} S cm⁻¹ at room temperature; however, it decreased due to the loss of absorbed water at temperatures above 100 °C. In contrast to this, hydrated PBI-PS exhibited a high proton conductivity at temperatures above 100 °C.

The large water uptake and high proton conductivity of PBI-PS at temperatures above 100 °C are due to the specific properties of the polymer and the physical state of absorbed water.

The proton conductivity of benzyldisulfonated PBI at different values of relative humidity has been studied.¹⁰² It was found that the proton conductivity increases as the degree of substitution increases. The polymer with a 75% substitution level exhibited a conductivity of $\sim 10^{-2}$ S cm⁻¹ at 40 °C and a relative humidity of 100%.

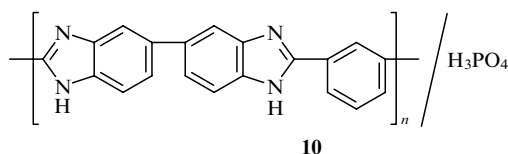
The results obtained in the above-mentioned studies suggest that alkylsulfonated aromatic polymer electrolytes exhibit sufficient thermal stabilities for fuel cell applications at 80 °C (a typical operating temperature for perfluorinated polymer electrolyte membranes). The water uptakes and proton conductivities of these polymers are close to the corresponding values for perfluorinated polymer electrolytes at temperatures below 80 °C but are larger than the latter at temperatures above 80 °C.

The absorbed water molecules are more strongly bound to alkylsulfonated rather than perfluorinated polymers. One can assume that this is related to the difference in the absorption mechanisms and to the physical state of the absorbed water in PBI-PS and perfluorinated polymer electrolytes.

IV. Proton-conducting electrolyte membranes based on acid–base polymer complexes

Proton-conducting membranes used in PEMFC operate under severe conditions (see above). Recently, complexes of basic polymers with strong acids have attracted a considerable interest. Such complexes are characterised by stable electrochemical properties and large water uptakes at high temperatures.

Recently, new proton-conducting polymer electrolyte membranes based on PBI–orthophosphoric acid complexes have been proposed for use in PEMFCs.^{103–106}



The most important advantages of this polymer electrolyte over perfluorinated polymer electrolytes and other acid–base polymer complexes are that PBI/H₃PO₄ possesses conductivity even at low activity of water and high thermal stability of these systems. The materials based on these complexes are expected to operate over a wide range from room to high temperature in both humid and dry gas. Such complexes are prepared by immersing PBI films into phosphoric acid solutions. In particular, the preparation of PBI–strong acid complexes by immersion of PBI films into solutions of strong acids in methanol was reported.^{107, 108} The absorption level of strong acid molecules increased with an increase in the concentration of the strong acid and reached up to 2.9 molecules per repeating unit for polymer complexes **10**. An IR spectroscopy study of the complexes revealed that the acid molecules, except for H₃PO₄, protonate the nitrogen atoms in the imidazole ring. Phosphoric acid (H₃PO₄) is incapable of protonating the imidazole groups in PBI but interacts with them *via* the formation of strong hydrogen bonds between NH and OH groups.

PBI films doped with phosphoric acid were prepared by immersion of PBI films in aqueous solutions of phosphoric acid for at least 16 h.^{103–106} Upon equilibration in an 11 M H₃PO₄ solution a doping level of ~5 phosphoric acid molecules per repeating unit of the polymer was achieved.

Anhydrous sulfonated aromatic polymers are highly brittle. Recently,¹⁰⁹ new materials with high mechanical strength were reported. They were prepared using polymer blending technique by combining PBI and sulfonated polymers (S-PEEK or *ortho*-sulfonated polysulfone **11**).

Such polymer blends exhibit high proton conductivities, moderate swelling values and high thermal stabilities. The specific interaction of SO₃H groups with basic nitrogen atoms was confirmed by FT-IR spectroscopy. The acid–base interaction between the sulfonated polymer and PBI provided a material with high mechanical strength and thermal stability.

The thermal stability of PBI–strong acid polymer complexes was studied by TGA and DTA. Figure 16 presents the TGA curves of polybenzimidazole and its complexes with strong acids. As can be seen, PBI exhibits an extremely high thermal stability over the entire temperature range. Small mass losses by all samples at temperatures below 200 °C are due to the loss of water and solvent present in the membranes.

Typical proton-conducting polymer electrolytes undergo considerable degradation in the temperature range under study.

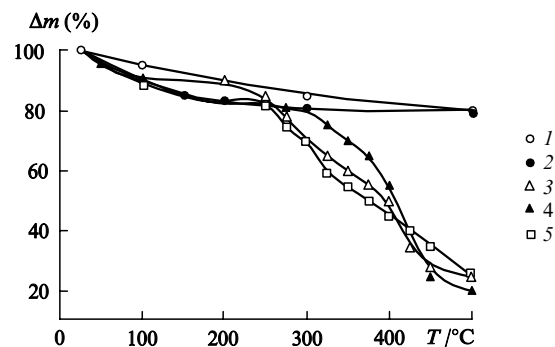
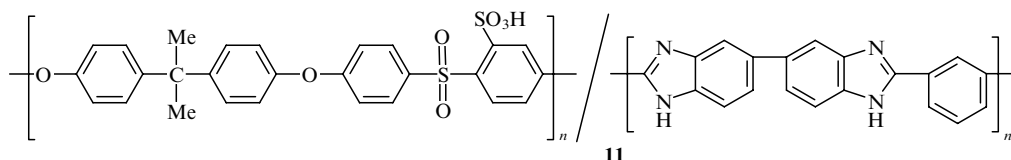


Figure 16. TGA curves of PBI (**1**) and its complexes with H₃PO₄ (**2**), H₂SO₄ (**3**), MeSO₃H (**4**) and EtSO₃H (**5**).⁷

A decrease in the degradation temperature of polymer complexes **10** was expected because of the complexation of acid molecules which easily corrode and oxidise the polymer macromolecules. However, no degradation was observed in nitrogen atmosphere. At the same time, thermal decomposition of PBI complexes with H₂SO₄, MeSO₃H and EtSO₃H begins at 330, 240 and 220 °C, respectively. After thermal decomposition of these polymer complexes in the temperature range 220–400 °C the residues were 50% of the initial masses of the samples. Therefore, complexation of PBI with H₂SO₄, MeSO₃H and EtSO₃H results in a loss of thermal stability. The decomposition of complexes is first of all due to elimination of acid molecules. This assumption was confirmed by the results of elemental analysis. At temperatures above 400 °C, the PBI chains gradually decompose under the action of high temperatures and strong acids.

Complexes **10** are thermally stable up to 500 °C. It was found that treatment of PBI with a phosphoric acid solution (27 mass %) improved the thermal stability of the polymer.¹¹⁰ This was associated with the formation of benzimidazonium cations. Samms *et al.*¹⁰⁴ studied the thermal stability of polymer complexes **10** and showed that these complexes are promising for use as polymer electrolytes in the hydrogen–air and methanol fuel cells. To simulate the operating conditions in a high-temperature PEMFC, the polymer complexes **10** were coated with platinum black, doped with phosphoric acid (4.8 H₃PO₄ molecules per repeating unit of PBI) and heated in an atmosphere of nitrogen and 5% hydrogen or in air in a TGA analyser. The degradation products were identified by mass spectrometry. In all cases the mass loss below 400 °C was found to be due to the loss of water. In addition, it was found that polymer complexes **10** coated with platinum black are thermally stable up to 600 °C.

Variation of the conductivity of polymer complexes **10** as a function of water vapour activity, temperature and acid doping level was studied.¹⁰⁶ It was shown that the conductivity of heavily doped complexes (500 mol.%) is nearly twice as high as that of the film doped to 338 mol.% at the same temperature and humidity. For instance, the conductivity of PBI doped with 500 mol.% H₃PO₄ (5 H₃PO₄ molecules per repeating unit of PBI) is 3.5×10^{-2} S cm⁻¹ at 190 °C and a water vapour activity of 0.1.

Raising the temperature and water vapour activity causes an increase in the conductivity of the polymers irrespective of the doping level of PBI with phosphoric acid. In addition, it was found that crossover of methanol molecules through the polymer complexes **10** is by an order of magnitude smaller than in the case of

perfluorinated polymer electrolytes and that the mechanical strength of such complexes is three orders of magnitude higher compared to that of Nafion membranes.

The proton conductivity of PBI polymer complexes prepared by the interaction of PBI with methanol solutions of strong acids was studied.⁷ The temperature dependences of the conductivities of anhydrous PBI–strong acid polymer complexes are shown in Fig. 17a.

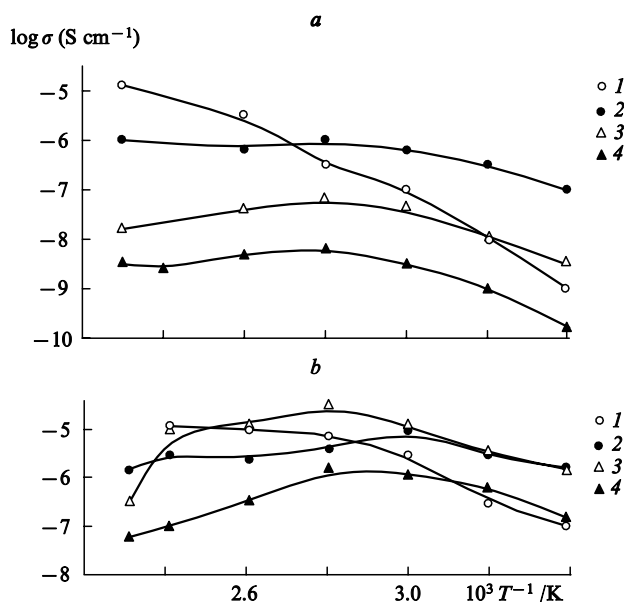


Figure 17. Temperature dependence of proton conductivity of anhydrous (a) and hydrous (b) PBI complexes with H_3PO_4 (1), H_2SO_4 (2), EtSO_3H (3) and MeSO_3H (4);⁷ (a): doping level, acid molecules per PBI unit: 2.0 (1), 1.8 (2), 2.0 (3), 1.9 (4); (b): water uptake (mass %): 13 (1,4), 19 (2) and 26 (3).

All anhydrous polymer complexes of PBI with strong acids possess a proton conductivity of the order of 10^{-6} – 10^{-9} S cm^{-1} at 100 °C. The conductivity of polymer complexes **10** can be as high as 10^{-5} S cm^{-1} at 160 °C, whereas other PBI–acid complexes showed a decrease in the conductivity at temperatures above 80 °C. These results point to high thermal stability of polymer complexes **10**.

To prepare hydrated systems, the films of PBI–strong acid polymer complexes were placed in a desiccator with a relative humidity of 90% for 72 h. The water uptakes of the complexes were 13 mass %–26 mass %. The proton conductivity of the hydrous PBI–strong acid polymer complexes was found to be nearly an order of magnitude higher than the conductivity of anhydrous polymer complexes (Fig. 17b). This difference can be explained by the improvement of charge carrier generation in the absorbed water. Changes in the proton conductivity at room temperature are especially remarkable. Figure 18 presents the temperature dependences of the conductivity of anhydrous complexes **10** with different acid contents. As can be seen, the conductivity of polymer complexes **10** increases with the concentration of H_3PO_4 .

The temperature dependence of the conductivity of polymer complexes **10** is quite different: in this temperature range the conductivity is low. This suggests that two H_3PO_4 molecules quantitatively react with the PBI units containing two imidazole groups. As a consequence, an excess of H_3PO_4 determines the necessary proton conductivity. A study of PBI/ H_3PO_4 polymer complexes by FT-IR spectroscopy showed that the spectra exhibited three characteristic absorption maxima near 1090 cm^{-1} (HPO_4^{2-}), 1008 cm^{-1} (POH) and 970 cm^{-1} (H_2PO_4^-).^{111–114} As

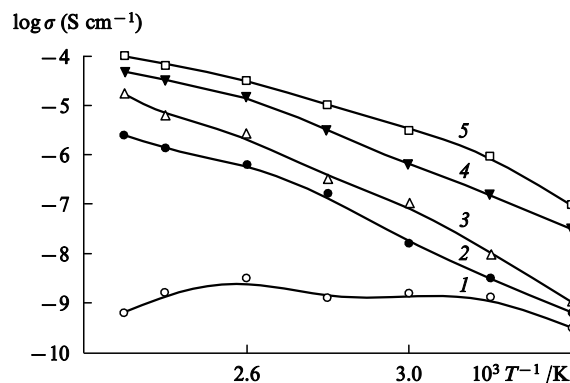


Figure 18. Temperature dependences of proton conductivity of anhydrous PBI/ H_3PO_4 complexes containing 1.4 (1), 2.0 (2), 2.7 (3), 2.3 (4) and 2.9 (5) H_3PO_4 molecules per PBI unit.⁷

the concentration of H_3PO_4 increases, the intensity of the absorption maxima of HPO_4^{2-} and H_2PO_4^- increases. This suggests that proton conductivity can occur by the Grotthuss mechanism¹¹⁵ involving an exchange of protons between H_3PO_4 and PO_4^{3-} or H_2PO_4^- .

V. Fuel cell applications of proton-conducting membranes based on aromatic condensation polymers

Two blend polymer electrolytes containing acid and basic functional groups (90 mass % PEEK and 10 mass % PBI or 95 mass % PES and 5 mass % PBI) were applied in H_2/O_2 fuel cells. The current-*vs.*-voltage curves of the membranes in the fuel cells were comparable with that of Nafion 112 membranes.¹⁰⁹

Fuel cell tests of membranes based on sulfonated PES showed⁷ a cell voltage of 550 mV at a current density of 700 mA cm^{-2} (atmospheric pressure, humidified gases, 70 °C). No significant loss of membrane performance was observed after long-term operation (1000 h) under fuel cell conditions.

The maximum power of fuel cells with S-PPBP membranes reaches 0.3 W cm^{-2} at a current density of 800 mA cm^{-2} . The conductivity of the electrolyte membranes was 3×10^{-3} S cm^{-1} ; the membrane thickness and surface area were 0.01 cm and 3.15 cm^2 , respectively.

The maximum power of fuel cells H_2/O_2 and $\text{CH}_3\text{OH}/\text{O}_2$ with membranes based on polymer complexes **10** (see Ref. 7) was as high as 0.25 W cm^{-2} at a current density of 700 mA cm^{-2} . The electrical resistance of electrolyte membranes was 0.4 Ω , the thickness and surface area of the membranes were 0.01 cm and 1 cm^2 , respectively, and the doping level was 500 mol.%. The measured electrical resistance of the cell was equivalent to a conductivity of 0.025 S cm^{-1} . It was found that the electrical resistance of the fuel cell is independent of the water content in the gas (water produced at cathode is sufficient for maintaining the necessary conductivity of the electrolyte). This type of fuel cells was characterised by continuous operation at a current density of 200 mA cm^{-2} over a period of 200 h (and for longer times) without reduction of the membrane performance.

The power of $\text{CH}_3\text{OH}/\text{O}_2$ fuel cells at 200 °C and atmospheric pressure reached 0.1 W cm^{-2} at a current density of 250–500 mA cm^{-2} . The conductivity of membranes operating under these conditions remained constant in the temperature range 30–140 °C.

* * *

To summarise, the aforesaid shows that the aromatic condensation polymers can be thought to be candidates for fuel cell

applications: the structure of ACP-based polymer electrolytes can be modified with ease; these polymer electrolytes possess large water uptakes and high proton conductivities at high temperatures and low humidities, as well as sufficient thermal and chemical stability. Further investigations to design proton-conducting materials exhibiting long-term thermal stability and mechanical strength, capable of operating at high temperatures without humidification and further improvement of fuel cells are required.

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^a — *Polym. Sci. (Engl. Transl.)*

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

Chemical modification of electrolytes for lithium batteries

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Abstract. Modern approaches to modifying chemically electrolytes for lithium batteries are analysed with the aim of optimising the charge-transfer processes in liquid-phase and solid (polymeric) media. The main regularities of transport properties of lithium electrolyte solutions containing complex (encapsulated) ions in aprotic solvents and polymers are discussed. The prospects for the development of electrolytic solvosystems with the chain (ionotropic) mechanism of conduction with respect to lithium ions are outlined. The bibliography includes 126 references.

I. Introduction

Direct energy conversion from chemical to electrical forms is a central problem of modern science and technology. At present, active research is carried out on the development of primary and secondary lithium cells with characteristics (high energy density, low self-discharge rate, applicability at low temperatures, high reliability, *etc.*) that should surpass those of traditional electrochemical systems^{1–6} and displace them in future. The research on lithium chemical power sources (CPS) was, first of all, stimulated by the progress in such industrial fields as electronics, new communication systems and transport (electrical vehicles). Lithium cells and rechargeable batteries are increasingly applied as autonomous power sources in various domestic, medical and computer devices. Special-purpose lithium CPS are used in night-vision devices, guidance systems, space equipment, and new weapon systems. At present, the yearly production of lithium CPS for special equipment and military branches is ~ 30 million cells, which is 3–4 times higher compared with other industrial branches.⁷

Elaboration of highly efficient lithium CPS is largely aimed at the development of electrolytic systems with high conductivities (10^{-3} – 10^{-2} S cm⁻¹) in a wide temperature range (from –50 to +70 °C) and chemical and electrochemical stabilities with respect to lithium and cathodic materials. Such systems should also enable sufficiently fast and reversible electrode processes. Insufficient conductivity of liquid-phase and, particularly, solid poly-

meric lithium electrolytes is a key factor impeding the development of CPS with lithium electrodes.^{8–11} The importance of solving this problem is determined by the fact that the internal resistance of a power source directly governs its main performance characteristics such as the power density and the discharge current.

Most approaches to choosing optimum electrolytic compositions for lithium CPS were based on theoretical concepts of the ion-migration mechanism of charge transfer.^{12–14} Hence, the aim of the latest studies was to create such conditions that would both enhance the migration rates of electrolyte ions as the main charge carriers in solution and in polymers and increase their concentrations. For this purpose, mixed low-viscosity solvents with sufficiently low dielectric constants were used as the electrolytic systems, macrocyclic ligands which can encapsulate lithium cations and different anions were added, lithium salts with low lattice energies which involve large anions with delocalised charges were synthesised, *etc.* It is known that a chain (prototropic) mechanism of conduction is brought about in aqueous solutions of acids and bases used as the electrolytes for traditional CPS, which is responsible for the conductivities of these solutions being 1–2 orders of magnitude higher as compared with solutions with the migration mechanism of charge transfer. It is also known that the ionotropic mechanism of charge transfer can involve not only protons in water and protic solvents but also some other ions in aprotic media. In this connection, the latest studies have considered a possibility of developing highly conductive nonaqueous electrolytes with a conduction mechanism different from the ion-migration one, as well as designing CPS based on such electrolytes with improved performance characteristics.

This survey analyses and generalises the results of studies published in the past 10–15 years and devoted to modifying chemically the conventional electrolytes applied in lithium CPS with the aim of optimising the charge transfer processes in liquid-phase and solid (polymeric) media. The analysis was carried out from the standpoint of dividing the electrolytes according to their phase compositions, *viz.*, liquid-phase and solid (polymeric) electrolytes. The latter type traditionally involves biphasic electrolytes, *i.e.*, gels, composites, *etc.* The survey also includes new systems which do not fit the traditional classification (*e.g.*, electrolytes with polymeric anions and ionic liquids). That is why it seemed reasonable to analyse the results of studies of different polymeric electrolytes according to the examples of concrete chemical modifications that were most interesting from our viewpoint, rather than to consider in detail the classes of electrolytes.

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II. Liquid-phase electrolytes

The main factors that affect the charge migration rate in electrolytes are the solvent viscosity and the processes of solvation and association. One of the first approaches to optimising electrolytic systems in lithium CPS consisted in the use of complex lithium compounds with low lattice energies, which involve weakly solvated and easily polarisable anions. This provided solutions with enhanced conductivities and higher concentrations of electrolyte ions. Within this approach, lithium electrolytes with coordinatively saturated fluorine-containing anions AsF_6^- , PF_6^- , BF_4^- and also with ClO_4^- , Ph_4B^- , all of which exhibited sufficiently high electrochemical stability, were extensively used.^{2, 8–11, 15–17} Moreover, the use of fluorine-containing salts allowed one to reduce the corrosion of cathodes with aluminium current leads at high positive potentials. However, the performance of power sources with the electrolytes mentioned entailed quite a number of problems. For example, lithium perchlorate is thermally unstable, and its solutions are explosive, especially, in ether-like solvents; lithium hexafluorophosphate can decompose in solution to give poorly soluble lithium fluoride and a Lewis acid PF_5 , which initiates polymerisation of cyclic ethers; hexafluoroarsenate ions are reduced electrochemically to give AsF_5 and As^0 which are environmentally hazardous; lithium tetrafluoroborate solutions do not provide a sufficient conductivity level and, moreover, BF_4^- ions initiate polymerisation of cyclic ethers. Therefore, the search for new lithium electrolytes which would exhibit better compatibility with solvents and electrode materials is still in progress.

Lithium salts with anions such as CF_3SO_2^- , $\text{B}_{10}\text{Cl}_{10}^-$, $\text{B}_{12}\text{Cl}_{12}^-$ and BMe_4^- turned out to be more stable but their solutions possessed low conductivities. Recently, new lithium electrolytes with large anions and minor polarisability have been proposed: $\text{Li}[(\text{CF}_3\text{SO}_2)_2\text{N}]$ (**1**) and the corresponding cyclic imides $\text{Li}[\text{N}(\text{SO}_2)(\text{CF}_2)_n(\text{SO}_2)]$ ($n = 1–3$) (**2**), lithium methanide $\text{Li}(\text{CF}_3\text{SO}_2)_3\text{C}$ (**3**), the family of lithium chelatoborates of the general formula $\text{Li}[\text{BR}_2]$ (**4–6**) (where bidentate ligands **R** are aliphatic or aromatic diols), and the corresponding lithium phosphates $\text{Li}[\text{PR}_3]$ which are highly stable chemically and electrochemically, well soluble ($> 1 \text{ mol litre}^{-1}$) and weakly associated.^{9, 18–25} The charge distribution in anions strongly affects the electrolyte association. With addition of electron-acceptor substituents such as F, CF_3 , COOR, SO_2OR and nitrogen atoms, which can delocalise the negative charge in anions, the association constants of lithium electrolytes decreased by several orders of magnitude. The effects mentioned favour the increase in the conductivity and extend the electrochemical window of solvents. Thus the specific conductivity of 1 M solutions of lithium

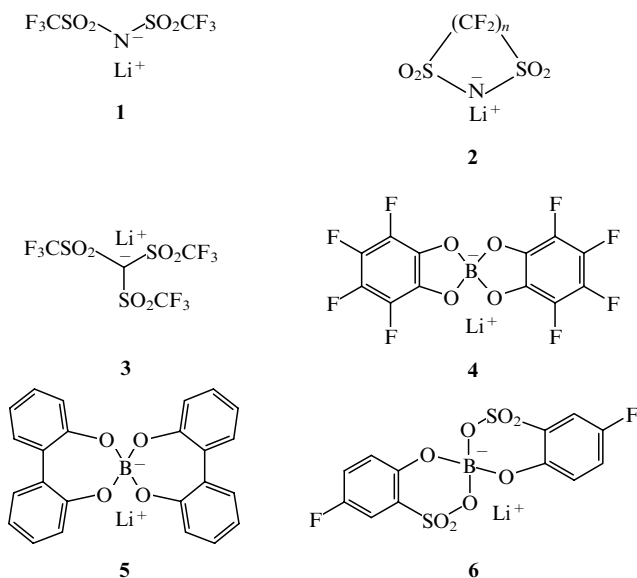
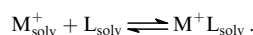
chelatoborates $\text{Li}[\text{B}(\text{C}_6\text{H}_x\text{F}_{4-x}\text{O}_2)_2]$ ($1 < x < 4$) in 1,2-dimethoxyethane (DME) increased by a factor of 4.4 at 25 °C and by a factor of 2.4 at –45 °C with substitution of fluorine atoms for four hydrogen atoms. A linear correlation between the limiting potentials of anodic oxidation of lithium borates and the energies of higher occupied molecular orbitals of anions, which was estimated using semiempirical quantum-mechanical methods AM1 and MNDO,^{9, 19} indicates that the electrochemical stability of these electrolytes depends on the degree of delocalisation of the negative charge in anions.

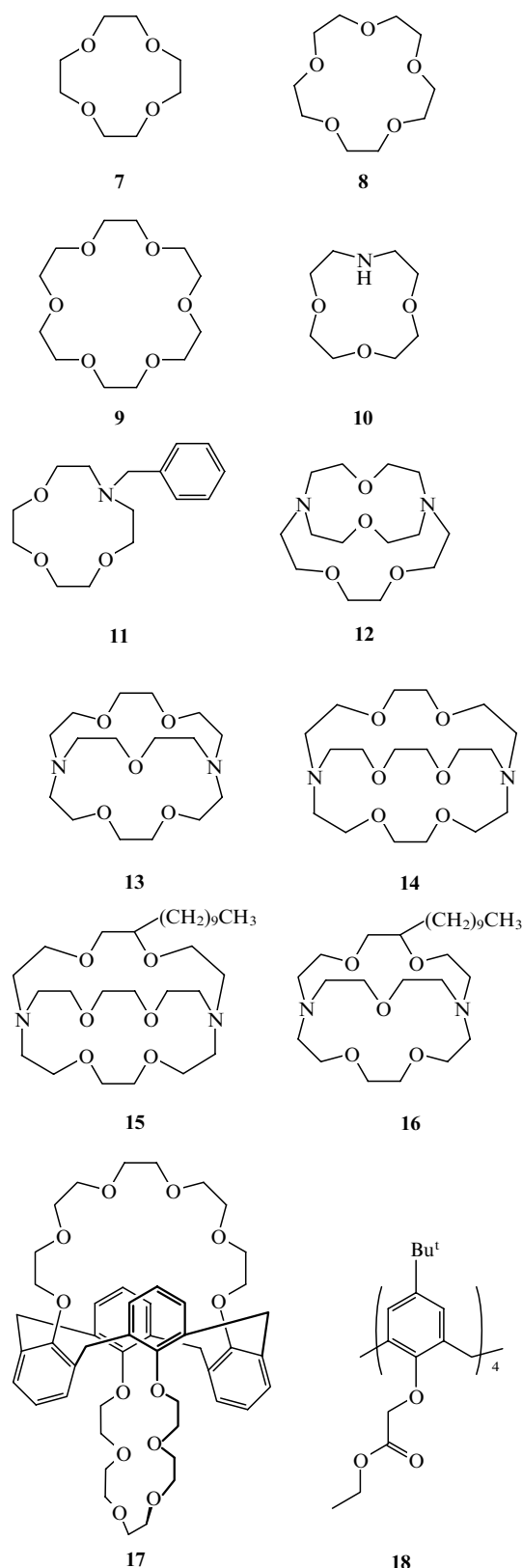
Lithium CPS most often employ cyclic and linear ethers and esters, *viz.*, DME, propylene carbonate (PC), γ -butyrolactone (γ -BL), tetrahydrofuran (THF) and inorganic sulfur compounds (SO_2 , SOCl_2 , SO_2Cl_2) as the solvents.^{2, 26–28} Solutions of lithium salts in such solvents demonstrated sufficiently high conductivities but often exhibited an enhanced activity with respect to both the lithium anode and cathodes. To enhance the stability of electrode materials, it was proposed to add dialkyl carbonates to solutions. In this case, due to a protective film formed on the anode and consisting mainly of solvent oxidation products, the cycling stability substantially increased. At present, the electrolytes for lithium power sources involve, as a rule, binary and ternary compositions based on PC or ethylene carbonate with addition of a certain low-viscosity solvent (DME, THF, *etc.*). At low temperatures, mixed solvents with low viscosities and sufficiently high dielectric constants proved to be most efficient.^{9, 10} Moreover, the possibility of using certain strongly associated and sufficiently viscous liquids, *viz.*, sulfones,^{29–31} sulfamides $\text{R}^1\text{R}^2\text{NSO}_2\text{NR}^3\text{R}^4$ and glymes (dimethyl ethers of polyethylene glycol) $\text{CH}_3\text{O}(\text{CH}_2\text{CH}_2\text{O})_n\text{CH}_3$ (see Refs 32–34), which allow preparing solutions of lithium salts with conductivities of an order of magnitude of $(0.8–2.5) \times 10^{-3} \text{ S cm}^{-1}$, was discussed.

1. Electrolytes with molecularly encapsulated lithium ions

The maximum conductivity and prevention of concentration polarisation during the discharge, were achieved if concentrated (1.5–3 M) electrolyte solutions were used in lithium CPS. However under these conditions, many lithium salts in solvents of low and medium dielectric constants dissociated incompletely to form ion pairs and other associates which cannot conduct current.³⁵ Insufficient solubility of lithium electrolytes also limited their practical application. The solubility and conductivity of lithium electrolytes could be enhanced by introducing macrocyclic compounds which contain oxygen or nitrogen atoms possessing appreciable affinity towards lithium ions into solutions. Several groups of mono- and bicyclic oxo- and aza(oxo)-ligands which form stable lithium complexes with the 1:1 composition are known. These comprise crown ethers: 12-crown-4 (**7**), 15-crown-5 (**8**), 18-crown-6 (**9**), 1,4,7-trioxo-10-azacyclododecane (**10**), *N*-benzyl-1,4,7-trioxo-10-azacyclododecane (**11**), *etc.*; cryptands: cryptand 211 (**12**), cryptand 221 (**13**), cryptand 222 (**14**); cryptand 222D (**15**), cryptand 221D (**16**), *etc.*; calixarenes: 25,27,26,28-bis[1,4,7,10,13,16-hexaoxa(hexadecamethylene)]calix-[4]arene (**17**), 4,10,16,22-tetra-*tert*-butyl-25,26,27,28-tetrakis-(ethoxycarbonylmethoxy)calix[4]arene (**18**), *etc.*^{36–43} Tricyclic ligands with cylindrical cavities can also form binuclear complexes with the composition 2:1 at high $\text{Li}^+ : \text{L}$ ratios.⁴²

Among all macrocyclic compounds known, cryptands form the most stable inclusion complexes (cryptates) with alkali metal ions. Such ligands have a spheroidal cavities that can encapsulate cations of suitable sizes, virtually screening the latter from interactions with solvent molecules and counterions.^{36, 37, 43–63} Due to their unique complexing properties, cryptands and crown-ethers favour the dissolution of metal salts and weaken their association in low-polarity media. The solubility increases due to a decrease in the free energy of ions as a result of their encapsulation in the ligand's internal cavity



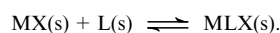


This effect and the solvation of hydrophobic groups of the ligand by organic solvent molecules compete with the increase in the free energy of ions as their radii increase upon complexing. By the example of cryptand **14**, it was shown that complexing of salts with macrocyclic ligands results in a decrease in the solubility of salts well soluble in this solvent and its increase for poorly soluble salts. For a given cryptate salt, the solubility increased with the transition to less polar media in which this salt is more strongly associated.

Table 1. Standard enthalpies of formation for lithium electrolytes in acetonitrile (AN) and propylene carbonate (PC) at 298.15 K.^{45–49}

Electrolyte	ΔH° /kJ mol ^{−1}	
	AN	PC
LiBF ₄	−14.57	−15.55
[Li(7)]BF ₄	4.74	9.69
[Li(8)]BF ₄	4.18	7.29
[Li(10)]BF ₄	0.85	3.73
[Li(11)]BF ₄	11.33	12.35
[Li(14)]BF ₄	6.7	—
[Li(18)]BF ₄	−21.0	—
LiClO ₄	−43.26	—
[Li(7)]ClO ₄	1.27	6.51
[Li(11)]ClO ₄	10.23	9.62
[Li(14)]ClO ₄	20.9	—
[Li(18)]ClO ₄	−9.17	—
LiCF ₃ SO ₃	−15.99	−12.50
[Li(7)]CF ₃ SO ₃	15.69	—
[Li(8)]CF ₃ SO ₃	9.17	13.34
[Li(10)]CF ₃ SO ₃	14.66	18.74
[Li(11)]CF ₃ SO ₃	18.96	22.50
[Li(14)]CF ₃ SO ₃	18.4	—
[Li(18)]CF ₃ SO ₃	−14.0	—
LiAsF ₆	−18.45	−15.14
[Li(7)]AsF ₆	7.17	14.92
[Li(8)]AsF ₆	10.62	13.19
[Li(10)]AsF ₆	3.72	4.84
[Li(11)]AsF ₆	8.75	13.91
[Li(18)]AsF ₆	−22.5	—

The strategy of choosing complex electrolytes for lithium CPS, which has been put forward in Refs 45–49, is based on studying the processes of complex formation and solvation in lithium salt solutions. The experimentally determined enthalpies of dissolution ΔH° for a number of lithium electrolytes in acetonitrile and PC (Table 1) showed that, as a rule, a lithium ion in the free state is much more strongly solvated ($\Delta H^\circ < 0$) than that incorporated into a complex with macrocyclic ligands ($\Delta H^\circ > 0$). A decrease in the degree of solvation due to complexing, which leads to an increase in the conductivity, was observed in less polar media. A number of lithium electrolytes with complex cations involving crown ethers, cryptands and calix[4]arenes as the ligands were isolated as solids. Studies of solvation of simple (M^+X^-) and complex ($[ML]^+X^-$) electrolytes as well as ligands (L) allowed the estimating of the changes in the enthalpy for solid-state complexing processes



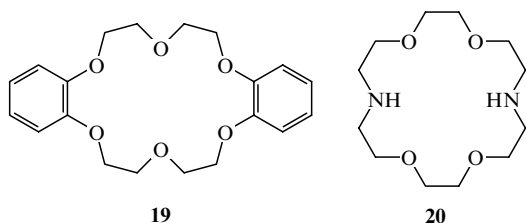
These values can be considered as the characteristics of complex formation in media with low dielectric constants.^{45–49} As was shown, the association of a complex cation with an anion in cryptand-containing solid electrolytes is weaker as compared with electrolytes containing crown ethers and calixarenes. For lithium salts (LiX), the coordination process becomes less exothermic with a decrease in the polarisability in the following sequence of anions: $I^- > ClO_4^- > Br^- > CF_3SO_3^- > AsF_6^- > BF_4^-$. In propylene carbonate at 298.15 K, the complexing of Li^+ with crown ethers resulted in a substantial increase in the ionic mobility (Table 2). Similar results were obtained for lithium complexes with **9** in PC and 2-cyanopyridine and complexes with **9** and **14** in a PC–dichloromethane mixed solvent.^{50,51}

Studies of the molar conductivity (Λ) of a 1 M LiBF₄ solution in γ -BL as a function of the [L]:[LiBF₄] ratio [L designates crown ethers **8** and **9** and dibenzo-18-crown-6 (**19**)] have shown⁵² that Λ increases with an increase in the crown ether content and reaches its maximum at the equimolar ratio. An electrolyte based on crown ether **8** which forms the most stable complex with a lithium

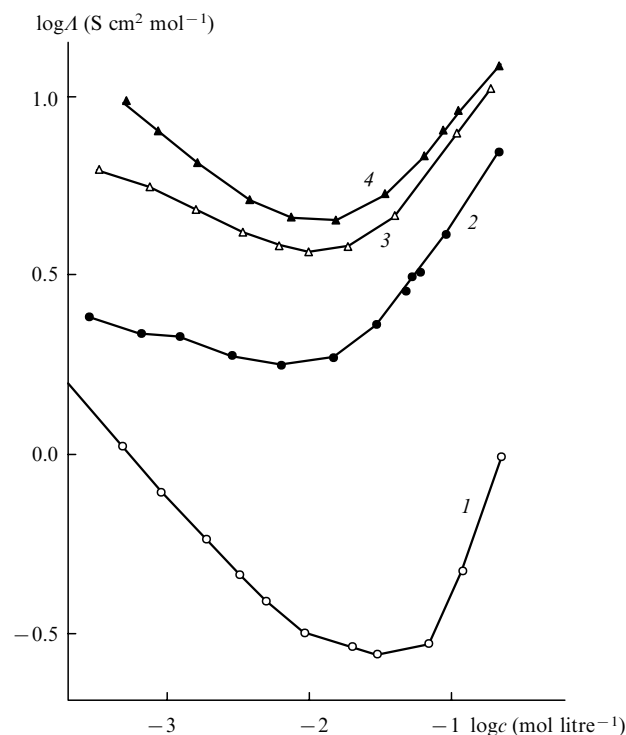
Table 2. Limiting mobility ($S\text{ cm}^2\text{ mol}^{-1}$) of Li^+ and $[\text{LiL}]^+$ cations at 298.15 K.

Cation	A_{LiL^+}	Ref.	Cation	A_{LiL^+}	Ref.
Solvent — PC			Solvent — nitromethane		
Li^+	7.86	46	Li^+	41.4	58
$[\text{Li}(\mathbf{7})]^+$	10.02	46	$[\text{Li}(\mathbf{8})]^+$	29.3	58
$[\text{Li}(\mathbf{8})]^+$	10.50	46	Solvent — AN		
$[\text{Li}(\mathbf{9})]^+$	8.41	50	Li^+	69.5	64
$[\text{Li}(\mathbf{10})]^+$	10.25	46	$[\text{Li}(\mathbf{7})]^+$	68.68	61
$[\text{Li}(\mathbf{11})]^+$	11.99	46	$[\text{Li}(\mathbf{8})]^+$	65.10	61
Solvent — methanol			$[\text{Li}(\mathbf{13})]^+$	63.20	64
Li^+	39.61	62	$[\text{Li}(\mathbf{14})]^+$	60.0	64
$[\text{Li}(\mathbf{7})]^+$	37.53	61	$[\text{Li}(\mathbf{15})]^+$	45.6	64
$[\text{Li}(\mathbf{8})]^+$	38.20	61	$[\text{Li}(\mathbf{16})]^+$	45.1	64
$[\text{Li}(\mathbf{14})]^+$	38.60	62			

ion exhibited the maximum conductivity ($1.1 \times 10^{-2}\text{ S cm}^{-1}$). The use of **8** enhanced the battery power. A possibility of using substances capable of forming charge-transfer complexes (CTC) as the functional additives to electrolytes was also considered.⁵² It was found that for solutions containing CTC of metal lithium with hexamethylphosphoric triamide (HMPA) $\text{Li}^+[(\text{CH}_3)_2\text{N}]_3\text{PO}^-$ in γ -BL (lithium was added in excess, the ratio $[\text{HMPA}]:[\gamma\text{-BL}] = 1:2$), the conductivity increased by three orders of magnitude as compared with the initial solution without CTC and reached $4.2 \times 10^{-2}\text{ S cm}^{-1}$. The potential drop vs. current density dependence has shown that the transport properties of a complex electrolyte are better compared with the ordinary one. It was assumed that in the presence of CTC in solution the charge transfer can be realised by the chain mechanism, where the discharge of an ion is not preceded by its desolvation.



Most of the studies observed a correlation between the stability of complex lithium ions and the increase in the conductivity of the solution. Thus it was found⁵³ that the addition of crown ethers **7** and **9** to LiAsF_6 solutions in DME and **9** to LiClO_4 solutions in DME has practically no effect on the conductivity in the range of salt concentration from 10^{-4} to $5 \times 10^{-2}\text{ mol litre}^{-1}$. The result obtained can be explained by the weak interaction between lithium ions and ligands due to strong solvation of ions by the solvent molecules with the chelate structure. The addition of crown ethers to NaClO_4 solutions in DME resulted in formation of more stable complexes of sodium ions with ligands, thus decreasing the electrolyte association and increasing its conductivity. For more strongly associated electrolytes, the addition of macrocyclic ligands led to a greater increase in conductivity as compared with less associated electrolytes. For instance, the molar conductivity of a LiClO_4 solution in a cyclic ether, namely, 1,3-dioxolane, in the absence of macrocyclic compounds was lower as compared with its solutions in DME due to the stronger association of the salt in the former case. At the same time, the conductivities of 1,3-dioxolane solutions of LiClO_4 containing equimolar additions of **7–9** with $c_{\text{LiClO}_4} > 10^{-3}\text{ mol litre}^{-1}$ were substantially higher compared with DME solutions. The greatest increase in conductivity was observed upon addition of crown ether **8** (Fig. 1). It was concluded⁵⁴ that the extent of the complex-

**Figure 1.** Dependence of the molar conductivity of LiClO_4 and LiClO_4 + crown-ether (1 : 1) solutions in 1,3-dioxolane on the salt concentration at 298 K:⁵⁴ (1) LiClO_4 , (2) LiClO_4 + **7**, (3) LiClO_4 + **9**, (4) LiClO_4 + **8**.

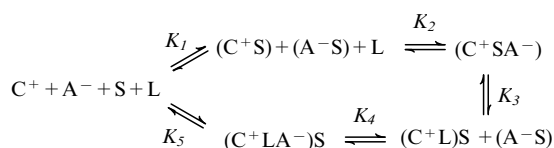
ing-induced increase in conductivity should be directly proportional to the increase in the solution dielectric constant (ϵ) observed in low-polar media due to the higher dipole moments of ion pairs comprising complex cations as compared with ordinary ion pairs.

Conductometric and spectroscopic studies of dissociation of salts $[\text{LiL}]^+[\text{ZPh}_3]^-$ and $[\text{LiL}]^+[\text{A}]^-$ ($\text{Z} = \text{C, Ge and Sn}$, **L** is cryptand **12** and **A** is an anion of a CH-acid) in solvents of low polarity have shown that the introduction of a cryptand to solutions of organolithium compounds resulted in the formation of 'cryptand-separated' ion pairs with light absorption maxima independent of the solvent nature.^{55,56} In nonpolar solvents, the ion pairs comprising anions with strongly delocalised charges (Ph_3C^-) were less strongly associated. In more polar media, the inverse order of anion stability (with respect to ion pairs) due to the stronger ion–dipole interaction of localised charges with solvent molecules was found. Thus, in polar solvents, the electrolytes with charges localised on anions are associated to a lesser degree.

For lithium salts containing anions of CH-acids with strongly delocalised charges, the dissociation constants (K_d) remained virtually unchanged with the formation of cryptates. The degree of association changed only for salts containing anions with localised charges. On going from THF ($\epsilon = 7.6$, $K_d = 10^{-6}\text{ mol litre}^{-1}$) to cyclohexylamine ($\epsilon = 4.7$), and *N*-methylmorpholine, the dissociation constants of cryptate-containing ion pairs decreased by 3–4 orders of magnitude, whereas the transition to benzene ($\epsilon = 2.3$) resulted in their decrease by 9 orders of magnitude. Moreover, the constants depended linearly on the reciprocal dielectric constant of the medium.

A series of studies^{57–64} dealt with conductivity of lithium salts in media with similar dielectric constants, viz., acetonitrile (AN) and dimethylformamide (DMF), methanol and nitromethane (NM), with the aim of elucidating how the molecular structure of the solvent and the presence of macrocyclic ligands affect the transport properties of solvents. It was shown that the limiting

molar conductivity (Λ_0) of a complex electrolyte [LiL]Pi [L is diaza-18-crown-6 (**20**), Pi is picrate ion] in AN is smaller than Λ_0 of a simple LiPi salt. However, with an increase in the LiPi concentration (at the constant L concentration of 10.2×10^{-3} mol litre $^{-1}$), the molar conductivity of an electrolyte containing **20** became higher than without this additive. At a constant salt concentration, the molar conductivity increased with an increase in the L concentration. At the same time, the molar conductivity of KPi in AN with addition of **20** ($c_{20} = 5.2 \times 10^{-3}$ mol litre $^{-1}$) was lower and decreased with an increase in the ligand content.⁵⁷ The results obtained were analysed with account of the following equilibria:



where C is the solute, A is a counterion, S is a solvent molecule and L is a ligand.

Assuming that $K_2 > K_5$ and taking into account the strong association of LiPi in acetonitrile ($K_5 = 10^3$ kg mol $^{-1}$), the increase in conductivity can be explained by dissociation of nonconducting ion pairs, which is caused by complex formation (K_2). For KPi, it was concluded that equilibria 3, 4 and 5 weakly affect equilibria 1 and 2 due to insignificant association of the salt ($K_5 = 77$ kg mol $^{-1}$). It was also found that the addition of L to solutions of KPi and LiPi in MeOH did not affect the value of Λ due to the specific solvation of the ligand by solvent with the formation of H bonds. However, upon addition of an alkyl-substituted diazacrown ether RL (R = Alk), which can form complexes with cations, the conductivity of solutions decreased. The addition of crown ether **8** to LiPi and LiClO $_4$ solution in MeOH and DMF, in which these electrolytes are weakly associated, did not affect the value of Λ . For strongly associated LiPi and LiClO $_4$ in AN and NM (Fig. 2), the introduction of macro-

cyclic ligand **8** enhanced the conductivity, decreased the association constants, and made the decay in Λ which occurs with an increase in electrolyte concentration less pronounced.^{58, 59} In an AN + NM mixed solvent, the association constants were practically independent of its composition (as might be expected for isodielectric systems); in the absence of **8**, the values of constants substantially differed from one another and depended nonlinearly on the mixed solvent composition.⁶⁰

Studies of the molar conductivity of solutions of lithium, sodium and potassium perchlorates in MeOH and AN containing crown ethers **7**, **8** and cryptands **13**, **14** have shown that the association constants, mobilities and Stokes radii of [ML] $^+$ complex ions are practically independent of the nature of the metal ion involved. As a rule, the association constants for complex ions were lower compared with 'free' ions; however, $\Lambda_0([ML]^+X^-) \leq \Lambda_0(MX)$ (Table 3).^{61–64} It was assumed that the formation of complexes levels off the differences in the degrees of solvation, charge densities and sizes of complex ions, so that their mobilities depend solely on the size of the ligand attached. A deviation from this rule observed for large cryptate ions was attributed to the changes in their degrees of solvation, because for 'free' alkali ions Λ_0 increases as their solvation weakens

Table 3. Molar conductivity values at infinite dilution and association constants for lithium electrolytes at 298.15 K.

Electrolyte	$\Lambda_0 / S \text{ cm}^2 \text{ mol}^{-1}$	$K_a / \text{litre mol}^{-1}$	Ref.
Solvent — AN			
LiClO $_4$	173.22±0.02	23±0.3	59
[Li(7)]ClO $_4$	172.30±0.01	7.97±0.01	61
[Li(8)]ClO $_4$	166.2±0.2	15±1	61
[Li(13)]ClO $_4$	167.01±0.01	8.81±0.04	64
[Li(14)]ClO $_4$	163.66±0.01	5.2±0.1	64
[Li(15)]ClO $_4$	149.41	15.90±0.06	64
[Li(16)]ClO $_4$	148.89	13.77±0.07	64
[Li(17)]ClO $_4$	127.67	16.98	52
Solvent — nitromethane			
LiClO $_4$	110.6±0.2	205±2	60
[Li(8)]ClO $_4$	97.03±0.2	13.1±0.3	60
LiPi	86.4	1.6×10^6	60
[Li(8)]Pi	73.31±0.06	84.7±0.5	60
Solvent — DMF			
LiClO $_4$	73.34±0.04	9±1	59
[Li(8)]ClO $_4$	70.32±0.2	10±1	59
LiPi	58.33±0.05	12	59
[Li(8)]Pi	57.9±0.2	16±1	59
Solvent — methanol			
LiClO $_4$	110.52±0.03	25±1	59
[Li(7)]ClO $_4$	108.50±0.03	7.967±0.001	61
[Li(8)]ClO $_4$	109.17±0.02	2.4±0.004	61
[Li(14)]ClO $_4$	109.55±0.05	15±2	63
[Li(17)]ClO $_4$	97.18	13.97	62
Solvent — PC			
LiClO $_4$	26.75	1.2	50
[Li(7)]ClO $_4$	28.91	—	46
[Li(9)]ClO $_4$	27.30	—	50
[Li(17)]ClO $_4$	23.52	0.48	62
LiBF $_4$	28.57	0.29	46
[Li(8)]BF $_4$	31.06	—	46
[Li(10)]BF $_4$	30.83	—	46
[Li(11)]BF $_4$	32.70	—	46
LiCF $_3$ SO $_3$	24.27	1.91	46
[Li(8)]CF $_3$ SO $_3$	27.14	—	46
[Li(10)]CF $_3$ SO $_3$	26.73	—	46

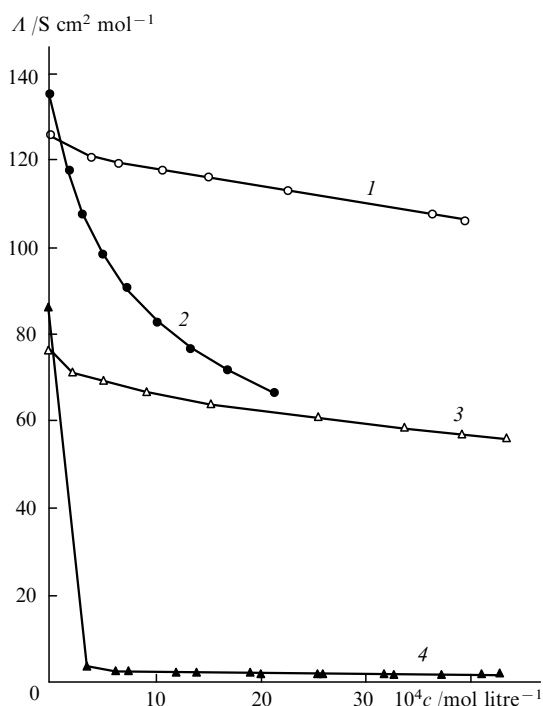


Figure 2. Dependence of the molar conductivity of lithium picrate LiPi solutions in (1, 2) acetonitrile and (3, 4) nitromethane on the salt concentration at 298.15 K.^{58, 59} Concentration of additive **8**: (1) 46.43×10^{-4} (3) 89.05×10^{-4} mol litre $^{-1}$, (2, 4) in the absence of **8**.

($\text{Li}^+ < \text{Na}^+ < \text{K}^+$) and Stokes radii increase. Similar results were reported in Ref. 65. The addition of dicyclohexyl-18-crown-6 to ethanol solutions of NaCl, KCl and RbCl ($c = 10^{-4}$ – 10^{-3} mol litre $^{-1}$) resulted in complete dissociation of the electrolytes. At the same time, the values of A_0 decreased. For the system KI + crown ethers in AN, the A_0 values were lower than in solutions without ligands, decreasing with a decrease in the r_1/r_2 ratio, where r_1 is the ionic radius and r_2 is the cavity radius. It is of note that electrolytes based on [K(12-crown-4)]I and [K(15-crown-5)]I ($r_1/r_2 > 1$) in AN exhibited association constants of 28 ± 4 and 23 ± 5 litre mol $^{-1}$, respectively, whereas the original electrolyte KI was completely dissociated. The explanation of this effect invokes the fact that the effective radii of complex ions are smaller than those of solvated ('free') ions. It is known that an increase in association constants due to complex formation is most pronounced for multicharged strongly solvated ions, e.g., halides of rare-earth elements with the cations strongly bound with organic ligands partially substituting their solvate shells.⁶⁶

The effect of the addition of crown ethers **9** and **19** and cryptand **14** on the thermodynamics of electrolytic dissociation and the conduction of KSCN in such solvents as AN, DMSO, PC and their binary mixtures with chlorobenzene was also studied.^{67,68} It was found that throughout the range of mixed solvent concentrations ($\varepsilon = 5$ –66), the association constants are smaller for electrolytes with complex cations than for simple salts. However, the conductivity in the systems studied ($c_{\text{KSCN}} = 10^{-3}$ – 10^{-4} mol litre $^{-1}$) increased with the addition of macrocyclic compounds as a result of a decrease in the degree of electrolyte association only for mixed solvents enriched with the nonpolar component. In individual solvents with relatively high dielectric constants (AN, DMSO and PC) and binary mixtures with high contents of these solvents, the degree of electrolytic dissociation of potassium thiocyanate was high; however, the conduction decreased upon addition of crown ethers and cryptands. This effect was attributed to the increase in the cation size with the formation of complexes comprising macrocyclic ligands, which reduced the cation mobility. In addition to the change in the ion size, the nature of the ligand attached also plays a certain role. It was shown⁶⁹ that, as compared with A_0 of free ions in AN, a decrease in $A_0(\text{ML}^+)$ ($\text{M}^+ = \text{Na}^+, \text{K}^+$) is more pronounced for complex ions containing macrocyclic ligand **9** with two *tert*-butyl substituents than for complex ions with similar but larger ligands with four *tert*-butyl substituents. The explanation of these results invoked the fact that in the latter case complex cations $[\text{ML}]^+$ were less stable and retained their association with anions.

The molar conductivity of potassium chloride solutions with additions of cryptand **14** was calculated for different interaction potentials using the Monte-Carlo method.⁷⁰ For KCl solutions with concentrations of 0.10 and 0.15 mol litre $^{-1}$ at 298 K, the values of Λ were found to be 128.82 and 126.52 S cm ^{2} mol $^{-1}$, respectively, whereas for the same solutions with additions of cryptand **14** the Λ values turned out to be substantially smaller, viz., 71.5 and 65.9 S cm ^{2} mol $^{-1}$, respectively. For a constant cryptand-to-salt concentration ratio, the molar conductivity decreased as the concentration increased in the range from 0.03 to 0.15 mol litre $^{-1}$. If the overall interaction potential took into account the hydrodynamic component in addition to the Coulomb attraction and repulsion forces, an adequate agreement of calculated and experimental Λ values was observed. However, the authors failed to derive a generalised interaction potential which would allow one to adequately simulate both the structural (neutron diffraction spectra) and dynamic (conduction) properties of the system studied.

2. Lithium electrolytes with molecularly encapsulated anions

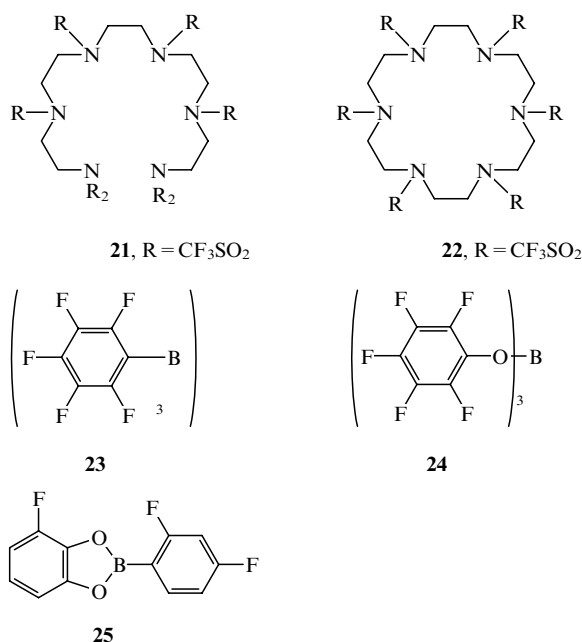
By binding anions of lithium salts into complexes, it is possible to reduce not only the conductivity of a solution (due to a decrease in the degree of ion association), but also the transport number of lithium. Most of the known ligands capable of forming anionic

complexes cannot be used in lithium CPS, because they either coordinate anions by forming hydrogen bonds or comprise positively charged fragments (or metal atoms) acting as Lewis acids. Recently, new neutral ligands, viz., cyclic and linear azacompounds, in which the electron-acceptor groups CF_3SO_2 were substituted for hydrogen atoms in NH groups [octakis(trifluoromethylsulfonyl)pentaethylene hexamine (**21**), hexakis(trifluoromethylsulfonyl)hexacyclene (**22**), etc.] were studied.^{71–73} Nitrogen atoms of nonsubstituted polyamines display electron-donor properties, which favour the formation of complexes with cations. Upon introduction of electron-acceptor groups, these ligands become the receptors of anions due to the local positive charge that appears on the nitrogen atoms as the electronic density shifts to the substituent. The formation of complexes by linear ligands and anions was confirmed by the NEXAFS method (X-ray absorption spectra in solution). For complexes with cyclic ligands isolated in the solid state, this was confirmed by X-ray diffraction technique. It was shown that, for an equimolar concentration ratio of ligands and lithium halides (LiCl, LiBr, LiI, $c = 0.1$ or 0.2 mol litre $^{-1}$), the conductivity of THF solutions increased by 1–3 orders of magnitude (Table 4). The conductivity also increased with an increase in the number of sulfonamide groups NSO_2CF_3 for both cyclic and linear ligands. For LiBr and LiCl solutions in THF, the conductivity increased with an increase in the ligand concentration, however, to a lesser extent; the conductivity of a THF solution of lithium iodide remained virtually unchanged as the ligand-to-salt concentration ratio changed from 1:1 to 1:2. The greatest increase in conductivity with the introduction of macrocyclic ligands was observed for solutions of the most strongly associated salt, viz., lithium chloride, which exhibited the lowest conductivity. It was noticed that, upon introduction of macrocyclic ligands comprising six and seven sulfonamide groups in a ring, the conductivity of lithium halide solutions in THF increased to practically the same value ($\sim 1.6 \times 10^{-3}$ S cm $^{-1}$), although their solutions without additives exhibited quite different conductivities.

Yet another group of anionic receptors comprises boron-containing ligands with fluorinated aryl and alkyl groups: boranes $[(\text{C}_6\text{F}_5)_3\text{B}$ (**23**), etc.], borates $[(\text{C}_6\text{F}_5\text{O})_3\text{B}$ (**24**), etc.], boronates $[(\text{C}_6\text{H}_3\text{F})\text{O}_2\text{B}(\text{C}_6\text{H}_3\text{F}_2)$ (**25**), etc.].^{74–77} As compared with borane (**23**), borate (**24**) has a higher solubility in solvents of low polarity

Table 4. The effect of the addition of equimolar amounts of boron- and nitrogen-containing anionic receptors on the conductivity of lithium electrolytes at 298.15 K.^{71–77}

Electrolyte	σ / S cm $^{-1}$
Solvent — DME	
0.2 M LiCl	5.0×10^{-6}
0.2 M LiCl + 0.2 M (24)	3.0×10^{-3}
0.2 M LiCl + 0.2 M (23)	2.6×10^{-3}
0.2 M LiI	7.3×10^{-4}
0.2 M LiI + 0.2 M (24)	3.2×10^{-3}
0.2 M LiI + 0.2 M (23)	2.2×10^{-3}
0.2 M LiCF $_3$ COO	3.3×10^{-5}
0.2 M LiCF $_3$ COO + 0.2 M (24)	3.3×10^{-3}
0.2 M LiCF $_3$ COO + 0.2 M (23)	3.2×10^{-3}
0.2 M LiCF $_3$ COO + 0.2 M (25)	1.2×10^{-3}
0.8 M LiF + 0.8 M (24)	6.4×10^{-3}
0.8 M LiF + 0.8 M (23)	6.6×10^{-3}
Solvent — THF	
0.1 M LiCl	7.5×10^{-6}
0.1 M LiCl + 0.1 M (21)	1.6×10^{-3}
0.2 M LiCl	1.6×10^{-6}
0.2 M LiCl + 0.2 M (22)	1.4×10^{-3}
0.1 M LiBr	2.9×10^{-5}
0.1 M LiBr + 0.1 M (21)	1.8×10^{-3}



(*e.g.*, their solubilities in dimethyl carbonate at room temperature were > 1 and $0.3 \text{ mol litre}^{-1}$, respectively). The complexing of these ligands with halide ions was also confirmed by X-ray absorption spectra of solutions (NEXAFS). The addition of boron-containing ligands to lithium halide solutions in DME substantially increased the conductivity and solubility (see Table 4). For example, lithium fluoride was practically insoluble in solvents with low dielectric constants; however, the addition of a compound **23** or **24** (1 : 1) to its 1 M solution in DME yielded solutions with conductivities of $(6.2\text{--}6.8) \times 10^{-3} \text{ S cm}^{-1}$. The conductivity was shown to increase with an increase in the number of fluorine atoms in the ligand molecules. Boron-containing ligands, especially boranes, are electrochemically stable and compatible with the lithium anode. Thus for the 1 M LiF + 1 M **23** solution in a mixed PC–ethylene carbonate–dimethyl carbonate (1 : 1 : 3) solution, the range of working potentials reached 5.0 V. Compared with such electrolytes as LiPF₆ and LiAsF₆, lithium halides are cheaper and less toxic. Taking into account that the starting reagents for the synthesis of boron-containing anionic receptors are also inexpensive and of a low toxicity, electrolytes with complex anions have the prospects of gaining a wide use in future.

III. Polymeric electrolytes

Currently, keen attention is drawn to the safety of application and utilisation of waste power sources. In this respect, metallic lithium is an environmentally clean material as compared with lead and cadmium. The safety of lithium CPS for the environment and human beings is ensured by the correct choice of nonaqueous electrolyte solutions.

Numerous studies in the field of polymeric lithium electrolytes were largely aimed at solving the problems of enhancing the stability of the electrolytic system with respect to the lithium anode and increasing the safety and reliability of the performance of lithium batteries used for energising domestic devices.⁷⁸

The main drawback of polymeric electrolytes is their low conductivities at room temperature. Under the conditions mentioned, these electrolytes are mostly in a quasicrystalline state ($\sigma = 10^{-6}\text{--}10^{-7} \text{ S cm}^{-1}$). The conductivity increases only with the transition to the amorphous state (as the temperature rises). To improve the characteristics of polymeric electrolytic systems, different additives were extensively used, along with the procedures of modifying the polymer structure itself (which allows, *e.g.*, the reduction of the glass transition temperature). The addition of

plasticisers that, as a rule, represent electrolyte solutions in low-molecular aprotic solvents led to formation of hybrid biphasic gel-electrolytes with acceptable conductivities. However, they were highly active with respect to lithium electrodes. Additions of macrocyclic compounds weaken the association of ions in non-polar polymeric matrices, thus increasing the conductivity.

The effect of cryptand **14** additives on the conductivity of sodium salt of an oxysiloxane polymer was studied.⁷⁹ It was found that with addition of the cryptand, the conductivity increased by a factor of 15 irrespective of temperature and concentration and was $1.7 \times 10^{-5} \text{ S cm}^{-1}$. It was concluded that, in the general case, the conductivity should increase with an increase in the equilibrium constant of the formation of cation–cryptand complexes and an increase in the association constant of the polymeric electrolyte. This agrees with the conclusions made in the studies of solutions of liquid-phase lithium electrolytes. Cations are free charge carriers despite their sufficiently strong solvation by the polymer, and a cryptand additive should not cause any substantial conductivity rise. This was confirmed in several studies.^{80–84} Additions of cryptand **14** or crown ether **8** to polymeric electrolytes based on NaSO₃CF₃, NaBF₄, NaI and NaSCN solutions in amorphous polyethylene oxide were shown to reduce their solubilities and conductivities.^{80,81} Using spectroscopic methods, it was shown that association of these salts is insignificant and all polymer–salt complexes studied were amorphous. At the same time, the solubility and conductivity of NaSO₃CH₃ which is poorly soluble in the polymer increased with the addition of the crown ether and cryptand but did not reach the values observed for the other electrolytes of this system. An analysis of parameters of the Vogel–Tamman–Fulcher (VTF) equation which describes the temperature dependence of conductivity showed that the addition of the cryptand decreases the number of charge carriers for electrolytes with weakly associated NaSO₃CF₃, NaBF₄, NaI and NaSCN salts, increasing it only for electrolytes containing the more strongly associated salt NaSO₃CH₃.

Solid electrolytes based on Li[CF₃SO₂N(CH₂)₃OCH₃] complexes with cryptands **12–14** and crown ethers **7–9** and Li[(CF₃SO₂)₂N] complexes with **9** were also studied (Fig. 3).^{83,84} It was assumed that amorphous phases are formed due to the difference in the radii of the macrocycle cavity and the cation. The method of differential scanning calorimetry has shown that the most stable macrocycle–salt complexes [ML]⁺X[−] (M is an alkali metal, L is a crown ether or cryptand), in which the sizes of the cation and the ligand's (**7**, **12**) cavity match most closely one another, form only crystalline phases. A series of amorphous complexes of macrocyclic compounds and lithium salts were

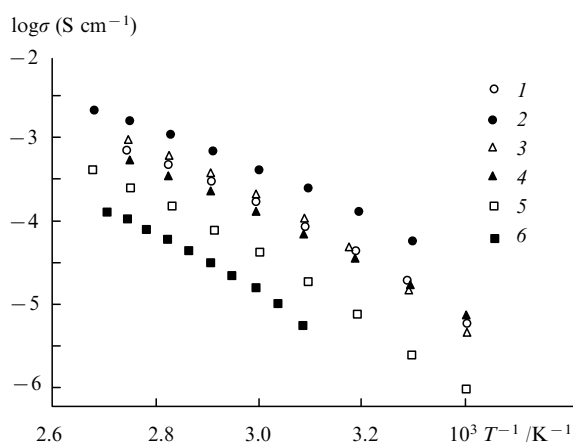


Figure 3. Temperature dependence of the specific conductivity (σ) of amorphous complexes: (1) [Li(**14**)]CF₃SO₂N(CH₂)₃OCH₃, (2) [Li(**13**)]CF₃SO₂N(CH₂)₃OCH₃, (3) [Li(**12**)]CF₃SO₂N(CH₂)₃OCH₃, (4) [Li(**9**)]CF₃SO₂N(CH₂)₃OCH₃, (5) [Li(**8**)]CF₃SO₂N(CH₂)₃OCH₃ and (6) [Li(**7**)]CF₃SO₂N(CH₂)₃OCH₃.⁸¹

synthesised where the size ratio mentioned was violated. Complexes with cryptands passed into the amorphous state at lower temperatures as compared with complexes with crown ethers. The presence of asymmetric anions favoured the glass transition.⁸⁴ Amorphous samples with the lowest glass transition temperature exhibited the greatest conductivity ($10^{-4.5}$ S cm⁻¹). An analysis of IR and Raman spectra has shown that cryptands most effectively screen lithium cations. The parameters of the VTF equation have shown that cryptate complexes exhibit higher concentrations of charge carriers as compared with complexes with crown ethers (see Fig. 3).

An increase in conductivity at room temperature by 2 orders of magnitude (up to 10^{-4} – 10^{-3} S cm⁻¹) for polymeric electrolytes based on LiClO₄ and polyethylene oxide observed upon introduction of crown ether **8** was explained⁸⁵ by the formation of stable complexes of crown ethers with lithium ions. However, the addition of 1,4,7,10,13-pentaoxa(13)orthocyclophane(benzo-15-crown-5) had practically no effect on the conductivity in the system mentioned, because the formation of complexes with lithium ions was complicated. The solid polymeric electrolytes synthesised were well compatible with the lithium anode and stable during long-term storage.

New synthetic methods for polymeric and liquid electrolytes of the series of nitrogen-containing compounds, *viz.*, aromatic amines, diarylamines and organosilicon compounds with ammonium groups and their practical applications as the additives have been reported.⁸⁶ Organosilicon derivatives of 4,4'-bipyridyl were referred to as most promising. The additives mentioned almost double the conductivity of polymeric electrolytes and prevent the capacity fade during cycling.

The mobility of ions in polymeric electrolytes is directly associated with the mobility of polymeric chain fragments, which is the main factor limiting the conductivity. An approach to enhancement of the conductivity and simultaneous increase in the transport number of lithium ion is the use of compounds which act as Lewis acids and can interact with anions. For example, good results were obtained where cyclic boron-containing compounds **26** ($n = 1-3, 7.2$), particularly, 2,4,6-tris(2-methoxyethoxy)boroxine were introduced into polymeric electrolytes based on LiSO₃CF₃ and poly(methyl methacrylate).⁸⁷ This was explained by the effective interaction of oligoether oxygen-containing fragments with lithium ions and the anion-acceptor nature of boroxine rings. Introduction of 11-acryloyloxy-3,6,9-trioxaundecyl biphenyl-2,2'-diyl borate (**27**) into solutions of strongly associated electrolytes of LiCl and CF₃CO₂Li in both polar and low-polar media, as well as of electrolytes formed by LiBF₄ and **1** in DME and dimethyl carbonate (DMC) increased the conductivity.⁸⁸ In contrast, introduction of the same additive to solutions of well dissociated salts, namely, LiBF₄ and **1** in polar solvents resulted in a decrease in the ionic conduction, which was explained by a decrease in viscosity (Table 5). It is of note that the conductivity increased for all gel-polymeric electrolytes, because the additive introduced was built-in into the polymer structure in such a way that the microviscosity of the solution surrounding the ions remained unchanged.

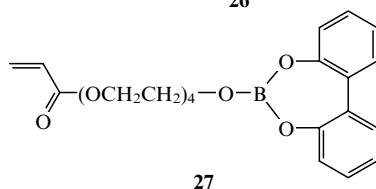
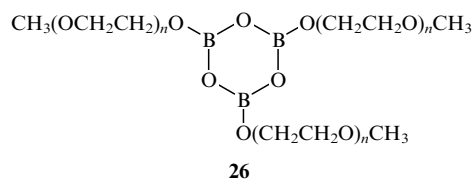
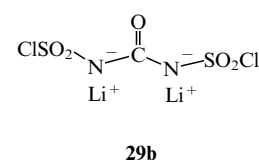
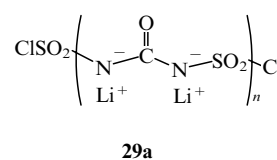
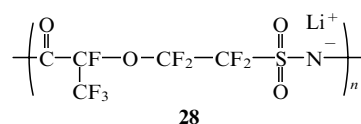


Table 5. The effect of the addition of equimolar amounts of **27** on the conductivity of lithium electrolyte solutions ($c_m = 0.2$ mol kg⁻¹) at 298.15 K.⁸⁸

Salt	Electrolyte	Conductivity (mS cm ⁻¹) in a medium of			
		PC	γ-BL	DME	DMC
LiCF ₃ COO	without addition	0.33	5.2	0.024	$< 5 \times 10^{-4}$
	with addition	0.82	1.2	0.19	2.8
LiBF ₄	without addition	2.7	4.3	0.19	1.5×10^{-3}
	with addition	2.2	3.1	2.5	0.027
Li(CF ₃ SO ₂) ₂ N	without addition	3.0	4.3	3.0	0.25
	with addition	2.4	3.3	6.9	0.42

In a number of studies, it was suggested to use lithium salts with polymeric anions. Thus for electrolytes based on acrylates of a co-polymer of ethylene oxide and propylene oxide and containing a lithium salt with a polyimide anion, *viz.*, lithium poly(5-oxo-3-oxa-4-trifluoromethyl-1,1,2,2,4-pentafluoropentamethylene-sulfonimide) (**28**), the conductivity was of an order of magnitude of 10^{-5} S cm² and the transport number of lithium > 0.7 substantially exceeded the value obtained for polymeric electrolytes with a 'monomeric' lithium salt **1**.⁸⁹ Polyanionic electrolytes prepared by introducing Lewis bases (imidazole) into the polymeric structure (the 'base in chain' method) were studied.⁹⁰ Plasticisation of the corresponding lithium polyimide salts (**29a, b**) by chloroaluminates (1 : 1) and AlCl₃ made it possible to substantially decrease the glass transition temperature (< -20 °C) and obtain liquid-phase systems with the electrolyte conductivity values currently best for polyanionic electrolytes. Thus the conductivity of lithium poly(carbamate sulfonylimide) (**29a**) reached the maximum value upon addition of 20% LiAlCl₄ ($10^{-2.9}$ S cm⁻¹ at 25 °C) (Fig. 4), whereas, for a similar complex with the 1,3-dichlorosulfonyl-1,3-dithiocarbamide (**29b**), the maximum conductivity value obtained upon introduction of 40% LiAlCl₄ did not exceed $10^{-3.3}$ S cm⁻¹. However, the presence of Lewis acids (AlCl₃, BF₃) in the system can initiate corrosion of the power source materials and other undesirable electrochemical processes. In this connection, it was proposed to 'fix' a Lewis acid directly in the polymer chain. For this purpose, the $-\text{O}-\text{B}-(\text{Ph})-\text{O}-([\text{CH}_2]_2\text{O})_n$ ($n = 2-23$) polymers synthesised by the 'acid in chain' method were transformed into polymeric anions by complexation with lithium salt anions representing Lewis acids (*e.g.*, Ph⁻, CN⁻).⁹¹ The largest conductivity values were obtained for short polyether chains $([\text{CH}_2]_2\text{O})_n$ which separated the anionic centres in the polymer. The polymers thus synthesised were reported to exhibit lower chemical activities and better compatibility with cathodic and anodic materials as compared with their analogues obtained by the 'base in chain' method. It is expected that higher values of ionic conduction can be reached by using lithium compounds with anions of a higher basicity, such as methoxide and formate ions, as well as with the methyl anion (CH₃⁻).



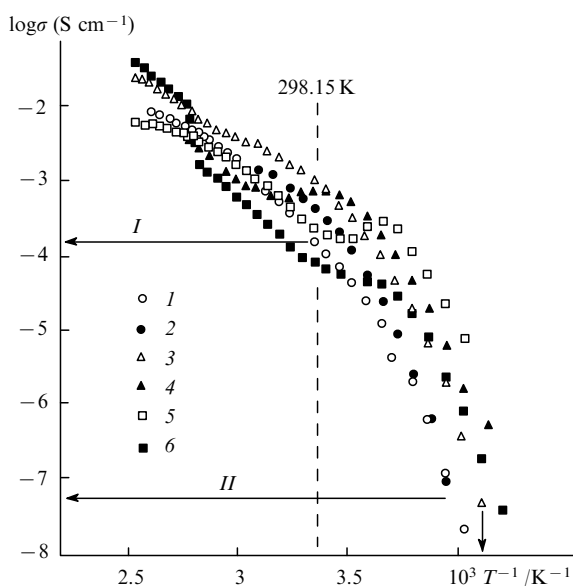
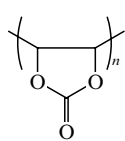
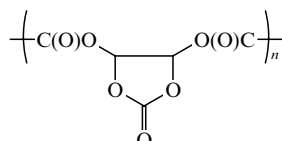


Figure 4. Temperature dependence of the specific conductivity of polymeric electrolytes based on lithium complexes with polyanions, *viz.*, $(1-x)\mathbf{29a}-\text{AlCl}_3$ (1:1)– $x\text{LiAlCl}_4$ (see Ref. 90). Arrows designate the conductivity of (I) an electrolyte without LiAlCl_4 at 298.15 K and (II) an electrolyte containing 20 mol.% LiAlCl_4 at the glass transition temperature; x : (I) 0, (2) 0.1, (3) 0.2, (4) 0.3, (5) 0.4, (6) 0.5.

Polymeric electrolytes with relatively high conductivities can be obtained not only in the amorphous state but also in the crystalline state. The following ‘rigid’ polymers were synthesised: poly(vinylene carbonate) (**30**) and poly(2-oxo-1,3-dioxolane-4,5-diyl oxalate) (**31**).⁹² In contrast to most polymeric electrolytes known, the addition of a lithium salt (LiCF_3SO_3) to these polymers decreased the glass transition temperature and the maximum conductivity was reached at a higher salt concentration (the molar concentration ratio of the salt to the monomeric units of polymers was 1:1). The crystalline structure of these polymers did not prevent the ionic transport, because the mobility of ions in the polymer is independent of the segmental mobility of polymeric chains.



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In a number of cases, solid polymeric electrolytes based on amorphous co-polymers of acrylonitrile with the maximum concentration of lithium salt were found⁹³ to exhibit unusually high conductivity, *viz.*, $\sim 10^{-3} \text{ S cm}^{-1}$. Moreover, the conductivity of systems studied was shown to be either virtually independent of the temperature or have a weakly pronounced inverse temperature dependence as compared with the Arrhenius-type dependence. Measurements of charge transfer numbers showed that it is mainly cations that are involved in the ionic transport. An analysis of IR spectra of electrolytes confirmed the presence of substantial amounts of ion pairs, triplets and more complex associates of lithium salts. Based on these results, the authors proposed that highly concentrated macromolecular polymeric solutions have a special structure which involves ionic clusters interacting with one another. The ionic transport in such solutions proceeds by an unusual, low-energy mechanism. The use of extremely high (close to the solubility limit) concentrations of lithium salts in polymeric matrices was assumed to be promising for the development of highly conductive solid polymeric electrolytes.

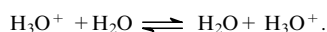
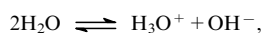
Recently, great success was achieved in studying the so-called ionic liquids, *viz.*, salts with unusually low melting points, which remain in the liquid state even at room temperature. Such systems are of great interest as the electrolytes for lithium CPS. Based on lithium salts and Lewis acids (AlCl_3), the following liquid electrolyte systems with conductivities of $> 10^{-3} \text{ S cm}^{-1}$ at room temperature were synthesised: $0.33 \text{ LiCF}_3\text{SO}_3 - 0.67 \text{ AlCl}_3$,⁹⁴ $0.4 \text{ LiSCN} - 0.6 \text{ AlCl}_3$.⁹⁵ It was assumed that, due to ion–molecule interactions, the following complex anions are formed in these systems: $[\text{Al}_n\text{Cl}_{3n+1}]^-$, $[\text{Al}_n\text{Cl}_{3n-m+1}(\text{SCN})_m]^-$, *etc.*, and the melt structure changes, which makes crystallisation difficult and is favourable for the system to retain its liquid or glassy state. Moreover, the charge transfer mechanism is virtually independent of the structural relaxation of the medium (the charge is transferred preferentially by cations).

The above methods for modifying chemically the electrolytic systems are different; however, they have a common theoretical basis determined by the ion-migration (Stokes) mechanism of charge transfer. These methods were largely applied to dilute solutions of lithium electrolytes in aprotic solvents and polymers. Concentrated electrolyte solutions in aprotic solvents, which are used in lithium CPS, still remain insufficiently studied. The results obtained to date^{9,53,54} suggested that, in low-polar solvents, the greatest increase in conductivity upon addition of macrocyclic compounds takes place at concentrations below the molar conductivity minimum point, *i.e.*, where ion pairs prevail in solution. For higher concentrations (in the ‘anomalous’ range), the conductivity increased to a lesser extent, apparently, due to the changes in the nature and composition of ions.

For strongly associated electrolytes in solvents with low and moderate dielectric constants and polymers, the conductivity increases mainly due to the weakened association and increased solubility. The most pronounced weakening in the ion association was observed with the formation of lithium–cryptand complexes as compared with lithium–crown ether complexes. As a rule, an increase in conductivity in these media is proportional to the increase in the stability constant of the complex ions formed. With an increase in ligand concentration, conductivity increases and reaches a maximum at the equimolar $\text{Li}:\text{L}$ ratio. In more polar solvents, where the electrolyte is sufficiently soluble and weakly associated, and the size of the ligand attached exceeds that of the solvating shell, the mobility of ions can decrease due to an increase in their Stokes radii. For electrolytes in polar media, in which the ions are strongly solvated (*e.g.*, for lithium salt solutions in propylene carbonate, $K_a \approx 0$), the conductivity can increase as a result of weakening in solvation, and, correspondingly, a decrease in the ‘free’ (solvated) ion radius with the formation of a complex with a macrocyclic ligand. At the same time, in certain cases, a substantial weakening in the lithium ion solvation upon its complexing can increase the association constants for the electrolytes involving complex cations as compared with ordinary electrolytes.

IV. Electrolytic solvosystems for lithium batteries and mechanisms of charge transfer in solutions

To understand the reasons for the electrochemical behaviour of electrolytic systems of different nature in wide ranges of electrolyte concentrations and temperatures, it is necessary to gain an insight into the nature of charge carriers and the mechanism of charge transfer. It is known that the high conductivity typical of concentrated aqueous solutions of bases and acids used as the electrolytes in conventional CPS is caused by the chain mechanism of conduction.^{13,96,97} This mechanism is distinguished by the exchange interaction between the electrolyte ions which correspond to the lyonium and lyate ions of the solvent and the solvent molecules (H_2O , H_2SO_4 , H_2SeO_4 , H_3PO_4 , HF). Thus in an aqueous solution, hydroxonium ions (hydrated protons) and water molecules exchange protons



Several approaches were proposed for estimating different contributions to the charge-transfer mechanism in solutions.^{13, 66, 98–103} However, to date, no sufficiently reliable criteria and methods were proposed for elucidation of the nature of charge carriers, which makes the studies of the conduction mechanism in nonaqueous media quite difficult.¹⁰⁴ The greater complications arise for concentrated electrolyte solutions for which the concepts of the Debye–Hückel–Onsager theory and the law of independence of ions' motions (the Kohlrausch law) are not fulfilled. One of the approaches to assessing the conduction mechanism in electrolyte solutions consists in comparing the activation energies of the conduction and viscous flow processes. For example, within the framework of this approach, it was assumed that the charge transfer in the $\text{LiCl}–\text{AlCl}_3–\text{CH}_3\text{NO}_2–\text{SOCl}_2$ system (see Refs 27, 28) with the electrolyte concentration $> 1 \text{ mol litre}^{-1}$ occurs by both the ion-migration and chain mechanisms. The latter mechanism provided high conductivity values during the lithium battery discharge irrespective of the observed increase in the solution concentration and viscosity.

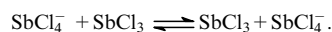
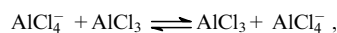
The conduction mechanism may be characterised by the transport number of ions (t_i), which however is insufficient to confirm the chain mechanism of conduction. Transport numbers of ions for most binary aqueous solutions of salts insignificantly deviate from the average value of 0.5; in aqueous solutions of acids and bases, t_{H^+} and t_{OH^-} are substantially higher, *viz.*, from 0.75 to 0.85. In nonaqueous solvents, transport numbers strongly depend on the differences in the degrees of solvation for cations and anions. For example, the greatest part of solvation energy for lithium salts in PC (up to 80%) falls to cations.¹⁷ Hence, as a rule, t_{Li^+} is smaller than the transport number of the corresponding anion and is equal to 0.3–0.5. The known attempts to analyse the experimental results on conductivities and the solution structure ambiguously assessed these data and often led to unorthodox conclusions. Thus it was suggested^{105, 106} that electrolyte solutions be considered as impurity conductors in which the charge is transferred by electrons and holes rather than by ions. Based on high-frequency studies, electrolyte solutions were concluded to have ionic lattices like those in crystals and the presence of a long-range order was assumed to be a key condition for enhancing the mobility of charge transfer in condensed media.

The possibility of realising the chain mechanism of conduction in solutions is largely determined by the structure and the degree of self-ionisation of the solvent, which depends (in protic solvents) on the strength of bridging hydrogen bonds between molecules.^{96, 97} For instance, in liquid ammonium the constant of self-ionisation (at -50°C) was found to be $\sim 10^{-23}$ due to a weak $\text{N}\cdots\text{H}\cdots\text{N}$ bond and a low ϵ , and the mobility of ions formed upon autoprotolysis was not anomalously high.^{107, 108} Such an order of magnitude is typical of self-ionisation constants of most nonassociated aprotic solvents. Nonetheless, the charge transfer by the chain mechanism can also occur in aprotic media. In this case, anomalous mobility values were observed for lyonium and/or lyate ions formed upon self-ionisation of solute associates.

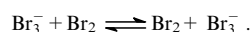
In binary liquid systems formed by protic (H_2SO_4 , H_3PO_4) acids and proton-containing organic bases (RH) (such as acetamide, *N*-methylacetamide, *N,N*-dimethylacetamide, *etc.*), in the range of high acid concentrations, the charge was shown to be transferred by the chain mechanism as in individual acids.^{109–113} Bearing in mind that, for binary systems of organic bases with strong aprotic acids (MX_n) (SbCl_3 , FeCl_3 , SnCl_4 , SbCl_5), the conductivity isotherm has a maximum, it may be assumed that the charge transfer in these systems also occurs by the chain mechanism in the range of high acid concentrations. The components of these systems are prone to autoionisation; hence, the acid–base interaction occurs between the lyonium ion MX_{n-m}^+ of the acid and the lyate ion R^- of the base to give a nonelectrolyte $\text{MX}_{n-m}\text{R}_m$. This results in the increase in the concentration of the

lyate ions of the acid MX_{n+1}^{p-} and the lyonium ions of the base RH_2^+ in the solution. It is the mobility of these ions that determines the conduction of solutions.

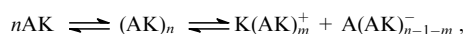
For chlorides (solvated chloride-containing ions, *e.g.*, SbCl_4^- or AlCl_4^-) in ultra-concentrated solutions based on antimony trichloride and aluminium chloride, the following halogenotropic mechanism of conduction was postulated:^{109–111, 114, 115}



For bromides and iodides (polyiodides, I_3^- , Br_3^-), PCl_5 and PBr_5 in liquid bromine and iodine, the same mechanism was suggested.^{116–118}



It was shown¹¹⁹ that the conduction of salt solutions in low-polar solvents in a wide range of concentration (from $0.1 \text{ mol litre}^{-1}$ to fused salts) is largely determined by self-ionisation (autosolvation) of the electrolyte



where $\text{K}(\text{AK})_m^+$ and $\text{A}(\text{AK})_{n-1-m}^-$ are the autosolvated cation and anion, respectively.

According to concepts put forward,^{116–118} ions in concentrated solutions form aggregates which are involved in the charge transfer. Moreover, with an increase in electrolyte concentration, upon passing its minimum at $0.01–0.1 \text{ mol litre}^{-1}$, the molar conductivity of low-polar solutions was shown to increase due to the increased number of such aggregates, irrespective of the simultaneous increase in the solution viscosity. A hypothesis that an electrolyte in a concentrated solution passes into a state similar to that of a melt, which was put forward in the studies under discussion, was confirmed by the results of studying the molten $\text{ZnBr}_2–\text{AlBr}_3$ and $\text{SbBr}_3–\text{AlBr}_3$ systems. With an increase in salt concentration, the molar conductivity values of these melts (with a correction made for viscosity) increased up to a point where the conductivity of the individual liquid electrolyte is reached. According to this hypothesis, for any concentration of an electrolyte solution, its molar conductivity (with a correction made for its viscosity) cannot exceed the corresponding value of a hypothetical molten individual electrolyte under equal conditions. The anomalous conductivity can be observed not only for solvents with low dielectric constants but also in polar solvents at sufficiently high electrolyte concentrations. For both cases, a similar type of the dependence of the molar conductivity on the concentration was suggested.

Similar conclusions were drawn in Refs 32–34. Based on the results of studying thermodynamic and transport properties of lithium electrolytes in a wide range of concentrations in solvents of different types (glymes, sulfamides, AN, γ -BL, PC and their mixtures), it was concluded that at least two conduction mechanisms should be taken into account, *viz.*, the ion-migration mechanism, which occurs at low electrolyte concentrations, and the chain mechanism (charge transfer accompanied by rotation of complexes-associates), which occurs at high concentrations. It was assumed that the state of a highly concentrated electrolyte solution is similar to that of a fused salt. The chain mechanism of conduction can occur in both low-polar and polar aprotic solvents with sufficiently high electrolyte concentrations. In highly concentrated solutions, as the distance between ions decreases, the chain mechanism prevails and the difference in the conductivity values for solvents with low and high ϵ values decreases. A low viscosity of the medium and a high solvation power of the solvent, which weaken the ion association and facilitate reorientation of dipoles in the electric field, favour the charge transfer to occur by the chain mechanism.

However, for the chain mechanism (in contrast to the ion-migration mechanism), many properties of electrolytic systems (viscosity, solvation, association) can exert the opposite effects on the conduction. For example, despite the high viscosity of anhydrous sulfuric acid, the mobilities of the lyonium H_3SO_4^+ and the lyate HSO_3^- ions are comparable with the mobilities of H^+ and OH^- ions in water; in aqueous solutions, the mobility of protons substantially exceeds those of other ions, even if the hydration energy of H^+ is the highest; among the large number of electrolytes completely dissociated in aqueous solutions, only acid and base solutions, *i.e.*, electrolytes that comprise the ions formed by the self-ionisation (autoprotolysis) of the solvent have anomalously high conductivity values. The prototropic conduction decreases with an introduction of both electrolytes and non-electrolytes into these solutions,⁹⁷ which is usually attributed to the hydration of ions and molecules accompanied by the changes in the water structure built by hydrogen bonds. Such a structure is best suited for the chain transfer of protons. At the same time, it was found¹²⁰ that the additivity of the molar conductivity is typical of the whole composition range of an isomolar $\text{HCl} + \text{KCl}$ mixture in methanol. A similar Λ vs. composition dependence was also observed for an aqueous $\text{HCl} + \text{LiCl}$ system ($c_{\text{Li}} \leq 8 \text{ mol litre}^{-1}$). Taking into account these results, it was concluded that the prototropic mechanism of proton transfer is retained even for high concentrations of aprotic electrolytes.

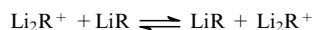
It should be also noted that, in contrast to other ions, the mobilities of H^+ and OH^- increase with an increase in the pressure.⁹⁶ The temperature coefficient of conduction is positive for both aqueous solutions of acids and bases and other electrolytes with the usual ion-migration mechanism of conduction. The effect of the temperature on the structure of hydrogen bonds in water is apparently less significant compared with the effects of pressure and chemical factors (solvation). A comparison of different physicochemical parameters of water and other liquids in a wide temperature range have shown that water retains a sufficiently distinguishable structure up to the critical point.¹²¹

An analysis of the conduction data for different kinds of aqueous and nonaqueous electrolyte solutions have shown that the chain mechanism of conduction is realised in aprotic media if, first, the chemical nature of the electrolyte is similar to that of the solvent (solutes comprise lyonium or lyate ions of the solvent) and, second, at high concentrations, the solvent and/or the electrolyte form a polymeric structure with intermolecular bonds.

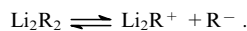
The presence of a certain solution structure is often characterised by high viscosity values (*e.g.*, H_2SO_4 , H_3PO_4 , H_2SeO_4 , concentrated electrolyte solutions). On the other hand, such associated liquids as water, $(\text{HF})_n$, SbCl_3 , *etc.*, in which the charge is transferred by the corresponding ions by the chain mechanism, exhibit relatively low viscosities. Evidently, under conditions necessary for the chain mechanism to occur, an additional decrease in the viscosity should facilitate the charge transfer.

To develop nonaqueous electrolytic solvosystems with the chain mechanism of conduction, it is necessary to carry out a quest for new-in-principle lithium electrolytes and nonaqueous media which will match the requirements described above. One of the approaches in such a research is to develop electrolytic solvosystems based on organolithium compounds. Organolithium compounds pertain to the group of the so-called electron-deficient structures, like organoelement compounds of the Groups II and III on the Periodic System (R_2Be , R_3B , R_3Al).^{122, 123} At the same time, organolithium compounds behave in reactions as the reagents with a deficit of electrons and react in the same manner as carbanions. The deficit of electrons manifests itself in a strong association of molecules $n\text{RLi} \rightleftharpoons (\text{RLi})_n$ ($n = 2-6$) by means of bridge bonds formed by the electrons of the $\text{C}-\text{Li}$ bond and free $2p$ orbitals of the lithium atoms. It was assumed¹²⁴ that the nature of $\cdots\text{Li}-\text{C}\cdots\text{Li}-\text{C}\cdots$ 'lithium' bonds in the associates of organolithium compounds is similar to that of hydrogen bonds.

A possibility that lithium ions of an electrolyte Li^+X^- and a solvent LiR are transferred by a mechanism similar to that of proton transfer in water, *i.e.*,



should be attributed to dissociation (self-ionisation) of the associate $(\text{RLi})_n$ (a dimer, in the simplest case)



The compound LiR should preferentially be of the nucleophilic nature, *i.e.*, have the affinity to lithium ions, and the lithium salt should contain a weakly basic anion (X^-) for these processes to be realised.

It is known that the complexes formed by aliphatic and aromatic organolithium compounds with lithium halides, which are less reactive than the original organolithium compounds, are stable in air and more handy in applications. The ability to form complexes depends on the nature of the radical (R), the lithium salt anion and the solvent. It is also of note that polyacetylene films ($\sigma = 10^{-12} - 10^{-9} \text{ S cm}^{-1}$) doped with organolithium compounds had an anomalously high conductivity ($20 - 160 \text{ S cm}^{-1}$)¹²⁵ typical of electron-conducting polymers and charge-transfer complexes.¹²⁶ In this connection, it seems interesting to explore the possibility of using organolithium compounds as one of the components of the medium (solvent) for electrolytes in lithium CPS.

* * *

In the past decade, the main research on electrolytic systems for lithium power sources was directed to modifying chemically the electrolytes and solvents traditional for this field. A key problem for these studies is the enhancement of conductivity of lithium salt solutions in aprotic solvents and polymers in order to optimise the electrochemical processes and improve the performance of lithium CPS. The advances in the field of physics and chemistry of solutions, chemistry of polymers and coordination chemistry allow one to understand and explain the specific features of charge transfer in condensed media and serve as the theoretical basis for the development of new electrolytic systems.

The most promising research directions involve the studies of highly concentrated solutions (including ionic liquids), the use of principles of molecular encapsulation of ions by macrocyclic ligands, and the quest for systems with nontraditional mechanisms of ionic transport. However, it is clear that the possibility of enhancing the conductivity within the framework of the approaches based on the ion-migration charge-transfer mechanism, *e.g.*, by reducing the solvent viscosity and the degree of ionic solvation (increasing their mobility), or decreasing the degree of association of the electrolyte (increasing the number of charge carriers) are limited.

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^e — *Russ. J. Gen. Chem. (Engl. Transl.)*

Applications of NMR tomography to mass transfer studies

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Abstract. Modern physicochemical applications of NMR tomography, or magnetic resonance imaging (MRI), to the investigation of mass transfer processes are described. The mass transfer involved in the sorption of gases, fluids and solutes, swelling of polymers and coal and drying of various materials is considered. Various methods of studying isotropic, anisotropic and restricted diffusion in porous media are discussed. The approaches to the investigation of filtration and the flow of fluids, gases and granulated materials are presented. The bibliography includes 373 references.

I. Introduction

This review concerns a number of the most widely used modern physicochemical applications of the method of NMR tomography, or magnetic resonance imaging (MRI), which mainly concern the studies in the field of the transfer (transport, flow) of fluids, gases and granulated materials. The studies devoted to the obtaining of spectral data and the NMR experiments carried out without spatial resolution are covered fragmentarily. The exception are the investigations involving the use of the pulsed magnetic field gradients for studies of the spatial molecular displacements due to diffusion, to the flow of fluids and other types of motion. These communications were covered in the review because of their great value and also for yet another reason, namely, because the corresponding experiments are often considered as the MRI studies in the molecular displacement space rather than in the conventional coordinate space. The title field of research is so broad that the published data are covered only partially. The salient features of the MRI techniques and their applications to studies of liquid-containing materials have been reported in a recent review.¹

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II. Sorption into porous materials

1. General remarks

Sorption has found a very broad spectrum of technological applications including, in particular, the drying and separation of chemical substances. Transport of fluids and gases through porous materials also plays an important role in catalysis. Permeability of building materials is critical to the development and use of engineering protective structures and containers for nuclear waste. Water and brine ingress into building materials can cause their accelerated degradation following different mechanisms including freezing, uptake of ions and corrosion and affects the gas permeability and thermal conductivity of materials.

The problem of how the structure of the pore space influences the transport processes in porous media is also topical. Application of the MRI technique to studies of this interrelation offers considerable prospects, since the method allows investigation of both structural and transport features for the same sample under the same conditions. Mass transfer can be strongly affected by not only microscopic inhomogeneities with the characteristic sizes lying in the pore size length scale, but also by macroscopic structural inhomogeneities inside porous materials including those due to specific features of the preparation procedure; therefore, MRI is widely used in the studies of transport processes.

Most modern building materials, as well as soil and many catalysts contain large amounts of paramagnetic ions, predominantly, Fe ions, which are responsible for appreciable shortening of the spin relaxation times of the fluids confined within the pores of such materials and for the appearance of local inhomogeneities of the magnetic field due to different magnetic susceptibilities of the chemical substances at the interfaces (if the experiments are carried out in strong magnetic fields). For instance, the T_2 time of water present in the fired-clay red brick containing a large amount of iron was found to lie between 180 and 360 μs .^{2–4} Correspondingly, the MRI studies are often carried out in relatively weak fields ($< 1\text{--}2\text{ T}$) using strong amplitudes of the applied field gradients and appropriate experimental techniques that provide a short effective echo time.^{5,6}

Large variations of the fluid content in the sample usually cause substantial changes in the relaxation times (see Section IV.2 in Ref. 1). Short T_2 times make a complete elimination of the relaxation weighting of MRI images virtually impossible; therefore, variations of the signal amplitudes are not in proportion to variations of the fluid content in the sample. In addition, adsorption can be accompanied by pronounced variation of the temper-

ature, which also affects the relaxation time values. Therefore, quantitative measurements require the use of some references and calibration curves.

Sorption of water usually causes large variations of the dielectric losses in the sample, while the presence of paramagnetic ions affects the electrical conductivity of the sample. This can be responsible for substantial variations of the sensitivity of the NMR spectrometer as a result of detuning the resonant circuit, which additionally complicates the quantitative interpretation of experimental data and in some instances makes it ambiguous due to nonmonotonic variation in the signal amplitudes upon a monotonic change in the water content.^{7,8} For this reason, a number of experiments were carried out on a tailor-made instrument designed to study the processes accompanied by substantial variations of the water content in the samples.³

2. Sorption studies

Investigations of one-dimensional (1D) capillary sorption of water into different building material bars showed⁹ that transport of water can be described using a nonlinear 1D diffusion equation in which the effective capillary diffusion coefficient, $D(C)$, depends on the water concentration, C . For gypsum and mortar bars⁹ and for some limestone rock bars^{9,10} the D value exponentially increases with the local concentration of water. Sorption of water into cylindrical hardened mortar samples¹¹ is described by an analogous equation with exponential dependence of D on C . Transfer of water in the sample dried at 105 °C was found to occur much faster than in the sample dried under milder conditions by extraction in isopropyl alcohol followed by drying at 40 °C. This can be due to the formation of a system of interconnected larger pores in the high-temperature drying. Shortening of the T_2 time of the adsorbed water in the region behind the adsorption front with time indicates a gradual redistribution of water from capillary pores into smaller gel pores that are formed around the cement grains upon hardening of the mortar.¹¹ Capillary sorption of water into different materials is characterised by the presence of a sharp front of water. In the case of 1D diffusion the front moves in proportion to the square root of time and the amount of the adsorbed water behaves analogously.^{5,9–11} Adsorption of D_2O into samples with large initial water content was studied using the ^2D NMR signals.⁵

Often, the results of the sorption dynamics studies are presented as the $C = C(x/t^{1/2})$ dependence using the Boltzmann coordinate transformation. In these coordinates, e.g., the 1D water distribution profiles obtained^{2–4} for water in the fired-clay red brick at different times that passed after the beginning of the adsorption process fall on the same curve.⁴ Numerical simulation of adsorption using the 1D diffusion equation and exponential dependence of D on the water content

$$D = D_0 \exp(\beta C),$$

where β is the fitting parameter, led to good agreement between the calculated and experimental data.

Absorption of aqueous NaCl solution into a cylindrical calcium silicate sample was studied by simultaneously recording the 1D water distribution profiles and sodium concentration profiles.¹² Similarly to the data obtained for water, the sodium concentration profiles fall on the same curve in the $C(x/t^{1/2})$ coordinates. However, the system exhibits no sharp sodium concentration front. Virtually no sodium is present in the vicinity of the water front; sodium falls far short of the water front, being adsorbed into the pore space. It was recognised that the profiles obtained using the ^{23}Na NMR signals correspond to the sodium ions present in solution, whereas the concentration of the adsorbed sodium can be found from the adsorption isotherm measured in that study. The results obtained for sodium cannot be described by the diffusion equation in the $C(x/t^{1/2})$ coordinates even assuming that the equilibrium local concentration of the adsorbed sodium (determined from the adsorption isotherm) is reached following an exponential dependence some time after the

beginning of the process rather than instantaneously. All calculations predict the presence of a more or less sharp sodium concentration front, which contradicts the experimental results.¹² Good agreement between the calculated and experimental data for water was obtained using an exponential dependence of D on C .

To reduce the water permeability of building materials, they are impregnated with some agents based on hydrophobic polymers and other compounds. An impregnation study of a hardened mortar sample with 5% solution of alkyltrialkoxysilane in methanol showed⁶ that the impregnating agent penetrates only a short distance (1.5 mm from the surface). After drying the sample water poured on its surface did not penetrate the material, in contrast to non-impregnated blank sample. Water uptake by hardened cement samples containing both clay (sodium aluminosilicate, 2%) and polyvinyl alcohol (4%) additives was much smaller as compared to the samples containing only one additive.¹³ This behaviour was explained by the formation of a hydrophobic material (as a result of cross-linking of the aluminosilicate particles and alcohol molecules), which fills the pores, thus preventing water ingress.

MRI allows visualisation of the spatial distribution of water and hydrocarbons in rock samples, which is necessary for the development of efficient procedures for improved petroleum recovery from petroleum pools based on the results of numerical simulation of the fluid diffusion in rocks (see also Section V). In particular, adsorption of water vapour into sandstone cores of various compositions, porosities and permeabilities has been studied.¹⁴ The 1D water distribution profiles recorded at relatively low saturations allowed visualisation of the ingress of water vapour into the core through its open end. Simulation of the results obtained was carried out based on the assumption of simultaneous diffusion transport of water vapour and the adsorbed water with inclusion of the local equilibrium between them and led to good agreement between the calculated and experimental data. Assuming an exponential dependence of the vapour pressure on the concentration of the adsorbed water, it was found that D exponentially increases with an increase in the water content in the sample until the vapour filtration threshold is reached at times longer than 100 h. At even longer times, the distribution of water along the core axis became relatively homogeneous and varied only slightly upon further keeping the sample over a water bath, which was due to blocking of narrow inter-pore channels with the liquid that prevented free diffusion of vapour. Carrying out a series of experiments at different temperatures allowed the determination of the activation energy for surface diffusion.¹⁴

Selective water sorbents (SWS)^{15–17} represent porous matrices impregnated with hygroscopic salts. The ability of such materials to efficiently absorb water vapour and alcohol vapours and release a great deal of energy offers considerable prospects for versatile applications of these materials, in particular, for dehumidification of gases, in heat pumps and in chemical heat accumulators. Adsorption of water vapours by individual $CaCl_2$ -impregnated silica gel granules exposed to a humid air stream leads to the appearance of a sharp front of the adsorbed water inside the granule^{7,8,18} (Fig. 1). Therefore, the presence of salt inside the millimetre-size granules makes capillary transport inefficient. The limiting stage of the process is transport of the adsorbed water into the interior of the granule. The results of numerical simulation of the process using the diffusion equation are in satisfactory agreement with the experimental data if one assumes an exponential increase in D with an increase in the water content.^{8,18,19} The use of $CuCl_2$ allows one to follow the salt redistribution as a result of successive sorption–drying cycles for the granules prepared with inhomogeneous salt distribution.^{7,18} Granules with large initial water content were characterised by the absence of a sharp water front during the adsorption process.¹⁸

Sorption of water vapour by a cylindrical pack of SWS granules exposed to a humid air stream has been studied.^{7,8}

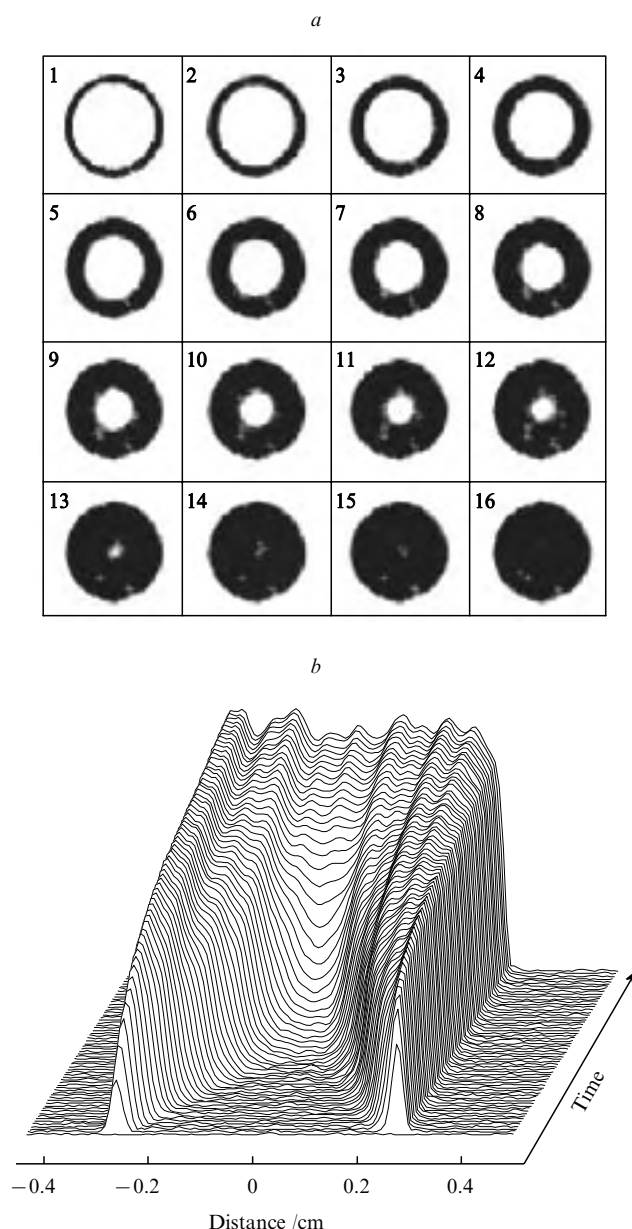


Figure 1. Visualisation of the adsorption of water vapours into a cylindrical silica gel granule impregnated with CaCl_2 (granule diameter: 6 mm).

Sixteen successively recorded two-dimensional images (acquisition time: ~ 15 min per image; the dark ring corresponds to the region containing the adsorbed water) (a); one-dimensional water distribution profiles along the diameter of the granule (acquisition time: 34 s per profile, the time taken to complete the experiment: nearly 5 h) (b).

Mention has been made that numerical simulation of the longitudinal movement of the sorbed water front requires the inclusion of (i) the effect of intragranular transport on the adsorption efficiency, (ii) flow dispersion effects in the porous medium and (iii) the character of the adsorption isotherm. Adsorption of water vapours by individual SWS granules and pellets and by SWS packs under vacuum has also been reported.^{8,20} It was found that transport of adsorbed water under vacuum is, by and large, much more efficient; however, it is to a great extent determined by the granule (pellet) composition and morphology.

Interest in mass transfer in zeolites is due to the wide use of these materials in separation processes, drying and catalytic reactions. MRI was used for studying adsorption of different gases and vapours by zeolites. The movement of the adsorbed

water front into the interior of the adsorbent (small crystals of zeolite 4A) has been studied in detail.^{21,22} The shape of the front and the character of its movement were found to be strongly dependent on the relative efficiency of transport in the intercrystalline space and intracrystalline transport within the adsorbent layer. For tiny crystals (several micrometres in size) one can expect that the limiting stage of transport process is the diffusion of water vapour in the intercrystalline space, while the equilibrium between the adsorbate concentration in the crystal and the vapour pressure above the surface of the crystal is described by the adsorption isotherm. In this case the process can be described using one nonlinear diffusion equation while the diffusion coefficient, D , depends on the amount of the adsorbed water and is expressed by a combination of constant diffusion coefficients of the water vapour and adsorbate inside individual crystals. When exponential adsorption isotherm is used, the D value increases as the water content increases and can be represented as the sum of a constant and an exponential term.^{21,23} Analogous experiments were carried out at different temperatures for two contacting layers comprised of 3 μm zeolite 4A granules with different initial water content.²³ Simulation of the results obtained showed that a decrease in the water content and an increase in temperature make the role of intragranular transport more significant. Equilibration of two contacting layers saturated with the light and heavy water occurs at a high vapour pressure and much faster, while the apparent (constant) diffusion coefficients of the adsorbed water and water vapour are somewhat higher than the corresponding values obtained in the equilibration experiments with a water-saturated layer contacting a dry layer. This difference becomes significant at higher temperatures and is probably due to the drawbacks of the mathematical model employed to describe the transport process. In particular, the intracrystalline vapour diffusion coefficient can also be strongly dependent on the vapour concentration. For instance, adsorption of *n*-hexane by a NaX zeolite layer is accompanied by a decrease in the intracrystalline diffusion coefficient with an increase in the adsorbed *n*-hexane.²⁴

In the beginning of adsorption process the concentration of adsorbate in the surface layer rapidly reaches a maximum value, which is followed by the movement of the sharp concentration front into the interior of the adsorbent.²² The concentration front is likely to move proportionally to the square root of time. In the later stages of the process the concentration front becomes somewhat diffuse and a wing appears in the region of low adsorbate concentration. The T_1 times obtained for water in the vicinity of and behind the adsorption front are different, which was associated with the changes in the mobility of water molecules that cannot be instantaneously located inside zeolite cavities.²² The gradual movement of a sharp adsorption front was also observed in studies of the adsorption of water or butane vapours by a layer comprised of tiny crystals (4 μm in diameter) of zeolite NaX (Ref. 25) and of the adsorption of *n*-hexane vapours by zeolite NaX layer.^{24,26} In contrast to this, experiments with zeolite NaX crystals 40 μm in diameter showed that intercrystalline transport is no longer the limiting factor and that butane remains uniformly distributed within the layer, whereas the overall amount of the adsorbed butane gradually increases.²⁵

The MRI technique can be used for studies of adsorption from solutions. For instance, the chemical shift of 1,3,5-*tert*-butylbenzene adsorbed on $\gamma\text{-Al}_2\text{O}_3$ differs from that of the bulk phase of 1,3,5-*tert*-butylbenzene. This allowed the determination of the variation of the adsorbate concentration with time and estimation of the effective diffusion coefficient for a CDCl_3 -filled granule from the NMR signal intensities.²⁷ Moreover, the chemical shift of the adsorbate can be pore size dependent. For instance, NMR studies of the samples of a carbon adsorbent characterised by a broad multimodal pore size distribution (from micropores to macropores) and saturated with solutions of acetonitrile, dichloromethane or benzene in CCl_4 revealed that the NMR spectra exhibit a superposition of several broad lines, each of them corresponding to the fluid confined inside pores of

different size. The chemical shift difference between the pore-confined and bulk-phase fluids varied from 1.4 ppm (large pores) to 9.6 ppm (small pores) for the three compounds studied. This indicates that the difference in the chemical shifts of the molecules inside pores of different size is due to different diamagnetic susceptibilities in the vicinity of the interfaces rather than donor–acceptor interactions. The ‘dips’ in the pore size distribution plot and slow inter-pore molecular exchange are two prerequisites for this conclusion. The linewidth is determined by intra-pore processes and is temperature independent in the range between 20 and 60 °C. From the surface areas of the signals in the NMR spectrum one can determine the fraction of the adsorbate inside the pores of different size (determination of absolute values requires the use of other measuring techniques). The method allows investigations of the role played by the pores of different size in the course of adsorption. As the adsorbate concentration increases from 0.2 to 1.2 mol litre⁻¹, the total amount of the adsorbate inside the micro- and mesopores is ‘saturated’, whereas the amount of the adsorbate in the large pores increases. Hence, preferred adsorption in micropores occurs initially. The T_1 and T_2 relaxation times of the peaks corresponding to different chemical shifts are also different. The T_2 times of the fluids confined in micropores remain constant as the adsorbate concentration varies, since the micropores are completely filled at a concentration of 0.2 mol litre⁻¹. At the same time, the T_2 times of the fluids confined in larger pores are lengthened as the concentration of adsorbate increases, since the fraction of the adsorbed molecules in these pores decreases. The amount of adsorbate in meso- and macropores increases with time, which is accompanied by displacement of the solvent molecules from the pores. The results obtained allowed construction of the isotherms of acetonitrile and benzene adsorption from CCl₄ separately for large, small and intermediate pores in the sample. Variation of the adsorbate concentration is accompanied by some variation of the chemical shifts of the NMR signals, which is consistent with their assignment to pores of different size.²⁸

Transport of fluids in soil is critical to soil contamination studies. Equilibration of soil and water after placing a sample of dried soil (humus) in water has been studied over a period of 50 days.²⁷ 2D spin density maps and the T_2 time maps of water were obtained. The sample was found to be inhomogeneous and characterised by a bimodal T_2 distribution and by the shift of the short- T_2 mode towards the short-time region. This is probably due to either a gradual filling of micropores with water or to gelation.

III. Swelling of polymers and coal during sorption of solvents

1. General remarks

The interactions between polymers and fluids or gases accompanied by swelling and dissolution of the polymers are of great practical value for fabrication, processing and use of polymeric materials as well as in the physical chemistry of coal. Swelling of polymers is often accompanied by gelation.

The polymer–solvent systems can exhibit various types of mass transfer. If the rate of solvent diffusion into the polymer is much lower than the segmental relaxation rate of the polymer, the diffusive transport of the solvent is usually observed, which obeys Fick’s laws (the so-called Case I transport). This type of transport is characterised by a gradual change in the solvent concentration along the direction of the solvent diffusion, movement of a diffuse solvent concentration front in proportion to the square root of time ($t^{1/2}$) and by nearly constant spin–spin relaxation time, T_2 , of the solvent in the solvent-filled regions of the polymer. A quite different behaviour is characteristic of Case II transport, which occurs if the solvent diffusion rate is higher than the segmental relaxation rate of the polymer. In this case, a clearly visible front of the solvent permeating into the polymer is observed, the solvent concentration front moves linearly with time, the solvent concentration behind the front is constant and the T_2 time is shortened

with the distance from the polymer surface contacting the solvent. The contour of the solvent front in 2D images matches that of the outer surface of the sample, through which the solvent ingress occurs, whereas in the case of Fickian transport the solvent contour acquires a circular shape after passage of a short time.

Fickian transport is usually observed in amorphous polymers characterised by the glass transition temperature lying below the temperature of the experiments. In contrast to this, realisation of Case II transport requires that the polymer be (initially) in the glassy state. Swelling of a polymer is usually accompanied by a decrease in the glass transition temperature, T_g , which can lead to transition of the polymer to the rubbery state. In addition to the two limiting cases, an intermediate type of transport (Case III transport) occurs. Often, the character of transport and its features can be revealed only using spatially resolved measurements.

Solvent transport into the interior of the polymer is often accompanied by cleavage of hydrogen bonds, weakening of other intermolecular interactions and by disentangling and moving apart the polymer chains. Infinite swelling leads to dissolution of the polymer.

Impregnation of polymeric materials with various solvents can be studied either by periodically interrupting the process to acquire MRI images or using real-time monitoring. The use of conventional techniques employed in the liquid-phase NMR allows selective monitoring of solvent transport,²⁹ whereas the signal of the solid matrix is often not observed due to short T_2 relaxation times. However, sometimes the mobility of the macromolecules becomes so high due to swelling that MRI imaging of the polymer is possible without using solid-state NMR techniques.^{30,31} It should be noted that MRI allows one to obtain separate images of the solvent and the polymer, as well as the images of individual solvents if their mixtures are used in the experiments (see Section III.1 in Ref. 1). Swelling of polymers and coal in solvents occurs at relatively low rates; therefore, corresponding experiments may take times from tens of minutes to tens of days.

2. Swelling of polymers and coal

Periodic recording of the 1D acetone distribution profiles in a vulcanised rubber sheet revealed³² a Fickian transport of the liquid. The acetone front moves from the surface into the interior of the sample in proportion to the square root of time ($t^{1/2}$), since the glass transition temperature of the polymer under study is below the room temperature (the experiment was carried out at room temperature). Nevertheless, no substantial dispersion of the acetone front was observed, which indicated an (exponential) increase in the diffusion coefficient with an increase in the acetone concentration (C) in the polymer. Transport of boiling water in a nylon-6,6 block also obeys Fick’s laws (the results obtained were described using an exponentially increasing dependence of D on C).³³ More recently,³⁴ transport of water in nylon-6,6 was studied at different temperatures between 20 and 100 °C; in this case, a linear dependence of D on C was used. The activation energy, E_a , for water diffusion in the polymer, extracted from the experimental data, was found to be 15 kcal mol⁻¹. This value is only slightly dependent on the water content. The temporal evolution of both the water distribution profiles and the spin relaxation times of water was described by the two-phase model, which implies the presence of two types of water molecules differing in degree of binding to the polymer. An increase in pressure caused an increase in both the diffusion coefficient and the maximum content of water in the polymer.³⁴

Analysis of the 2D MRI images of radial transport of 1,4-dioxane in a poly(vinyl chloride) rod showed³⁵ that the system is characterised by Case II transport and the movement of the 1,4-dioxane front into the interior of the rod is proportional to $t^{0.91}$. At the same time, the swelling-induced variation of the rod diameter was proportional to $t^{1/2}$, since the increase in the volume occurs in the polymer region that is behind the liquid front and is

in the rubbery state for which transport of liquids obeys Fick's laws.³⁵ The solvent region behind the front is characterised by a constant spin density and by lengthening of the T_2 time with the distance from the surface. A more complex picture was observed for swelling of a bisphenol A polycarbonate rod in acetone. The movement of the solvent front was proportional to $t^{1/2}$, thus indicating Fickian transport. The solvent concentration decreased from the surface towards the core of the rod, while the T_2 time was nearly constant. At the same time, the 2D images exhibited a contracting, high-intensity ring-shaped zone of the NMR signal around the core; the concentration and the T_2 time (mobility) of the solvent inside this zone were higher than outside.³⁵ This was associated with crystallisation of the polymer, accompanied by the displacement of the solvent into the interior of the sample, which causes the solvent front to move in proportion to the square root of time. Crystallisation of the sample leads to the appearance of wedge-like cracks oriented from the surface into the interior of the cylinder; on further swelling, stress cracking is developed and the cracks become larger.

The butadiene rubber–toluene,³⁶ isobutyl rubber–toluene³⁷ and methylsiloxane rubber–hexafluorobenzene³⁶ systems exhibit Fickian transport while the poly(ethyl methacrylate)–methanol and bituminous coal–pyridine systems are characterised by Case II transport (a sharp solvent front is clearly visible in the corresponding 2D MRI images and moves at a constant velocity).^{36,37} It was found that, due to attenuation of the signals characterised by short T_2 times, the solvent front in the MRI images can appear to be sharper than that which actually exists.³⁶ A relatively simple model proposed for the description of the kinetics of the process couples the solvent diffusion and the polymer network relaxation upon transition from the glassy state to the rubbery state.³⁶ The experimentally measured solvent front velocities were used for calculations of the constant solvent diffusion coefficient in the glassy polymer and the polymer relaxation rate constant. The poly(methyl methacrylate)–methanol system exhibits Case II transport, which is probably due to the presence of the initial Fickian induction period.³⁸ The 2D images of poly(methyl methacrylate) rods partially saturated with deuteromethanol (CH_3OD) or acetone and the 2D maps of both the spin relaxation time distribution and the diffusion coefficient of the solvent were also obtained using the NMR signal of the solvent.³⁹ The presence of a sharp solvent front and a constant solvent concentration in the region behind the front are indicative of Case II transport. When moving from the glassy core into the interior of the swollen region, the T_1 and T_2 times and the diffusion coefficients of both solvents increase and then reach a plateau. This behaviour can be due to gradual increase in the polymer mobility along the polymer chain that is fastened at one end (in the glassy domain of the sample) and to the effect of the polymer mobility on the mobility of the solvent molecules. In practice, the behaviour of the system can strongly depend on the presence of residual amounts of the monomer or water in the polymer. For instance, an increase in the initial water content in poly(methyl methacrylate) increased the diffusion rate of methanol during the absorption process. If the water content exceeds 1 mass %, a passage from the Case II transport to Fickian transport of methanol occurs.⁴⁰ The absorption–desorption cycling of water and methanol followed by drying of the polymer also accelerate the diffusion of methanol in poly(methyl methacrylate) and the diffusion kinetics alters from Case II diffusion to Fickian diffusion. In all cases the initial period of absorption was characterised by a specific type of methanol diffusion, intermediate between the Fickian diffusion and Case II diffusion.⁴⁰

Studies of the swelling of a poly(vinyl chloride) rod in toluene for 15–50 h revealed^{41,42} a sharp solvent front characteristic of Case II diffusion. The solvent front contour matched the cross-sectional shape (round or square) of the sample. When toluene penetrated into the rectangular rod through two oppositely lying surfaces, two parallel solvent fronts moved to meet each other.⁴² At the same time the high-density polyethylene–n-pentane system

exhibited a diffuse circular n-pentane front⁴¹ typical of Fickian diffusion. The sample of stretched poly(vinyl chloride) used in yet another study⁴¹ was prepared as follows. A poly(vinyl chloride) pipe was heated above the glass transition temperature of the polymer and expanded in a radial fashion. Then, slices were cut from the pipe, parallel to the pipe symmetry axis. Investigation⁴¹ revealed strong anisotropy of solvent diffusion during the swelling process. In this case, the diffusion of toluene or trichloroethylene in the polymer occurred only in the direction corresponding to the radial direction for the initial pipe and was accompanied by elongation of the sample in the same direction and by contraction of the sample along the axis orthogonal to the direction of solvent diffusion. The anisotropy of the properties of the polymer was found to be hard to detect by high-resolution solid-state NMR techniques irrespective of the presence or absence of solvent in the sample.

Swelling of a copolymer of 2-hydroxyethyl methacrylate (HEMA) and tetrahydrofurfuryl methacrylate (THFMA) in water has been studied.²⁹ The diffusion coefficient of water ($D_{\text{H}_2\text{O}}$) in polyHEMA is $(1.5\text{--}2) \times 10^{-7} \text{ cm}^2 \text{ s}^{-1}$; in the copolymer the $D_{\text{H}_2\text{O}}$ value decreases with an increase in the THFMA content due to the lower polarity of THFMA. The NMR images obtained revealed a Fickian diffusion and the peaks corresponding to increased content of water in the region between the diffusion front and the glassy core of the sample at the mole fractions of HEMA greater than 0.6. The peaks are thought to be due to the formation of small cracks appeared in peripheral regions of the glassy core owing to stress induced by swelling of the outer part of the sample; the cracks are filled with water. Further swelling of the polymer leads to closure of the cracks, while the region with the increased water content moves through the sample along with the diffusion front. As the diffusion front reaches the core of the sample, the peaks in the MRI images disappear along with the glassy core.

The character of diffusion for the same polymer–solvent pair can change appreciably with temperature. For instance, the diffusion of methanol in poly(methyl methacrylate) is Fickian at temperatures above 60 °C and Case II diffusion at temperature below 30 °C, whereas in the temperature range between 30 and 60 °C one can expect a combination of the two diffusion mechanisms.^{43,44} The character of diffusion can also strongly depend on the degree of cross-linking of the polymer. For instance, the diffusion of dioxane in a material prepared by polymerisation of styrene with divinylbenzene (DVB) additives can obey Fick's law (5% DVB), be Case II diffusion (1% DVB) or exhibit an intermediate diffusion type (2.5% DVB).⁴⁵ An increase in the degree of cross-linking of the polymer chains is accompanied by substantial reduction of the velocity of the movement of the dioxane front into the interior of the polymer sample.

Ageing of polymers strongly affects the diffusion processes. This was shown,⁴⁶ in particular, in the study of swelling of natural rubber exposed to high-temperature ageing at 170 °C in C_6D_6 . At the ageing times of the order of 50–100 min, the diffusion and swelling rates in the surface layer, in which the ageing occurs most intensely, increase. At prolonged ageing, radical polymerisation in the presence of oxygen induces cross-linking of the polymer chains, which precludes the changes in the size of the sample due to swelling, but has no effect on diffusion. The anisotropy of the polymer structure strongly affects its swelling behaviour, *e.g.*, the change in the size of the sample.

Swelling of a polymer proceeds differently when a mixture of two or more liquids is used instead of the individual liquids. Swelling of a bisphenol A polycarbonate rod in a mixture of acetone and methanol (a good and a poor solvent for the rod material, respectively) has been studied using the difference between the chemical shifts of the solvents.³⁵ It was shown that the presence of methanol reduces the rate of acetone diffusion in the polymer, whereas the diffusion coefficient of methanol increases in the presence of acetone. Analogous studies of the diffusion of individual components of acetone–methanol mix-

tures with different component ratios were carried out using deuterated compounds.⁴⁷ A square-root-of-time dependence of the movement of the solvent front and a constant T_2 time of acetone in the region behind the solvent front were interpreted as manifestations of Fickian diffusion. In mixtures with the mole fraction of acetone being less than 50% both solvents diffuse with the same rate, whereas diffusion of acetone in the mixtures with higher content of this component occurs faster. Swelling of a cylindrical vulcanised rubber sample in an acetone–methanol mixture has been studied based on large difference between the chemical shifts of the mixture components.⁴⁸ It was found that both liquids diffuse in the mixture with the same rate equal to 80% and 250% of the diffusion rates of benzene and acetone, respectively, in the case of single-component impregnation. The creation and recording double-quantum coherence of the nuclear spins allowed one to follow isooctane diffusion in identical cylindrical sample impregnated with cyclohexane.⁴⁸ Swelling studies of cross-linked polystyrene in C_6F_6 revealed the presence of the absorption front. However, no clearly visible absorption front was observed for polystyrene initially saturated with C_6H_6 ; structural inhomogeneities favoured diffusion transport of liquid.⁴⁹

A polymer gel based on poly(*N*-isopropylacrylamide) and H_2O/D_2O with CH_3OD additive, in which cross-linking of the polymer chains occurs in the presence of different amounts of *N,N'*-methylenebisacrylamide, is known to have the lower critical solution temperature.⁴⁶ As the temperature exceeds the critical value or as the concentration of the organic component of the solvent increases, the gel undergoes a transition from the swollen to the 'compressed' state. This behaviour can be used for fabrication of automatic chemomechanical valves. The 2D NMR images of a cylindrical sample revealed a decrease in the diameter of the sample with an increase in the temperature of water. The process was accompanied by the change in the T_2 -contrast due to the variation of the mobility of the polymer and water molecules. Experiments with a D_2O-CH_3OD mixture showed that the initial stage of CH_3OD diffusion in the polymer gel obeyed Fick's laws. Since the degree of swelling of the polymer gel depends on the local component ratio in the solvent, this causes some changes in the polymer gel structure, followed by deviation of the diffusion mechanism from Fickian diffusion. Sometimes the formation of a surface layer was observed, which slowed down or precluded further ingress of the solvent into the polymer gel.

Not only the solvent behaviour, but also the changes in the properties of polymers have been studied. In particular, a study of the swelling of the peroxide vulcanised natural rubber in decane^{21, 50} revealed a correlation between the T_2 time of the polymer and the local concentration of decane in the sample. An empirical relationship was suggested to describe the correlation. It was also found that the diffusion coefficient of decane exponentially increases as its local concentration increases. The study⁵¹ of swelling of poly(ethylene oxide) in water showed that both diffusion of water in the swollen hydrogel and the swelling process are diffusion controlled and not accompanied by the change in the overall volume of the polymer and water. It was also found that monitoring simultaneous ingress of H_2O and D_2O into the polymer from the opposite ends of the sample allows one to observe the redistribution of the light and heavy water in the sample even after the two solvent fronts meet. The use of CD_2Cl_2 as solvent permitted the observation of the ^1H NMR signal of the polymer prepared by cross-linking the liquid-crystalline nematic prepolymer chains.⁴⁶ The ^1H NMR signal of the polymer was shown to increase with the degree of swelling of the sample. In this case, solvent diffusion along the polymer chains occurs much faster than lateral diffusion, the latter being jumpwise.

Sodium polyacrylate is a hydrophilic polymer capable of absorbing large amounts of water (several hundred times its own mass).⁵² The 1D H_2O profiles obtained in the course of swelling of the polymer in water indicate a Fickian diffusion of water. Swelling was accompanied by shortening of the T_2 time of water due to gelation. By recording the NMR signal of the polymer it

was shown that the swelling of the polymer followed by gelation occurred nearly two times faster than the movement of the water front into the interior of the polymer. It was found that distilled water diffuses faster than water containing salts and other impurities due to different chemical potential gradients.

Swelling of polymers occurs not only when the polymers contact liquids, but also when they are exposed to vapours. For instance, the ionic conductivity of polymer electrolytes $(Pb,Zn)(CF_3SO_3)_2(PEO)_n$ [PEO is poly(ethylene oxide)] is enhanced by several orders of magnitude upon adsorption of water vapours.⁵³ The 1D spin density and T_2 profiles for the adsorbed water and for the water-soaked polymer were obtained. In a number of experiments the contributions of water and polymer were separated using D_2O . The experiments confirmed that the adsorbed water exhibits a Fickian diffusion despite the presence of a sharp front. At the same time, the results obtained using the NMR signal of the polymer are quite different, namely, the signal amplitude is constant in the region behind the water front, while the T_2 time is shortened along the direction from the adsorbing face into the interior of the sample. The apparent velocity of the H_2O front movement was much higher than in the case of D_2O ; this was explained by different dynamic properties of water and the polymer. An amorphous film with high content of poly(ethylene oxide) contained crystalline domains of the pure polymer with characteristic sizes from 500 to 800 μm . The 2D NMR images of the films totally exposed to water vapours showed that adsorption of water by the sample occurred due to the amorphous phase and caused a transition of the crystalline domains to the amorphous state.⁵³

Similar discrepancies between the results obtained using the NMR signals of the solvent and polymer were also observed during adsorption of acetone vapours by poly(vinyl chloride) samples.⁵⁴ In this case, the solvent exhibited a Case II diffusion with a constant acetone concentration behind the liquid front; however, a 'Fickian precursor', that is, a long wing of low intensity and substantial extension into the interior of the polymer, was observed ahead of the solvent front. Variation of the signal behind the liquid front was rationalised by gradual softening of the swollen polymer. Another possible explanation is low segmental mobility of the polymer chain in the glassy region of the sample and gradual increase in this parameter with an increase in the depth of penetration into the rubbery swollen region.³⁹ The acetone and polymer signals were distinguished⁵⁴ using both deuterated acetone and the difference in the T_2 times. Despite the fact that the samples studied were synthesised in the United Kingdom while studied in Germany, it was stated that no errors were introduced. The charge carrier distribution in the polyelectrolyte-based electrochemical cells has been studied.⁵⁵

Analysis of the profiles acquired using the NMR signals of polymers characterised by high segmental mobility [experiments on adsorption of the deuteriochloroform or carbon tetrachloride vapours by poly(methyl methacrylate) or polystyrene bars] revealed⁵⁶ a Fickian diffusion in these systems. This conclusion is based on the assumption of proportionality of the local concentration of the mobile polymer to the local concentration of the adsorbed solvent. However, the T_1 profiles showed that the T_1 time of the polymer varies along the length of the sample even after establishment of homogeneous swelling after long-term impregnation with the liquid. This was interpreted as a consequence of the polymer mobility gradient.

Water diffusion is of great importance for food polymers since the presence of water affects the quality and the shelf life of food products. Studies of amylose pellets prepared from corn starch revealed⁵⁷ a Fickian diffusion of water in the sample exposed to water vapours and a Case II diffusion of water in the polymer sample contacting liquid water; in addition, polymer swelling in the latter case occurred much faster than in the former. The signal amplitudes were converted into actual water content using an empirical calibration relationship.

The 2D NMR images obtained in the course of swelling of bituminous coal in deuterated solvents (pyridine, acetone) exhibited⁵⁸ a gradual increase in the concentration of proton-containing substances in solution, which was attributed to the removal of loosely bound solvent molecules from coal. The NMR signal of protons inside the coal sample was detected only after 48 h monitoring, thus reflecting the appearance of mobile proton-containing components. A sample of another type of coal exhibited conventional swelling; however, only the NMR signal of the surrounding liquid was observed.⁵⁸

In a number of studies the NMR images of polymers and coals partially saturated with a certain solvent were presented 'as is' without reporting the swelling dynamics data. Rod-like samples of bisphenol-acetone epoxy resin reinforced with a glass fibre swell in water at 93 °C in different manners depending on the character of the curing agent used in the sample preparation.⁵⁹ The difference is first of all due to the character of the microcracking of the sample. The distribution of water in the samples remains inhomogeneous even after swelling over a period of 90 days. The surface swelling occurs mainly in the vicinity of the glass fibre bundles.⁵⁹ The 2D images of the signal intensity and T_2 time distributions obtained for a rod-like sample of polybutadiene rubber completely saturated with 1,4-dioxane⁶⁰ revealed inhomogeneity of the polymer structure, which is due to, *e.g.*, poor mixing of the components or nonuniform heating in the course of the preparation and vulcanisation of the polymer. Saturation of a sample of natural rubber with hot water allowed visualisation of pores connected to the outer surface while the NMR images of a sample of vulcanised rubber completely saturated with cyclohexane allowed one to find the regions characterised by increased degree of cross-linking of the macromolecular chains.⁶¹

In spite of very broad NMR signals (300–800 Hz), the B₁-imaging technique¹ was successfully employed to acquire the 2D images of cellulose exposed to acetic acid vapours for 48 h and polystyrene swollen in liquid n-pentane for 72 h.⁴² The images of coal samples swollen in acetone, DMSO or pyridine over a period of several hours allowed studies of the coal morphology and its changes caused by swelling.⁶² It was found that permeation of solvents into coal was essentially inhomogeneous. The presence and arrangement of microcracks, cavities, mineral inclusions and other coal structure peculiarities was found using pyridine and pyridine-d₆.⁶³

Studies of solvent desorption from a polymer are also of interest. If swelling of a polymer exhibits a Case II diffusion, one can expect a transition of the polymer from the rubbery state to the glassy state in the course of desorption, which must affect the efficiency of solvent transport. The dynamics of changes in the NMR images of a poly(methyl methacrylate) rod in cyclohexane-d₁₂ at 30 °C (the sample was preliminarily kept in CH₃OD at the same temperature) has been studied.⁶⁴ During the first 60 min period the concentration of methanol in the surface layer of the sample substantially decreased and then varied only slightly over a period of 100 h. The results obtained suggested that the near-surface layer of the polymer undergoes a glass transition faster than other regions of the sample, which strongly hampers transport of the desorbing methanol.

Studies of infinite swelling resulting in dissolution of polymers are of interest from the standpoint of, *e.g.*, the development of controlled drug release systems based on dissolution of polymeric supports. For instance, water diffusion in a polyvinyl alcohol pellet (the molecular mass of the polymer lies between 35 740 and 133 000) causes a transition of the polymer to the rubbery state under normal conditions.⁶⁵ The 1D water content profiles exhibit a steep liquid front, thus indicating a relaxation-controlled (Case II) transport. For the rubbery domain, the water distribution profiles have a plateau and suggest a low diffusion resistance. As the molecular mass of the polymer increases, the diffusion rate decreases. Numerical simulation showed that the diffusion coefficient of water decreases with the distance from the pellet surface, since restricted mobility of the polymer chains in the vicinity of the

glassy core hampers transport of water. As time passes, the diffusion coefficient in the vicinity of the pellet surface contacting the solid surface increases while remains constant near the free surface contacting the solvent.

A gel layer surrounding the pellet reduces the rates of dissolution and outward diffusion of drugs.^{66,67} Swelling of a hydroxypropylmethylcellulose (HPMC) pellet in water was characterised⁶⁶ by gradual permeation of water into the pellet and by swelling-induced movement of the interface. The penetration depth of water is a function of the square root of time, $t^{1/2}$. The T_2 relaxation times of water were converted into the 1D polymer concentration profiles along the direction of swelling using the results of NMR calibration experiments. After swelling for 37 h the pellets became four-fold thicker. The regions with the HPMC content greater than 30% remained solid; reduction of the HPMC fraction to 10%–30% was accompanied by gelation, while in the regions with the HPMC content less than 10% the polymer slowly dissolved and diffused into the bulk water phase.

Osmosis-based substance release mechanisms were found to act for water in a silicon matrix containing NH₄F.⁶⁸ In the presence of salt the T_1 and T_2 times of water are shortened and the ability of the cylindrical polymer sample to absorb water is enhanced considerably. Water diffusion in the matrix was accompanied by the formation of concentrated brine droplets that grew under the action of osmotic pressure. The process was monitored over a period of three months. The spatial distribution of water in a cylindrical sample containing 1% NH₄F was more or less homogeneous during the observation time. At 5% NH₄F, after swelling for seven days the content of water in the inner region of the sample was lower than in the outer region. After swelling for 35 days at the same concentration of NH₄F the content of water in the outer region of the sample decreased. This is due to the development of stress cracking in the matrix and to release of the content of brine 'pools'. Cracking of the sample was initiated at the surface and gradually moved into the interior.

Poly(hydroxyalkanoates) form a family of semicrystalline biopolymers. They are of interest because of biocompatibility and the ability to undergo biodegradation under the action of enzymes released by microorganisms. Enzymatic degradation of thin polymer films (0.2 mm) has been studied.⁶⁹ Since the crystalline domains do not contribute to the NMR signal, the signals observed in the experiments carried out at 50–60 °C after washing and drying the sample corresponded to the spin density in the amorphous domains. At the beginning of the process the content of amorphous polymer exponentially decreased and after some time became a linear function of time. In the deeper stages of the process enzymatic degradation of both the amorphous and the crystalline polymer occurred, which was confirmed by comparing the results of NMR imaging experiments and mass loss measurements.

IV. Drying

1. General remarks

Drying has found numerous technological applications. For instance, quality of cement and concrete articles depends on the water content in set and dried materials. Drying is used in film technologies (adhesives, binders, paints, coatings, *etc.*), synthesis of catalysts and treatment of food products and vegetable materials.

Violation of the drying regimes is often accompanied by deformation and cracking of articles and coatings. Because of this, the development of methods for controlling the water content in the samples in the course of the drying process is of great importance. MRI allows one to obtain necessary information and real-time monitoring makes it reliable.

The spin relaxation times of water in many porous materials are short due to the presence of paramagnetic impurities, reduction of molecular mobility owing to binding H₂O molecules and to the interactions of water molecules with the developed surface of

solids. This situation occurs, in particular, in the studies of cement and concrete. For instance, the relaxation times of hydrated white Portland cement are as follows: $T_2 = 320 \mu\text{s}$, $T_2^* = 170 \mu\text{s}$ and $T_1 = 1.2 \text{ ms}$.⁷⁰ Therefore, quantitative studies require the use of solid-state NMR techniques.^{71–77} For instance, the use of strong gradients of the stray fields of a superconducting magnet in the STRAFI technique¹ allows the recording of the proton signals even for the hydrated and gel phases during hydration of cement.⁷⁸ The single-point imaging (SPI) technique is also promising,^{1,70} though these methods do not allow the imaging of the whole amount of water in hydrates^{78,79} [this water has a T_2^* time of $20 \mu\text{s}$ (Ref. 79)]. Samples tens or hundreds of micrometres thick are studied using the GARField device, which produces a homogeneous magnetic field in the plane of the sample and a strong static gradient in an orthogonal direction.^{80,81} The advantage of the design is that the sample is placed on the surface of the probe rather than inside it.

It should be noted that the relaxation times are usually shortened as the water content decreases; therefore, the signal amplitude is not proportional to the actual water content in the sample. Often, the signal amplitudes are corrected using some calibrations obtained by independent methods of water content determination.⁸² This allows one to exclude, in particular, the influence of other factors on the amplitude of the NMR signal. For instance, large variations of the water content in the sample cause detuning of the resonant circuit and change the sensitivity of the NMR probe.

2. Drying of materials and films

As mentioned above, MRI allows one to monitor the processes associated with the presence of water in cement, mortar and concrete. Hydration of cement during the first 48 h after the preparation of the cement paste has been studied by periodically recording the 1D water content profiles along the axis of the sample placed in a glass ampoule.⁷⁸ The experiments showed that water displaced from the bulk of the sample is present above the cement surface and the linear dimensions of the sample are reduced owing to shrinkage. The appearance of hydrates caused appreciable shortening of the T_2 time of a fraction of the H_2O molecules; therefore, even with an echo time of $30 \mu\text{s}$ the signal amplitude is attenuated and does not correspond to the actual content of water. Gypsum and lime additives cause a decrease in the degree of shrinkage of the samples and a faster attenuation of the signal amplitude.

The drying of cement^{70,79,83} and concrete^{79,83,84} after long-term moist curing has been studied. The samples were of different compositions and had different initial water content, the drying time being also different. During the first 24 h of drying, the water content in the sample decreased appreciably in the region near the open surface and to a lesser extent along the full length of the sample up to its closed end (due to capillary flow).⁷⁰ Capillary transport plays a more important role in the samples with high initial water content, since in this case the amount of hydrate formed is insufficient for filling the volume that was initially filled with water.⁸³ As the water-to-cement mass ratio decreased to 0.3–0.4, almost the whole amount of water was involved in the hydrate formation. For longer moist curing periods the porosity and permeability of the samples decreased, thus substantially reducing the efficiency of capillary transport of water in the course of drying.^{79,83} In the deeper stages of the drying process, capillary transport of water changed to diffusion transport, which was accompanied by the movement of the drying front into the interior of the sample.^{83,84} Compared to cement, the loss of water in concrete occurred faster in the early stages of the drying process, while in deeper stages the loss of water occurred more slowly. The presence of large aggregate particles in concrete prevented the material from cracking under the action of the surface tension forces due to the presence of the residual water in the pores of size 2.5 to 50 nm.

Interpretation and quantitative analysis of the data on the drying of cement and concrete first of all require detailed analysis of the relaxation behaviour of water in order to elucidate the correspondence between the NMR data and the actual water content in the sample. Probably, sometimes the signal amplitude reflects the distribution of only that fraction of water, which can be removed by drying,⁷⁹ and does not reflect the water in the gel pores.⁸⁴ For concrete samples moist cured for a long time (28 and 90 days), variation of the amplitude of the MRI profile was proportional to the change in the water content, whereas for the samples moist cured for no longer than 24 h this proportionality was observed only after drying over a period of a week.⁷⁹ This is probably due to the presence of at least three types of water molecules characterised by different (and variable) T_1 and T_2 times and, hence, by different (and variable) relative contributions. At the same time, in some instances the T_2^* time is independent of the water content, *i.e.*, the amplitude of the MRI profile is proportional to the water content.⁷⁰ When the T_1 times are analysed using the stretched exponent

$$M_z(t) = M_0 \left\{ 1 - 2 \exp \left[- \left(\frac{t}{T_1} \right)^\alpha \right] \right\} \quad (1)$$

(M_z is the longitudinal magnetisation of the nuclear spin system), the parameter α characterises the size distribution of the filled pores, which allowed the detection of the onset of microcracking 28–90 days after the beginning of the drying process.⁸³ The T_1 , T_2 and T_2^* maps for mortar and partially dried concrete were obtained.⁸⁵

Analysis of the 2D images and relaxation parameters of water in cylindrical samples of cement at low temperatures showed that the addition of superplasticiser favours a decrease in porosity, reduction of the pore sizes and precludes the formation of macropores in which water freezes at relatively high temperatures.⁸⁶ The variation of T_1 [determined according to Eqn (1)] during the hydration process revealed that the addition of the superplasticiser causes an increase in the setting time of cement and the rate of subsequent hydration. The fact that the parameter α reaches the maximum value at long times is thought to be associated with the formation of microcracks.

Drying of fired clay brick, lime-and-sand brick and gypsum by blowing air with a relative humidity of 45% (at 20°C) over the open end of cylindrical samples has been studied by periodically recording the 1D water distribution profiles along the axis of the samples.^{3,87} In all cases, a relatively homogeneous decrease in the water content along the full length of the sample was initially observed. As time passed (7 to 20 h), the drying front moving into the interior of the sample was observed. The gypsum and lime-and-sand brick samples exhibited a nonzero residual water content in the region behind the drying front. Transport processes were simulated using the diffusion equation, which allowed one to obtain the dependence of the effective diffusion coefficient on the water content for the materials under study. Namely, for all the samples the D value decreased with decreasing C (for C lying in the range from 5% to 20%), was minimum at $C = 2\%–5\%$ and increased again on further decreasing the water content. The last-named feature is associated with increasing importance of the diffusion transport of water vapour at low water content and with the presence of a plateau in the adsorption isotherm.⁸⁷ To obtain a more reliable $D(C)$ dependence in this range of water contents, the movement of the drying front was simulated using a constant velocity model. The velocity of the front movement was strongly dependent on the type of the material and inversely proportional to the length of the sample.

Drying of a cubic limestone block at 105°C was studied by periodically interrupting the drying process to acquire the NMR images.⁸⁸ It was found that the completely dried block exhibits an NMR signal of unknown nature, which is characterised by rather long relaxation times ($T_1 = 300 \text{ ms}$, $T_2 = 30 \text{ ms}$). If the water content exceeds 15% of the maximum value, drying is accompa-

nied by a relatively homogeneous decrease in the water content in the entire block; at lower water content, the drying front moving into the interior of the sample was observed. In this stage, the water present in the sample was confined in a spherical 'pool' contracting in the course of the drying process.⁸⁸

Drying of liquid-saturated porous cylindrical granules (Al_2O_3 , SiO_2 , TiO_2) by blowing dry air has been studied.^{7, 8, 89, 90} Due to the fact that the acquisition time of the 2D images was much longer than the complete drying time of the sample (< 1 h), attempts at obtaining time-resolved profiles for quantitative data analysis failed.⁸⁹ Recording the 1D water content profiles along the diameter of a cylindrical granule allowed substantial reduction of the time taken to complete a single experiment (0.5–1 min), thus providing a way of studying radial transport of liquid inside the granules in the course of the drying process.^{7, 90, 91} A special series of experiments was carried out to plot a calibration curve relating the amplitude of the experimental profile to the actual water content. The results obtained and their numerical simulation^{91, 92} showed that in the early stages the drying process proceeds at a constant rate, the slow drying regime being maintained due to efficient capillary transport of the liquid inside the granule. This was confirmed by nearly homogeneous dehumidification of the sample. Only after removal of nearly the whole amount of water the drying rate decreases, which is accompanied by creation of strong water content gradients within the sample. The effective 'capillary diffusion' coefficient, D , depends on the concentration, C , of water in the sample and much exceeds the self-diffusion coefficient of water at high C . The $D(C)$ dependence is closely related to the pore size distribution and can exhibit local extrema against the trend towards decreasing D with a decrease in the water content for the samples with complex pore size distribution patterns (e.g., bimodal). Experimentally, this manifests itself in nonmonotonic variation of the curvature of the water content profile during the drying process. The character of the profile transformations is related to the degree of homogeneity of the granules.⁷ In particular, the granules having small pores in the near-surface region are characterised by higher water content near the surface in the course of the drying process compared to the interior of the granules, though evaporation of water occurs from the surface. Inhomogeneities inside the granules cause significant distortion of the shape of the profiles. Experiments with organic liquids (acetone, cyclohexane or benzene) showed that redistribution of the liquid due to capillary flow is much less efficient and the liquid content profiles acquired during the drying process have a clearly visible dome-like shape.^{7, 90}

Drying of the monolithic alumina catalysts saturated with water by passing a stream of dry air through their transport channels has been studied. The apparent uniform decrease in the water content along the length of the monolith is due to redistribution of water owing to the action of capillary forces.^{7, 8, 93} A modified catalyst sample of identical shape, in which longitudinal transport of water in the transport channel walls was impossible, exhibited a decrease in the drying rate with the distance from the inlet flat wall of the monolith.^{8, 20} Slow drying of the monolithic catalyst in the absence of air circulation and adsorption-contact drying of a monolithic catalyst using fine-grained alumina or zeolite powders has also been studied.

A number of studies have been concerned with the drying of various water-saturated granular packs, such as glass bead packs (bead size: 0.3–1 mm),^{94, 95} sand packs (grain size: 50–100 μm), potato starch packs (granule size: 20–50 μm), silica gel packs (granule size: 40–60 μm)⁹⁵ by blowing the pack surface with dry air. The NMR images obtained exhibit inhomogeneous patterns of drying inside the packs.⁹⁴ Investigations of the effect of surface tension on the drying process were carried out with an aqueous detergent (sodium dodecylsulfate) solution.⁹⁵ The experimental results were discussed using a model, which included the diffusion transport of water and the influence of the capillary and gravity forces that play a significant role in the case of packs of larger particles.⁹⁵ Drying of (i) packs comprised of water-saturated

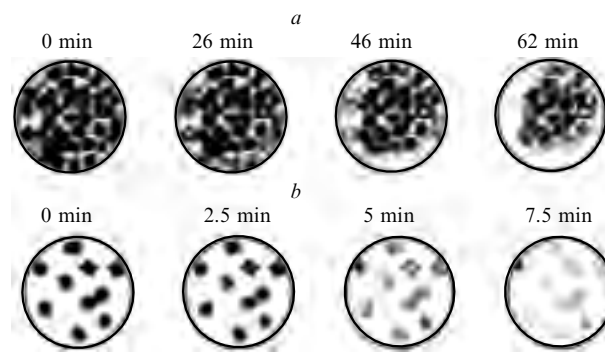


Figure 2. Two-dimensional MRI images obtained in the course of drying water-saturated alumina granules by blowing dry air through a cylindrical pack.

A pack of alumina granules 2.8 mm in diameter and 3.2 mm long (slice selective imaging technique; a slice 5 mm thick) (a); a pack comprising non-porous glass granules 2.4 mm in diameter and 2.2 mm long (invisible in the images) and a total of ten alumina granules (imaged without slice selection) (b).

porous alumina granules and (ii) mixed packs of non-porous and liquid-saturated porous granules^{7, 8} (Fig. 2) has been studied. These experiments allow studies of the details of mass transfer processes for grains located at different distances from the reactor walls.

A sample comprising a number of parallel, constant-diameter capillaries closed at one end is characterised by inefficient capillary transport. Exposure of the open end of a water-saturated sample to air stream led to establishment of fast drying regime, which was characterised by the movement of the sharp evaporation front along the capillaries towards the closed end.^{7, 96} The propagation of the evaporation front was proportional to the square root of time, while the estimate of the diffusion coefficient ($D = 0.24 \text{ cm}^2 \text{ s}^{-1}$) coincided with the diffusion coefficient of water vapour in air.

Evaporation of water from sodium silicate based films was studied by recording the 1D water content profiles in the direction normal to the film surface.⁸² Experiments on drying of the films at 22–62 °C showed that water is faster removed from the near-surface region and that strong humidity gradients appear inside the films. Analysis of the T_2 distribution suggested a decrease in the molecular mobility in the course of the drying process, the molecular mobility at a particular water content being independent of the drying regime. Despite the introduction of corrections for short relaxation time, the hydration values calculated for the most dry films were found to be nearly twofold underestimated. Therefore, quantisation was performed using a calibration obtained by weighing the samples with homogeneous water content. The spatial resolution of the technique (100 μm) was determined by the accuracy of orientation of the film plane normal to the direction of the (static) magnetic field gradient and by the magnitude of stepwise displacement of the sample in the course of the measurements.

The deposition of solid colloidal particles onto a surface *via* the drying of waterborne dispersions is an important process in nature and in many technologies. Recently, this process has attracted increased interest due to ecological problems. The drying of thin colloidal films occurs in the horizontal direction. Changes in the water distribution in the films are accompanied by transport of the solute molecules. Horizontal drying of the dispersions of acrylic latex and polystyrene latex with systematic variation of the particle size, film thickness and evaporation rate has been studied.⁹⁷ For relatively large particles, low evaporation rates and small film thickness the film edges are not completely dried over a rather long time and the central region of the film remains more wet than the peripheral zones. Then, the drying

front comes into play, moving inward from periphery, the interface between the dry and wet regions being diffuse. Ahead of the drying front, a clearly visible particle-packing front moves. In the second limiting case, the drying and particle-packing fronts overlap and move inward from the periphery just after the beginning of the drying process.⁹⁷ If a droplet of aqueous dispersion of acrylic latex is dried by exposing to air stream, a 'skin' is formed on its surface.⁹⁸ The formation of a film upon simultaneous drying and photo-induced cross-linking of the aqueous dispersion of (vinyl acetate)-*co*-ethylene copolymer based latex indicates a complex picture of changes in the concentrations and molecular mobility with the thickness of the sample. This is due to different processes, such as diffusion of water, oxygen and cross-linking agent, transmission of light and free-radical polymerisation.⁹⁹

Alkyd polymers prepared from natural substances (*e.g.*, fatty acids and oil) have found increasing use as paints. Unlike solid particles of colloidal dispersions, alkyd droplets are readily deformable in emulsion, which can affect the drying process. Therefore, drying of aqueous emulsions of an alkyd resin has been studied.^{81, 98} The difference between the chemical shifts of oil and water is sufficiently large to obtain separate NMR images.¹ It was shown that drying of a droplet deposited onto a solid surface and exposed to either stationary air or air stream was accompanied by a decrease in the size and thickness of the droplet.⁹⁸ The water loss rate was minimum at the edge and maximum at the centre of the droplet due to horizontal outward transport of water. The total amount of water decreased linearly with time over the whole observation time.^{81, 97} No increase in the alkyd resin concentration at the edge of the droplet was observed. The experimental data were compared with the results of model calculations. When the film was dried in stationary air, the film thickness linearly decreased with time during the first 13 min.⁸¹ The 1D T_2 distribution profiles obtained after 18 min exhibit a clearly visible near-surface layer, or a 'skin', characterised by much shorter T_2 time and by an increase in the thickness with time, while the underlying region of the film remains wet. The presence of a sharp interface indicates a strong dependence of the diffusion coefficient on the water content. After 190 min, the 'skin' extends throughout the full thickness of the film and the sample is characterised by one T_2 value.⁸¹ In auto-oxidative cross-linking of an alkyd resin film in the presence of a cobalt catalyst, a decrease in the amount of solvent is accompanied by shortening of the T_2 time as a result of cross-linking.⁸⁰

Drying of composite liquid packaging cardboard by exposing both surfaces to air flow (20.5–60 °C) has been studied.¹⁰⁰ The air flows were of different rates and humidities. The 1D water content, T_1 and T_2 profiles were acquired. Initially, the concentration of water in the two outer layers was higher than in the middle layer. During drying the profiles became narrower due to shrinkage of the cardboard sheet. Under faster drying conditions the water loss was predominantly from the near-surface regions, while with slower drying conditions the water loss occurred uniformly throughout all layers. Initially, the drying rate was nearly constant, and then decreased.

Knowledge of water distribution in wood is of great importance for wood-working industry. Drying of white oak lumber samples has been studied by periodically recording the cross-sectional 2D NMR images over a period of two weeks.¹⁰¹ The drying rate was found to be strongly dependent on the thickness of the sample and on the orientation of the wood rays and the growth rings with respect to the outer surface. Water loss from the surface of the wood was accompanied by the formation of a more dry near-surface region and more wet inner region, while outward transport of water could occur through wood rays.¹⁰¹ Polyexponential analysis of the spin relaxation times in different stages of the drying of cedar and fir samples allowed one to distinguish and follow the behaviour of different types of water molecules (water on the walls and inside the walls of the earlywood tracheids, latewood tracheids and wood rays) for the sap-wood and heart-wood regions.¹⁰² The T_2 time is determined by exchange of water

molecules between the surface and the bulk water phase, and the experimental values were consistent with the cavity sizes typical of tracheids and wood rays. Acoustic drying of wood has also been studied.^{103, 104} The acoustic field was shown to induce a substantial redistribution of water in the sample, which favours water recession.

Drying of food products and vegetable materials has been studied. For instance, the cross-sectional 2D NMR images of a corn spadix exposed to air flow at 60 °C exhibited a decrease in the water content inside the corn grains and reduction of the grain sizes.¹⁰⁵ A drying study of individual grains has been reported.¹⁰⁶ Drying of textile articles provides an example of drying of synthetic fabrics.¹⁰⁷

V. Diffusion

1. General remarks

NMR diffusion studies have been carried out for more than five decades.^{108, 109} One of the modern NMR applications, the multi-dimensional DOSY (diffusion ordered spectroscopy) technique, provides a tool for the analysis of the NMR spectra of complex mixtures based on the differences between the diffusion coefficients of different molecules, for estimation of the molecular sizes and for detection of molecular aggregates.^{110–114} MRI also allows spatially resolved diffusion studies.

Recently, considerable attention has been given to investigations of restricted diffusion of fluids and gases in porous materials (in this case, the presence of some obstructions/barriers imposes restrictions on the molecular displacements and, in particular, diffusion transfer).^{115, 116} Observation of the diffusive motion of the molecules in a porous medium permits extraction of information on the structure of the pore space. Generally, the apparent diffusion coefficient of the molecules in the pore space, $D(\Delta)$, depends on the observation time, Δ . At short Δ , the $D(\Delta)$ value is independent of the morphology of the porous structure and is defined as follows^{117–119}

$$\frac{D(\Delta)}{D_0} = 1 - \frac{4}{9\sqrt{\pi}} \frac{S}{V} \sqrt{D_0 \Delta} + O(D_0 \Delta). \quad (2)$$

Thus, diffusion studies at short Δ allow the determination of the pore surface-to-volume ratio, S/V . In addition, in the limiting case ($\Delta \rightarrow 0$) the molecules have no time to 'sense' the presence of barriers (see below) and the measurements give the self-diffusion coefficients of fluids.

In the long-time limit ($\Delta \rightarrow \infty$), one gets

$$\lim_{\Delta \rightarrow \infty} \left[\frac{D(\Delta)}{D_0} \right] = \frac{1}{T}, \quad (3)$$

where T is the tortuosity factor of the pore space.^{117, 118} There are also some interpolation formulae,^{117, 120} which make it possible to calculate the $D(\Delta)/D_0$ ratio at intermediate Δ values in the range between ~ 0 and $\sim \infty$.

Determination of the tortuosity factor of the pore space from the asymptotic behaviour of the diffusion coefficient requires that the molecule migrate over a distance of the order of the characteristic inhomogeneity size in the sample during the observation time. At the same time, pore size distribution measurements based on the results of analysis of the spin relaxation behaviour of a fluid assume an insignificant role of the inter-pore migration of the molecules. As can be seen, the two types of measurements are in some sense mutually exclusive.¹²¹ Gases usually diffuse much faster than fluids. Therefore, the short-time limit is hard to study for gases; however, the long-time limit can be investigated with ease.^{122–124} This can be of use in, *e.g.*, the studies of the samples with extended structural inhomogeneities.

In studies of the properties of the pore space considerable advances can be achieved using an analogy between diffusion and hydrodynamic (or gasodynamic) dispersion of flow through a

porous medium (see Section VI.4), since the dispersion coefficient can be much larger than the effective diffusion coefficient.¹²⁵

For the molecules in voids (in contrast to the interconnected pore space) the maximum migration length is limited to the void size and the product $D(\Delta)\Delta$ reaches a plateau while the $D(\Delta)$ coefficient tends to zero as Δ increases.^{117, 126} This can be used for the determination of the characteristic volume of droplets, cells, *etc.*, which imposes restrictions on the diffusion. At the same time, in contrast to relaxation porosimetry data (this technique is sensitive to the smallest characteristic size of essentially non-spherical pores, such as long cylinders and slits), the results of diffusion coefficient measurements obtained in the long-time limit depend on all characteristic pore sizes; therefore, it is not necessarily true that the asymptotic limit for $D(\Delta)$ is reached over the observation time [$\Delta < (3-5)T_1$].¹²⁷

Multiple-quantum coherence (MQC) technique with $n > 1$ is known to be more sensitive to inhomogeneities of the magnetic field than the NMR signal ($n = 1$).^{128, 129} This can be useful in measuring small diffusion coefficients. Intramolecular MQC can be created for both single quadrupolar nuclei¹³⁰ and for the system of interacting spins within the same molecule.¹³¹ If the samples have strong NMR signals, the intermolecular MQC can be created using the nonlinear echo technique¹³² based on the long-range intermolecular dipolar interaction between the nuclear spins, or the dipolar demagnetising field (DDF) technique. Experiments with a number of fluids showed¹³³ that for intermolecular multiple-quantum coherence one gets $D_{\text{ap}} \approx nD$, where D_{ap} is the apparent value (*cf.* $D_{\text{ap}} = n^2D$ for intramolecular n -quantum coherence).

The methods described below allow one to obtain information on the molecular diffusion over distances of the order of 0.1 μm , which is much better than the spatial resolution of the MRI technique. Thus, by considering the 'displacement space' it is possible to substantially improve the spatial resolution of the NMR experiments.¹³⁴

2. Methods of diffusion studies

One approach to the investigation of diffusion processes with the NMR technique involves the use of the concentration gradient of tracers or labelled compounds. In the presence of stable radicals and paramagnetic metal ions the relaxation times of the fluid or gas molecules contacting the unpaired electron spin are shortened. Diamagnetic compounds containing different nuclei and their isotopes, including mixtures of proton-containing compounds and their deuterated analogues, are also used. These experiments are most often carried out using the spatially resolved NMR imaging techniques in order to follow the temporal and spatial redistribution of tracers and then to determine the diffusion coefficient using numerical simulation methods.

A simple 'null-point' technique^{135, 136} proposed for the studies of diffusion of paramagnetic substances involves the observation of the displacement of the concentration front of the paramagnetic tracer over relatively short distances, with the concentration variation being small compared to the average tracer concentration in solution. This allows reduction of the time taken to measure the diffusion coefficients to tens of minutes instead of much longer time (*e.g.*, several days) required when using the methods based on the recording of variations of the total concentration profiles with time. Experimentally, the 1D concentration profile is acquired some time after inversion of the equilibrium magnetisation. The delay time is chosen in such a way that the desired concentration of the paramagnetic tracer corresponded to the passage of the magnetisation through zero when the signal is acquired. After calculations of the absolute values of the signal the profile exhibits a clearly seen, sharp minimum corresponding to the position of a given concentration of the diffusing paramagnetic tracer. A 2D version of the technique was also proposed.¹³⁷

MRI also allows diffusion studies without creating the gradient of the diffusing substance. In this case, selective inversion or saturation of the signal from a certain region of the sample can be

used as 'marker'. If no convection occurs, the 'dip' in the signal amplitude curve is recovered as a result of diffusion and spin-lattice relaxation.

Diffusion displacements of various molecules can be studied using the well-known¹⁰⁹ pulsed magnetic field gradient NMR techniques (pulsed field gradient, or PFG, and pulsed gradient spin echo, or PGSE). By modifying the conventional echo pulse sequence and by using strong pulsed field gradient amplitudes (up to 2500–5000 G cm⁻¹)^{138, 139} one can measure the diffusion coefficients of the order of 10⁻¹⁰ cm² s⁻¹. The measurement error is usually 5% to 10% of the measured values and depends on many factors^{140, 141} including finite duration of the gradient pulses^{142–144} and gradient-induced eddy currents,^{112, 145–147} local field gradients due to the presence of interfaces between materials with different magnetic susceptibilities,^{148–151} convection,¹⁴⁷ temperature errors and radiation damping effects.¹⁴⁸ Thorough consideration of these factors allows¹⁴⁰ the experimental error to be reduced to less than 1%. Diffusion studies can also be carried out using (quasi-)static field gradients.

The PFG technique is based on analysis of the dependence of the spin-echo signal amplitude on the magnitude of the applied field gradient. For a system of immobile spins the dephasing of precession of the nuclear spins experiencing different magnetic fields is reversible. However, random molecular displacements in inhomogeneous magnetic fields lead to incomplete rephasing of the NMR signal when the spin echo signal is created. Currently, the pulse sequences employed in PFG experiments utilise a pair of gradient pulses applied to the spin system after the transverse magnetisation is created. The gradient pulses have the effective amplitudes $-g_i$ and g_i ($i = x, y, z$), the same duration δ and are delayed by the time Δ [if a 180°-radiofrequency (RF) pulse is applied between the gradient pulses in order to rephase the transverse magnetisation, the gradient pulses must be of the same sign]. In this case, the expression for the spin-echo signal amplitude derived in the short gradient pulse approximation assuming unrestricted diffusion has the form¹⁰⁹

$$E(b) = \exp(-Db), \quad (4)$$

where

$$b = \gamma^2 g^2 \delta^2 \Delta_{\text{ef}} \quad (5)$$

(γ is the gyromagnetic ratio for the nuclei under study).

For the normal distribution of diffusive displacements one gets

$$\Delta_{\text{ef}} = \Delta - \frac{\delta}{3}. \quad (6)$$

Thus, the plot of the $-\ln[E(b)]$ dependence is a straight line with the slope D (see Ref. 109)

$$-\ln[E(b)] = Db. \quad (7)$$

Since varying the durations of the gradient pulses and delay times in the pulse sequence can affect the signal amplitude due to relaxation effects, the experiments usually involve variation of the gradient amplitudes g_i by using multiple repetition of the pulse sequence. Often, these measurements take a long time (see Section II.2 in Ref. 1); therefore, a number of fast techniques for diffusion studies have been developed.^{123, 152} In the case of multi-component solutions or mixtures the measurements can be performed for each component.

The experiment in question involves measurements of the projections of the molecular displacements on the direction of the field gradient. Often, diffusion is spatially anisotropic. The diffusion anisotropy can be detected by projecting the diffusion displacements on different spatial coordinates, which can be achieved by judicious choice of the direction of the field gradient. However, obtaining more detailed information on the diffusion anisotropy requires the determination of the 3×3 -diffusion tensor rather than scalar D_i values ($i = x, y, z$). Different elements of the diffusion tensor (including off-diagonal elements) can be deter-

mined from a special-purpose experiment in which the gradient pulses are applied along different directions (i, j) and the scalars b_i are replaced by a tensor with the elements

$$b_{ij} = \gamma^2 g_i g_j \delta^2 \Delta_{\text{ef}}, \quad (8)$$

which determine the contribution of each element of the diffusion tensor D_{ij} to the signal attenuation.^{152, 153} In principle, carrying out a total of six experiments with different orientations of the gradient vectors and one experiment without diffusion weighting (at $g = 0$) is sufficient for the determination of the elements of symmetrical diffusion tensor.

Sometimes, it is sufficient to know, *e.g.*, the spur of the anisotropic diffusion tensor, which is equivalent to the orientation average of the diffusion coefficient tensor. This can be achieved by performing one experiment with non-zero gradients (and one experiment with $g = 0$), in which the spin echo signal amplitude is proportional to the spur of the diffusion tensor.¹⁵⁴ However, the obtaining of an NMR image, in which the signal amplitude is proportional to any characteristic of the anisotropy of the diffusion tensor, *e.g.*, the dispersion and asymmetry coefficients (the second and the third moments, respectively), requires the same number of measurements ($6 + 1$) as that needed for the determination of all elements of the symmetrical diffusion tensor.¹⁵⁴

Diffusion is strongly affected by the presence of impermeable barriers (pore walls) to molecular motions. In this case, the $E(b)$ dependence cannot be described by the simple expression (4) and can also be nonmonotonic. This makes it possible to use the NMR technique in studies of the morphology of the materials in which restricted diffusion occurs.

The effects accompanying diffusion between two impermeable barriers were described¹⁵⁵ using three characteristic sizes [characteristic diffusion length l_d , pore size l_p and the parameter $l_g = (D_0/\gamma g)^{1/3}$]. Three limiting cases were considered, where one size was much smaller than the other two sizes. Since at $l_d \ll l_p$ most of the molecules do not ‘sense’ the barriers, one can expect that the corresponding experiments must give a correct value of the self-diffusion coefficient of the fluid, D_0 . However, the unrestricted diffusion regime can be attained only if the condition $l_d \ll l_g$ is simultaneously met. Then the spin-echo signal amplitude is given by expression (4). If $l_g \ll l_p$, l_d , a ‘localised’ diffusion regime is realised. In this case, the largest contribution to the observed NMR signal comes from the spins located in the near-wall region. In MRI, this leads to the so-called ‘edge enhancement’ effect and to a decrease in the observed D value. The third regime (at $l_p \ll l_g$, l_d) corresponds in MRI to the collapse of an image to a single-peak. Experimentally, the three regimes can be distinguished based on the shape of the $E(b)$ dependence. The first and second regimes were demonstrated taking the diffusion of water in a slit 160 μm wide between parallel glass plates (the slit is too wide to allow realisation of the third regime). The geometry of the experiment permits comparison of the results obtained for unrestricted and restricted diffusion by applying the field gradient parallel or normal to the plates.¹⁵⁵

Consideration of molecular diffusion in a regular system of voids or in an interconnected pore system exhibits an analogy between the PFG NMR and diffraction in optics.^{116, 134, 156, 157} As the observation time (Δ) passes, the diffusion-‘diffraction’ effects cause the appearance of extrema on the $E(q)$ dependence ($q = \gamma g \delta / 2\pi$) for a void of diameter a . Positions of the minima are close to the integer values of the product aq , which can be used for estimating the pore size. The situation becomes more complicated in the case of non-spherical pores. Numerical experiments on the diffusion in a cylindrical pore at arbitrary orientation of the axis of the cylinder with respect to the direction of the field gradient show the presence of two systems of minima on the plot of the dependence of the echo amplitude on q . These minima correspond to the motion along and normal to the axis of the cylinder, their amplitudes increasing with the increase in the $D\Delta$

product.¹⁵⁸ In one limiting case (large molecular displacements and small q values) the effective diffusion coefficient, $D = D_{\text{ef}}$, equals $L^2/12\Delta$ and $R^2/4\Delta$ if the field gradient is applied along and normal to the axis of the cylinder, respectively (L is the length and R is the radius of the cylinder). In the small-displacement limit, the $E(q)$ dependence in the form

$$E(q, \Delta) = E_A(q) = \exp(-4\pi^2 q^2 D \Delta_{\text{ef}}) \quad (9)$$

is observed only at small q ; at large q , the $E(q)$ dependence obeys a power law. An ensemble of randomly oriented non-spherical pores and the system of aligned pores are characterised by different functions $E(q)$. However, the pore orientation distribution and the pore size distribution can be distinguished only using a special-purpose experiment involving two successive ‘scattering’ acts, as was used in studies of the shape of the yeast cells.¹⁵⁹

The effect of the pore space geometry is of particular interest when following the spin motion in interconnected pore systems.^{125, 134, 160} For a regular system of pores interconnected by narrow channels the coherence effects are also manifested as extrema on the $E(q)$ plot in the $\Delta \rightarrow \infty$ limit. If the regularity of the pore space is not perfect, the $E(q)$ plot will exhibit a diffuse peak at $q \approx 1/b$ corresponding to the nearest environment, similarly to X-ray diffraction in liquids (b is the distance between the adjacent pores). The coherence effects are also substantially weakened due to orientational disordering of the pore necks; however, the effect of the structure of the pore system on the $E(q)$ dependence is still retained. Meeting the condition $2D_{\text{ef}}\Delta \approx b^2$ is optimal for obtaining information on the structure of the pore space. At $D_{\text{ef}}\Delta \gg a^2$ (a is the pore diameter) one can distinguish three regimes, *viz.*, $q \ll 1/b$, $q \sim 1/b$ and $q \sim 1/a$. The case $q \ll 1/b$ [initial portion of the $E(q)$ dependence] corresponds to large molecular displacements and allows the determination of the D_{ef} value, the D_{ef}/D_0 ratio tending to $1/T$ at $\Delta \rightarrow \infty$ (T is the tortuosity factor of the pore space). At $q \sim 1/b$, the $E(q)$ dependence for a regular pore structure exhibits a peak. This is true assuming equilibration of the situation inside the pore, when the characteristic time of migration over a distance of the order of the pore size is shorter than the characteristic time of inter-pore migration. At $q \sim 1/a$, the $E(q)$ dependence passes through a minimum, as in the case of isolated pores. At short diffusion times, Δ , the D value is independent of the morphology of the pore space, being determined by the S/V ratio for the pore space [see formula (2)].

Integration of the $E(q)$ dependence over q gives the probability for a particle to return to (or remain in) the vicinity of its initial position after a given diffusion time Δ .^{144, 161} This parameter can be used in studies of the pore space in materials with the broad size distributions of pores and solid grains constituting the material. For instance, the studies of rock cores revealed a correlation between the above-mentioned probability and hydraulic permeability of the samples.

NMR imaging in the displacement space (q -space, in contrast to NMR imaging in the k -space, or coordinate space) allows one to obtain not only the averaged diffusion characteristics (*e.g.*, the diffusion coefficient), but also complete information on the molecular displacement distribution over the observation time. Diffusion displacements can be characterised by the function $P(\mathbf{r}|\mathbf{r}', \Delta)$, which represents the probability density for a molecule initially located at the point $\mathbf{r}$ to appear at the point $\mathbf{r}'$ after time Δ .^{116, 141} The quantities measured in the NMR experiments are inevitably averaged over a large molecular ensemble present in the entire sample or in its macroscopic region. In addition, the $P(\mathbf{r}|\mathbf{r}', \Delta)$ parameter can vary in the microscopic length scale. Averaging of $P(\mathbf{r}|\mathbf{r}', \Delta)$ allows passage to the formalism of the averaged propagator $P(\mathbf{R}, \Delta)$, which gives the probability density for a molecule to migrate (or to be displaced) over the distance $\mathbf{R} = \mathbf{r}' - \mathbf{r}$ over time Δ irrespective of its initial position $\mathbf{r}$. At long observation times, Δ , the propagator can be considered as the autocorrelation function of the molecular displacements^{143, 156} or

as the autocorrelation function of the pore shape in the direction of the applied field gradient;^{159, 162} this allows the determination of the pore size as the half-width of the $P(\mathbf{R}, \Delta)$ peak, which describes the shape of the propagator as a function of $\mathbf{R}$.

The averaged propagator $P(\mathbf{R}, \Delta)$ is often measured using the above-mentioned pulse sequence with two pulsed gradients. In this case, the spin-echo signal amplitude is represented as a function of the following parameter

$$\mathbf{q} = \frac{\gamma \mathbf{g} \delta}{2\pi}. \quad (10)$$

The vector $\mathbf{q}$ is analogous to the wave vector $\mathbf{k}$; however, the $\mathbf{q}$ space is the reciprocal of the displacement space $\mathbf{R}$ rather than the coordinate space $\mathbf{r}$. If the gradient pulses are short, the spin-echo amplitude $E(\mathbf{q}, \Delta)$ and the averaged propagator are mutually conjugate:^{116, 141, 163}

$$E(\mathbf{q}, \Delta) = \int P(\mathbf{R}, \Delta) \exp(i 2\pi \mathbf{q} \mathbf{R}) d\mathbf{R}, \quad (11)$$

$$P(\mathbf{R}, \Delta) = \int E(\mathbf{q}, \Delta) \exp(-i 2\pi \mathbf{q} \mathbf{R}) d\mathbf{q}. \quad (12)$$

In the new notations, expression (4), which holds for unrestricted diffusion, takes the form of Eqn (9). The corresponding propagator describes a Gaussian distribution of diffusive molecular displacements centred at $\mathbf{R} = 0$:

$$P(\mathbf{R}, \Delta) = \frac{1}{\sqrt{4\pi D_{\text{ef}} \Delta}} \exp\left(-\frac{R^2}{4D_{\text{ef}} \Delta}\right). \quad (13)$$

q -Spectroscopy experiments involve multiple repetitions of the pulse sequence upon stepwise variation of the q parameter (as a rule, using a constant increment of the gradient amplitude). Some advanced techniques with variable q increment (in particular, this permits shortening of the measurement time) have also been developed.^{164, 165}

Dynamic q -space NMR imaging allows the determination of the spatially resolved averaged propagator $P(\mathbf{r}, \mathbf{R}, \Delta)$ and extraction of information on the displacements $\mathbf{R}$ that can be much smaller than the spatial resolution of the imaging experiments. In dynamic NMR imaging the signal amplitude, $S(\mathbf{k}, \mathbf{q})$, is experimentally measured as function of the $\mathbf{k}$ and $\mathbf{q}$ vectors at fixed Δ values

$$S(\mathbf{k}, \mathbf{q}, \Delta) = \iint \rho(\mathbf{r}) P(\mathbf{r}, \mathbf{R}, \Delta) \exp 2\pi i (\mathbf{k} \mathbf{r} + \mathbf{q} \mathbf{R}) d\mathbf{R} d\mathbf{r}, \quad (14)$$

where $\rho(\mathbf{r})$ is the spatial distribution of the spin density.

The multidimensional Fourier transformation technique makes it possible to derive the averaged propagator $P(\mathbf{r}, \mathbf{R}, \Delta)$ as a function of the coordinate $\mathbf{r}$ and to separately measure the propagator for each pixel of the NMR image using the formula^{116, 141}

$$\rho(\mathbf{r}) P(\mathbf{r}, \mathbf{R}, \Delta) = \iint S(\mathbf{k}, \mathbf{q}, \Delta) \exp(-2\pi i (\mathbf{k} \mathbf{r} + \mathbf{q} \mathbf{R})) d\mathbf{k} d\mathbf{q}. \quad (15)$$

Like usually, in this case the direction of the measured molecular displacement component is determined by the applied field gradient, *i.e.*, the $P(\mathbf{R}_i, \Delta)$ value is measured experimentally, where $\mathbf{R}_i$ is the projection of the displacement vector on the direction of the applied field gradient. However, independent stepwise variation of two or three orthogonal field gradients allows the determination of the probability $P(\mathbf{R}, \Delta)$, where $\mathbf{R}$ is the displacement vector in the 2D or 3D space, though these experiments are time-consuming and, hence, rare.

The averaged propagator formalism is applicable to the description of the experiments with short gradient pulses. Experiments with the gradient pulses of arbitrary duration and shape can be described using the formalism which is not based on the

averaged propagator and thus can also be applied to the description of non-Markovian processes.¹⁶⁶

The maximum observation time in the PFG NMR experiments is determined by the T_2 time or by a combination of the T_1 and T_2 times of the diffusing molecules. To increase the observation time, the stimulated echo sequence is often employed instead of the spin echo sequence, which makes it possible to extend the time Δ up to the times of the order of T_1 rather than T_2 or T_2^* . Experiments with inert gases can also be useful, since their spin relaxation times are much longer than those of fluids. However, the relaxation times can be substantially shortened upon pore filling with a fluid or a gas. The relaxation times also impose restrictions on the observation time in the experiments with the diffusion recovery of the NMR signal after local disturbance by the RF pulses. In the tracer concentration gradient experiments the observation time is limited to the time taken to equilibrate the tracer concentration over the sample. It should be noted that these types of experiments are inequivalent in the sense that the corresponding diffusion coefficients can be different since different measuring techniques are sensitive to the structure of the pore space in different length scales.¹⁶⁷

Another approach to the description of displacements of molecules is to use the velocity autocorrelation function.¹⁶³ The frequency analysis of this function can be performed by judicious choice of the frequency spectrum for the time integral of the effective field gradient. A study of the gradient sequences that allow one to determine the spectral densities of the velocity autocorrelation function in the frequency range (ω) from 10 Hz to 100 kHz has been reported.¹⁶³ The $D(\omega)$ coefficient of bulk water was shown to be constant in the frequency range studied (210–1670 Hz).

Due to a finite switch on–switch off time of the pulsed field gradients the molecular displacements are hard to measure at times of the order of 100 μs . In this case, the oscillating field gradients are sometimes employed.¹⁶⁸ A single field gradient pulse diffusion study technique based on the effects of long-range dipolar interaction in liquids has been proposed.¹⁶⁹ Diffusion and relaxation time studies (including spatially resolved ones) can also be carried out with the gradients of the radiofrequency field B_1 instead of the gradients of the static magnetic field B_0 .^{129, 170, 171}

As mentioned above, a feature of porous materials placed in a magnetic field is the appearance of internal field gradients due to the presence of interfaces with different magnetic susceptibilities. Diffusion in the presence of local field gradients also causes attenuation of the NMR signal; however, an increase in the observation time causes the signal amplitude to reach some constant level rather than to decrease down to zero. The characteristic time taken to reach the asymptotic limit is determined by the time of diffusive displacement of a molecule over a distance of the order of the pore size.¹⁷² If the pore system exhibits a pore size distribution, the decay of the signal is characterised by a set of characteristic times. The inverse Laplace transform allows the determination of the characteristic decay times and the pore size distribution for the sample under study.¹⁷³

3. Use of tracer concentration gradients

Diffusion in a cylindrical zirconia granule pre-saturated with water and placed in an ampoule with D_2O was studied¹⁷⁴ using the ^1H NMR signal of the 1D projections of the sample on the direction normal to the axis of the cylinder. The radial distribution of water was reconstructed using the Abel transform. The use of the 1D technique allowed the recording of a large number of profiles over the complete diffusion mixing time of two liquids. The effective diffusion coefficient and the tortuosity factor of the pore space ($T = 1.98$), which appeared to be close to the reciprocal of the sample porosity, were determined using numerical simulation of diffusion in a cylinder.

Diffusion of water in Laponite gel (synthetic smectic clay) was studied by recording the 1D profiles along the same axes of two cylindrical samples placed in contact through the flat walls to

initiate diffusion.¹⁷⁵ One of the two samples was prepared using heavy water (D₂O). Fitting of the experimental profiles was performed with inclusion of fast H/D exchange and corrected for the dependence of the NMR signal amplitude on the local light/heavy water ratio, which causes appreciable changes in the T_2 -weighting degree of the NMR signal. The (macro)diffusion coefficient of light water ($1.50 \times 10^{-9} \text{ m}^2 \text{ s}^{-1}$) was found to be close to the (micro)diffusion coefficient obtained using the PFG technique ($1.75 \times 10^{-9} \text{ m}^2 \text{ s}^{-1}$); both values are only slightly smaller than the self-diffusion coefficient of bulk water ($2.1 \times 10^{-9} \text{ m}^2 \text{ s}^{-1}$) under these conditions. This is thought to be due to the 'open' structure of the gel consisting of platelets.¹⁷⁵

Fractal systems exhibit anomalous self-diffusion and the mean square of molecular displacements is time dependent

$$\langle r^2 \rangle \sim t^{2/d}. \quad (16)$$

For unrestricted diffusion, $d = 2$; visualisation of light water diffusion in the pores of a percolation model object pre-saturated with D₂O gave a d value of 2.6.¹⁷⁶

Low-temperature conservation of *in vitro* grown living tissues requires the use of cryoprotective agents. Cryoprotective solutions are usually introduced at a low temperature to prevent the development of osmotic stress and to reduce the toxic action on the tissues. A study¹⁷⁷ of DMSO/D₂O mixture ingress into artificial dermal replacement saturated with H₂O revealed a decrease in the rate of water diffusion with an increase in the DMSO concentration due to the strong interaction between the DMSO and water molecules, which leads to higher ultimate (equilibrium) concentrations of H₂O. Analysis of the behaviour of two samples (one of them was freeze dried) showed that the presence of living cells causes acceleration of water diffusion due to osmosis effects. As the temperature decreases below room temperature, diffusion slows down. Permeation of aqueous solutions of three cryoprotective agents into a dechorionated fish embryo has also been studied.¹⁷⁸ Methanol was found in the embryo after 15 min, whereas no DMSO and propylene glycol were detected even after 2.5 h. It was concluded that the syncytial layer of yolk is impermeable for DMSO and propylene glycol and prevents them from being transferred into the interior of the embryo.

Measurements of the diffusion coefficients of copper ions or 4-amino-TEMPO[†] nitroxyl radical from aqueous solution into various gels along the axis of cylindrical samples have been reported.¹³⁵ Due to the more 'open' gel structure with larger pores, diffusion of copper ions in agarose gel ($D = 4.8 \times 10^{-10} \text{ m}^2 \text{ s}^{-1}$) occurs faster than in acrylamide gel ($D = 3.3 \times 10^{-10} \text{ m}^2 \text{ s}^{-1}$) and silica gel ($D = 3.5 \times 10^{-10} \text{ m}^2 \text{ s}^{-1}$). The diffusion coefficients of nitroxyl radical in gels were found to be nearly 80% of the corresponding values for the copper ion due to the larger size of 4-amino-TEMPO. Diffusion of Fe(II) and Fe(III) ions in a cylindrical sample of agarose gel has been studied by simulating the 1D diffusion process and led to $D = 2.7 \times 10^{-10} \text{ m}^2 \text{ s}^{-1}$ for Fe(III) and $D = 3.3 \times 10^{-10} \text{ m}^2 \text{ s}^{-1}$ for Fe(II) at room temperature.¹³⁶ Radial diffusion of copper ions in a hollow cylinder made of polyacrylamide gel, whose cavity was filled with an aqueous CuSO₄ solution ($D = 3.5 \times 10^{-10} \text{ m}^2 \text{ s}^{-1}$), has also been studied.¹³⁷ The acquisition time was less than 3 min per 2D NMR image, which is shorter than the time taken to move the diffusion front over a distance of the order of the characteristic spatial resolution achieved in the experiment (0.15–0.5 mm). Diffusion of Mn²⁺ ions from aqueous solution into agarose gel has been reported.¹⁷⁹ The radical 4-hydroxy-TEMPO was used¹⁸⁰ to investigate diffusion from aqueous solution into silk fibroin gel ($D = 8.1 \times 10^{-11} \text{ m}^2 \text{ s}^{-1}$). The NMR images obtained were both T_1 - and T_2 -weighted;¹ because of this, an increase in the local

concentration of the radical in gel initially caused an increase and then a decrease in the water signal amplitude.

Diffusion of paramagnetic tracers in liquid-saturated porous media has been studied¹⁸¹ using a tailor-made cell with an impermeable horizontal barrier between two sand layers (grain size: 250 μm). In the first experiment the upper layer was saturated with an aqueous NaCl solution while the lower layer was saturated with the same solution to which NiCl₂ (5 mmol litre⁻¹) was added. The experiment started with removal of the partition and the 2D images were obtained by acquiring the NMR signal of water, which was directly proportional to the concentration of the Ni²⁺ ions in the concentration range studied (0–5 mmol litre⁻¹) due to judicious choice of the experimental parameters. In the second experiment the upper (lower) sand layer was saturated with aqueous KCl (NaCl) solution and the 1D fluid distribution profiles were obtained by directly acquiring the ²³Na NMR signal. The diffusion coefficients obtained after fitting the experimental data were $2.7 \times 10^{-10} \text{ m}^2 \text{ s}^{-1}$ for Ni²⁺ and $1.04 \times 10^{-9} \text{ m}^2 \text{ s}^{-1}$ for Na⁺. The difference between these and actual values can be due to the effect of the Cl⁻ ions present in solution on the diffusion process. Despite the thin barrier (200 μm), the apparent diffusion coefficients for the lower layer were found to be substantially (by a factor of 3.5) overestimated due to a non-ideal contact between two sand layers.¹⁸¹

4. Diffusion studies without use of tracers

As mentioned above, an extensive literature has evolved, concerning the studies of fluid diffusion in various materials. Measurements of the D and S/V values for water diffusion in a glass bead pack,¹⁶⁰ of the D value and the pore space tortuosity factor for porous granules and catalyst powders^{182–184} and of the temperature dependence of D for anions and cations diffusing in concentrated electrolyte solutions¹⁸⁵ can serve as examples of these studies. The diffusion coefficients of hexadecane in silica and of MgO/n-octanol paste have been measured.¹⁸⁶ The experiments aimed at investigating the effects of the local field gradients were carried out using a Fe₂O₃ powder additive to MgO/n-octanol paste. Studies of water and brine diffusion in carbonate and sandstone rock cores have been reported.^{117, 121, 187} It was shown¹¹⁷ that in the short-time limit ($\Delta \rightarrow 0$) the D value tends to the self-diffusion coefficient, D_0 , of the bulk fluid. Measurements carried out at short Δ allowed the determination of the S/V ratio [formula (2)] and the surface relaxivity. At long Δ , the D/D_0 ratio decreases^{117, 187} and tends to $1/T$; however, this limit was reached for none of the samples studied.¹¹⁷ In some experiments, the expected monotonic decrease in D/D_0 with an increase in Δ was not observed at all.¹²¹ Analysis of the relaxation data showed that the samples exhibiting an anomalous behaviour were characterised by a complex pore size distribution pattern. Macroscopic structural heterogeneities of the porous medium can strongly affect transport of fluids and, in particular, be responsible for an increase in the apparent tortuosity factor.¹⁸³

For water in kraft cellulose¹⁶² at short Δ the propagator has a Gaussian shape and allows the determination of the S/V ratio. For cellulose with a reduced water content the distance between the diffusion barriers estimated from the propagator peak width at long Δ was 7 μm . The possibility of separating the contributions of free diffusing water in the inter-fibre space and of restricted water diffusing inside the fibres was recognised. Experiments showed that intra-fibre diffusion of water is anisotropic. In particular, the D values of water in a three-layer composite cardboard sheet were found to be the same for all layers at different water contents; however, the diffusion coefficient along the direction parallel to the surface of the cardboard sheet is larger than in the cross fibre direction due to the corresponding fibre orientation.¹⁰⁰ Drying of cardboard is accompanied by demonstrated shrinkage (a decrease in the pore size) and the D value also decreases. Numerical simulation was based on the model which included an exchange between two ensembles of water molecules with different D . Experiments¹⁴⁷ with a celery stalk also demon-

[†] TEMPO — 2,2,6,6-tetramethylpiperidine-1-oxyl, stable nitroxyl radical.

strated the anisotropy of water diffusion, especially in the vascular tissues. The measured D values were found to be 1.6×10^{-5} for longitudinal and $8.3 \times 10^{-6} \text{ cm}^2 \text{ s}^{-1}$ for lateral diffusion. The experimental diffusion coefficient of water in a developing wheat grain is $8.3 \times 10^{-6} \text{ cm}^2 \text{ s}^{-1}$.¹⁸⁸

The orientation of fibres in living tissues can be determined by, *e.g.*, measuring the diffusion tensor. Functional disorders are often accompanied by changes in the tissue structure, which is intimately related to the diffusion tensor.¹⁸⁹ For instance, a MRI evaluation of post-stroke patients by constructing the 3D diffusion tensor maps showed that the greatest changes in the diffusion tensor are observed for the white matter of human brain.

Measurements of the diffusion coefficient in voids can be used for sizing the droplets of the dispersed phase in emulsions.^{190, 191} Though the inverse problem (reconstruction of the size distribution from the NMR data) belongs to the class of ill-posed problems, the use of regularisation methods provides a tool for solving this problem in the absence of *a priori* information on the type of the size distribution. By employing flow-compensated PFG NMR techniques one can determine the size of emulsion droplets under flow. Measuring the $E(q)$ dependence also permits calculations of the diffusion coefficients and size distribution of molecular aggregates (*e.g.*, micelles and phospholipid vesicles).¹¹⁴ The contributions of the entire molecular aggregates, individual molecules in them and individual molecules in solution to the NMR signal can be separated based on the difference between their diffusion coefficients.

For a number of systems the $E(q)$ dependence exhibits extrema due to diffraction-like diffusion effects in the quasi-periodic porous systems. In particular, a coherent peak was observed for water in a polystyrene bead pack.^{161, 192} The $E(q)$ curves obtained for suspensions of human erythrocytes with different hematocrit exhibited some features (extrema and shoulders) due to both intra- and intercellular diffraction-like diffusion effects.¹⁹³ Cell death during the freeze–thaw cycles leads to disappearance of these features. Position of the ‘intracellular’ peak depends on the rate of transmembrane water exchange between the cell and its environment, which was confirmed experimentally by varying the temperature and by adding a transmembrane exchange inhibitor. Application of the pulsed field gradients parallel or perpendicular to the external magnetic field led to observation of different $E(q)$ dependences. This suggested that the diffusion anisotropy in the samples, which were in equilibrium with dioxygen, is a result of alignment of erythrocytes in the magnetic field (7 T) due to the difference between the diamagnetic susceptibilities of the suspension and the erythrocytes bearing oxygen-containing hemoglobin. In this case, a disk-shaped erythrocyte is aligned in such a way that the axis of the disk is directed normal to the external magnetic field. The addition of NaNO_2 to the suspension is accompanied by transition of hemoglobin to the paramagnetic state, which causes alignment of the axis of erythrocyte along the magnetic field. This was indirectly confirmed by the change in the shape of the $E(q)$ dependence. This mechanism was assumed to be responsible for the effect of the magnetic field on the blood flow in living organisms. (The experiments were carried out at 25 °C.)

When studying diffusion in porous media, spin relaxation induced variations of the NMR signal cannot be correctly included by simply multiplying the signal amplitude by the corresponding coefficient because of the effects of coupled restricted diffusion and surface relaxation.^{183, 194} In this case carrying out relaxation measurements allows a correct determination of the diffusion coefficients, relaxation times and the contributions of the components experiencing different environments.^{195, 196} Such experiments have been performed for water in a glass bead pack¹⁹⁴ and other fluids, for plants^{195, 196} and for the cat brain *in vivo*.¹⁹⁵ The authors of the last-mentioned study succeeded in separating the contributions of brain tissues and cerebrospinal fluid and in observing a decrease in the D value in an artificially created ischemic region.

Gas diffusion measurements have also been reported. For instance, the diffusion coefficient of a xenon–dioxygen mixture was determined by recording a time profile of the changes in the 1D signal projections after inversion of the magnetisation in a slice 12–24 mm thick oriented normal to the spatial coordinate of the 1D NMR image.¹⁹⁷ The diffusion coefficient of ^3He in a porous slice at a pressure of several atmospheres was determined in analogous experiments involving inversion or saturation of the signal followed by simulation of the results.^{198, 199} The spin–lattice relaxation time, T_1 , of the gas was calculated from the changes in the area under the curve of the 1D NMR signal profile.¹⁹⁸

Diffusion of xenon from the bulk gas phase into an aerogel sample causes attenuation of the NMR signal from peripheral regions of the sample after selective inversion of the signal of the bulk Xe phase.²⁰⁰ If the amplitude of the field gradients employed to obtain the image is increased, the signal of the bulk gas phase becomes weaker which allows the selective visualisation of the occluded xenon phase characterised by a relatively low diffusion rate.²⁰¹ The D values for the mixture of thermally polarised xenon with oxygen²⁰² and for hyperpolarised xenon^{123, 202} were determined using the $E(q)$ dependences. Diffusion of thermally polarised xenon in a glass bead pack has been studied.²⁰² The diffusion coefficient of xenon decreases with the observation time (12.5–1000 ms) and reaches the asymptotic limit. Measurements of the asymptotic behaviour of D values in the long-time limit in the experiments with fluorinated gases permitted the determination of the tortuosity factor of the pore space for partially sintered Y-stabilised tetragonal zirconia polycrystals.¹²²

Considerable attention has been given to diffusion of adsorbates in zeolites (*e.g.*, diffusion of water, acetone, isopropyl alcohol, propane and propene in the NaX and CsNaX zeolites,²⁰³ diffusion of alkanes in NaCaA zeolites¹³⁹) under different conditions.¹¹⁵ Since zeolites are most often used in the form of fine crystalline powders, transport of adsorbate is affected by both intracrystallite molecular diffusion and diffusion in the intercrystallite space.

Diffusion of ethane adsorbed into NaX and NaCaA zeolite powders at different observation times, temperatures, average crystallite sizes and adsorbate concentrations has been studied.²⁰⁴ The experimental conditions were chosen in such a way that the fraction, p , of the ethane molecules in the intercrystallite space was small. Therefore, at short observation times the diffusion (average) propagator had a Gaussian shape. At long observation times, when the average molecular displacement exceeds the crystallite size, the shape of the propagator depends on the ratio of D_1 and pD_2 , where D_1 is the intracrystallite diffusion coefficient of ethane and D_2 is the diffusion coefficient of ethane in the intercrystallite space. A feature of the ethane–NaCaA zeolite system is equality of the D_1 and pD_2 values at 173 K. Since the parameter p exhibits the most pronounced temperature dependence, at lower temperatures the propagator is mainly determined by intracrystallite diffusion even at long observation times; in addition, the smaller the crystallite size, the narrower the propagator peak. At higher temperatures, the propagator exhibits a wing extended towards large molecular displacements ($\mathbf{R}$), since a fraction of molecules has time to diffuse out of the crystallites. Therefore, the smaller the crystallite size, the broader the propagator peak. The average propagator observed on further extension of the observation time is due to exchange of the gas molecules between the inter- and intracrystallite space.

A study²⁰⁵ of ethane diffusion in H-ZSM-5 zeolite powder and of methane and butane diffusion in silicalite crystals and ZSM-5 zeolite at 123–383 K (see Ref. 206) revealed a decrease in D with an increase in the observation time Δ .²⁰⁵ The effect becomes less pronounced on raising the temperature and is virtually independent of the displacement $\mathbf{R}$ for methane at high temperatures. Variations of D on changes in the root-mean-square molecular displacements are due to the presence of intracrystallite barriers to diffusion (*e.g.*, intergrowth). The results obtained were

simulated using the Monte Carlo technique.²⁰⁶ The limiting stage of diffusion of benzene adsorbed into loose or compressed zeolite H-ZSM-5 is intraparticle diffusion.²⁰⁷ The D value was found to be $10^{-10} \text{ cm}^2 \text{ s}^{-1}$. The effect of coke formation in zeolite on the diffusion process was also studied.

Nitrogen ($^{15}\text{N}_2$) diffusion in CaNaA and NaX zeolites at different pressures and temperatures has been reported.¹²⁴ Small crystallite sizes and large diffusion coefficient of the gas permit only the D value for large molecular displacements to be experimentally determined, thus allowing calculations of the D_2 value.

Many technological applications of zeolites involve multi-component adsorption, which gives an impetus to research in the field of simultaneous diffusion of several adsorbates. For instance, diffusion of ethane–ethene mixture in zeolite NaX has been studied.²⁰⁸ Compared to the single-component systems, the diffusion coefficient of ethane in the binary system becomes much smaller and approaches the diffusion coefficient of ethene, which was found to be nearly constant in the single-component and binary systems.

Reagent and product diffusion during catalytic conversion of cyclopropane into propene on zeolite NaX has been investigated.²⁰⁹ In the binary system the diffusion coefficients of the two compounds were found to be equal and constant throughout the process, being coincided with the value obtained by extrapolating the results obtained when no reaction occurred. Catalytic conversion of ethene on silicalite or zeolite H-ZSM-5 was studied with CF_4 as an inert probe.²¹⁰ A three-fold decrease in the diffusion coefficient of CF_4 was observed after 240 min from the beginning of the reaction. No further decrease in D was detected; however, regions with different mobility of the probe molecules appeared in the sample. It was found that ‘short’ alkanes are mainly formed at 370 K, whereas aromatic compounds are mainly formed at 575 K. After conducting the reaction under the above-mentioned conditions the D value of CF_4 changed by an order of magnitude. The same differences were also observed for the CF_4 –hexane and CF_4 –benzene systems in the same zeolites without carrying out the reaction.

Experiments with zeolite single crystals allow one to reveal correlations between different components of the diffusion tensor, associated with the structure of the zeolite cavities and transport channels. To this end, water diffusion in natural chabazite has been investigated.¹³⁸ Diffusion anisotropy studies can also be performed with powders; however, this requires simulation of the $E(q)$ dependence.

MRI allows the determination of the dimension of the space in which diffusion occurs. For instance, one-dimensional diffusion can be established even for a sample comprising randomly oriented crystallites. A diffusion study of ethane in large crystals of $\text{AlPO}_4\text{-5}$ molecular sieves has been reported.²¹¹ The $\text{AlPO}_4\text{-5}$ crystals have a system of parallel cylindrical channels 7.3 Å in diameter and no interconnections. The mean square displacements depends on the square root of the observation time ($t^{1/2}$), which indicates a ‘single-file’ diffusion when the molecules cannot ‘bypass’ one another. At the same time, both ‘single-file’²¹² and unidirectional (rather than ‘single-file’) diffusion of methane in $\text{AlPO}_4\text{-5}$ were observed.²¹¹ A continuous-flow generation system of hyperpolarised gas was employed in studies of xenon diffusion in the 1D channels of porous nanocrystallites.²¹³ The amplitude of the NMR signal acquired using the saturation–recovery technique was used as a direct measure of the average penetration depth of the xenon atoms in the interior of the crystallites. The time dependence of the NMR signal corresponded to ‘single-file’ diffusion. The advantage of the technique is the possibility of studying molecular displacements at times from hundreds of milliseconds to tens of seconds.

5. ‘Edge enhancement’ effect

One interesting and useful consequence of the attenuation of the NMR signal in the case of diffusion in inhomogeneous magnetic field is the so-called ‘edge enhancement’ effect. The molecules

located in the vicinity of impermeable barriers migrate over shorter distances compared to the molecules present far from the barriers; therefore, they are less sensitive to signal attenuation, which is equivalent to extension of the decay time, T_2^* of the transverse magnetisation. As a result, the signal from the near-wall region will be more intense in the images. Indeed, reconstruction of the 2D diffusion coefficient maps of water and octanol in glass capillaries provided an experimental proof of the reduction of the diffusion coefficient of water in the near-wall layer up to 150 µm thick at an observation time of 0.8 s.²¹⁴ Often, reduced signal attenuation in the near-wall region compared to the bulk of the sample was experimentally observed in the diffusion-weighted NMR images of different dimension, *e.g.*, in the 1D and 2D images of water in glass capillaries 600 and 190 µm in diameter (see Ref. 215) and in the 1D images of water in a slit 2.6–2.8 mm wide.²¹⁶ The effect of the amplitude and duration of the gradient pulses²¹⁵ and of the observation time²¹⁶ on the ‘edge enhancement’ effect has been investigated. The characteristic range of the molecular displacements over the observation time under the experimental conditions was found to be 12–22 µm.²¹⁶

Rather large diffusion coefficients of gases can cause significant distortions of the NMR images. The character of these distortions strongly depends on the sample size, the field gradient amplitude and the diffusion coefficient. The possibility of attenuation of the signal from the bulk gas phase compared to the signal of gas in the near-wall region was demonstrated in experiments with xenon.^{217,218} As the relative efficiency of diffusion increases due to decrease in the field gradient or reduction of the sample size, the near-boundary peaks are broadened, approach each other and then coalesce into one peak.²¹⁸ In this case, the MRI ‘image’ does not correspond to the spatial structure of the object under study. The experimental mean diffusive displacement of gas molecules in a rectangular ampoule differs from zero at the sample boundaries and is of different sign near the oppositely lying boundaries, while the root-mean-square diffusive displacement near the boundaries is smaller than inside the ampoule. Combining these effects and diffusion weighting provides a tool for implementation of selective edge imaging; however, a drawback of this technique is a substantial reduction of the signal-to-noise ratio. The edge distortion of the 1D NMR images of gas confined between impermeable parallel walls of a rectangular ampoule has also been observed in the experiments with hyperpolarised ^3He .^{199,219} Possible reasons for distortion of the NMR images include the ‘edge enhancement’ effect and the magnetic field disturbance near the tube walls due to different diamagnetic susceptibilities of materials. In the case of hyperpolarised gas, the long-range dipolar demagnetising field produced by the spin ensemble at the location of an individual spin also causes the ‘edge enhancement’ effect.²¹⁹ Helium also exhibits a lower diffusion coefficient in the vicinity of the tube walls;¹⁹⁹ however, this was thought to be unrelated to the restricted diffusion mechanism, since the diffusive displacement over the measuring time (0.1 mm) is much smaller than the spatial resolution achieved in the experiment (0.8 mm).

On the one hand, the ‘edge enhancement’ effect can find some useful applications in, *e.g.*, the experiments involving selective NMR spectroscopy of the near-wall regions,²¹⁵ enhancing the NMR signal in the regions of impermeable boundaries and revealing partitions that would be invisible otherwise.²²⁰ On the other hand, this effect can cause significant distortions of the NMR images of microscopic objects. Broadening of spectral lines due to fast near-wall relaxation and partial penetrability of the barriers can suppress this effect.²²⁰

The ‘edge enhancement’ effect on the 1D, 2D and 3D images in linear and spherical geometries has also been the subject of theoretical studies.²²⁰ Calculations for objects with a characteristic size of 40 µm showed that an increase in the diffusion coefficient causes averaging of the ‘edge enhancement’ effect due to faster molecular motions and leads to the appearance of a single peak with the maximum at the centre of the model object.

Calculations for two hollow spheres filled with water (one sphere was placed inside the other) showed that the 'edge enhancement' is observed only inside each sphere but not at the outer surface of the smaller sphere.²²⁰

An expression for the description of the 'edge enhancement' at an arbitrary shape and duration of the pulsed field gradients has been derived.²¹⁶ The echo amplitude was expressed through the molecular motion correlation function while the inhomogeneous spatial distribution of the magnetisation phase was expanded into a plane-wave series. In this approach incoherent molecular displacements cause a discord of plane waves, thus leading to improvement of the signal-to-noise ratio in the near-wall region. The maximum signal amplitude (or minimal root-mean-square molecular displacement) is observed at some distance from the walls rather than in the immediate vicinity of the walls. This distance, as well as the width of the peak, is independent of the amplitude of the applied field gradient but increases with the observation time. The Monte Carlo simulations lead to 'sharper' near-wall peaks compared to those observed in the experiments.²¹⁵

VI. Application of magnetic resonance imaging to flow studies

1. General remarks

This Section concerns flow studies including filtration; however, one should keep in mind that the experimental methods considered here also allow investigation of other types of motion, *e.g.*, a translational or rotational motion of the entire body, deformation, *etc.* Therefore, we use the term 'flow' in a wider sense.²²¹ In addition to studies of the motion of individual molecules and molecular aggregates (by measuring the nuclear spin relaxation times and magnetisation transfer processes) and diffusion, MRI allows investigations of the transport of macroscopic mass quantities of, *e.g.*, liquids, gases and solids.^{116, 222, 223} The technique does not require introduction of tracers into the flow, imposes no limitations on the refraction indices of the media under study and provides a tool for studying optically opaque flows, *e.g.*, multiphase flow and flow of granulated solid materials through the entire volume of the flowing substance. Usually, the results of MRI studies are in good agreement with those obtained using other flow investigation techniques including optical methods.^{221, 224, 225} In contrast to many conventional methods, MRI also allows reliable visualisation of unstable flow regimes²²⁶ and investigation of transverse velocity dispersion.

The minimum flow velocity measured in the experiments is limited to diffusive molecular displacements (nearly $10 \mu\text{m s}^{-1}$ for unbound water and $1 \mu\text{m s}^{-1}$ for macromolecules²²⁷). The maximum velocity is determined by the outflow of the sample from the RF coil during the measuring time. The relative accuracy of the velocity measurements is usually several per cent. Knowledge of the velocity field allows, in particular, mapping the deformation rates of the medium and calculations of the volumetric flow of the fluid, which can be compared with the experimental results.²²⁸ It should be noted that the quantities measured by the MRI technique are statistically averaged over space and time and that the averaging scale can be varied; this provides a way for comparing the experimental data with the predictions of the theories based on the averaged quantities.²²¹ For instance, in most cases the experimental data were found to be in satisfactory agreement with the results of hydrodynamic calculations for different fluids and flow geometries.^{224, 229–240}

In studies of, *e.g.*, the flow of fluids the results are often represented as the spatial velocity distribution maps; however, the experimental techniques discussed below involve measurements of the molecular displacements over the observation time. These measurements are equivalent to the velocity measurements provided that the velocity remains constant over the observation time. This should be kept in mind, in particular, in the molecular diffusion or hydrodynamic dispersion studies.

This review concerns only a few applications of the MRI technique to flow studies in biology and medicine. At the same time, there is a wealth of such applications and a number of problems can be solved using the NMR imaging techniques employed in medical MRI evaluation. For instance, MRI has long and successfully been used in transport studies of blood and other fluids in living organisms.^{241–243} For instance, it was established that the arterial blood flow velocity can be as high as 150 cm s^{-1} (see Ref. 244) at the Reynolds numbers of up to 12 000. It should be noted that the demand to study the pulsatory flows in elastic branching vessels in the presence of spiral, vortex and reversible (in particular, valvular regurgitation induced) flows led to the development of special techniques.^{228, 245–248}

2. Methods of flow studies

The method of spatial tagging is based on the creation of tags (magnetic stripes) by changing the NMR signal in a particular region of the sample followed by tracing the movement and change in the shape of the markers in the NMR images.^{221, 249} A tag can be created using, *e.g.*, inversion or saturation of the NMR signal. In particular, the use of selective pulses and field gradients allows local manipulation of the signal in the specified slice. If the tag plane is not parallel to the image plane, the tag looks like a contrast stripe in the NMR image (Fig. 3*a*). With an increase in the delay time between the instant at which the tag is created and the instant at which the image is acquired the relative and absolute displacements of different parts (regions) of the sample will be followed by displacement and change in the shape of the tag (Fig. 3*b,c*). The lifetime of the tag is determined by the longitudinal relaxation time, T_1 , of the nuclear spins.

Creation of a single tag is usually sufficient to study low-dimensional flows. For instance, creation of a tag in the plane orthogonal to the developed flow in a straight tube and imaging the tag shape after some time immediately gives the flow velocity field (see Fig. 3*b,c*). Studies of more complex flow patterns involve creation of many tags. One can, *e.g.*, simultaneously create a number of parallel stripe-like (or planar) tags and then to create the second set of perpendicular tags.^{226, 237, 250–254} In this case the displacement of the tag cells in the NMR image permits the determination of the local flow velocity while distortion of the cell shape is related to the shear deformation.²²¹

The time-of-flight technique is also based on disturbance of the NMR signal in a particular region of the sample by the RF pulses using the signal inversion or saturation techniques. However, this approach usually involves observation of subsequent changes in the NMR signal amplitude due to displacements of the disturbed and undisturbed spins in the sample. NMR signal

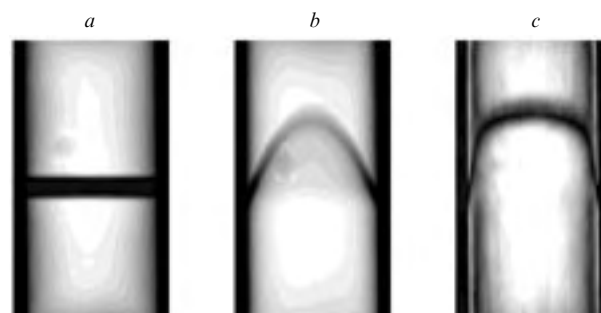


Figure 3. MRI images of water in a tube of 7.6 mm i.d. Stagnant water, $Re = 0$, the delay between the tag creation and image acquisition is 4.1 ms (*a*); laminar flow, $Re = 250$, the delay is 83.1 ms (*b*); and turbulent flow, $Re \approx 8300$, the delay is 7.1 ms (*c*). The tag was created using the spin saturation technique in the slice 1.4 mm thick and perpendicular to the plane of the two-dimensional image obtained without slice selection. Image size: 1 cm (horizontal dimension) $\times$ 3.1 cm (vertical dimension).

recovery in the disturbed region occurs due to inflow of the spins with equilibrium polarisation from undisturbed upstream regions. Simultaneously, the signal amplitude in the undisturbed downstream regions will decrease due to replacement of the undisturbed spins by the disturbed ones. In this case, variation of the signal amplitude will depend on the flow velocity (the time of flight) in a given region of the sample.

The time-of-flight technique can also be implemented without disturbance of the NMR signal by the RF pulses, since the initial magnetisation of a fluid inflowing into the magnet is close to zero and the spin relaxation rate of the fluid will depend on the time of flight taken to reach the RF detection coil, *i.e.*, it will be different for the spins experiencing different flow velocities.²⁵⁵ Signal inversion can be achieved by adiabatic passage through resonance if the fluid flows along the direction of the field gradient. The use of time-of-flight technique without spatial resolution gives the average flow velocities.²⁴² The spin disturbance and signal acquisition regions can be different. For instance, one RF coil can be used for signal disturbance while the second (detection) coil can be placed downstream.^{242, 255} It should be noted that in the literature the names of the two methods considered above are often used as synonyms since they involve creation of a spin disturbance in a particular region of the sample followed by observation of variations of the NMR signal.

Quantification of the molecular velocities and mapping the fluid velocity fields are often carried out using the phase (phase contrast) technique.^{253, 254, 256–258} In this case the pulse sequence is designed in such a way that the phase of the signal to be acquired be proportional to the spin motion velocity. For instance, if the pulse sequence includes two field gradients with the effective amplitudes $-g_i$ and g_i , duration δ and the time delay Δ between them, the phase of the transverse magnetisation will change by

$$\phi = \gamma v_i M_1 = \gamma v_i \int t g_i(t) dt = \gamma v_i g_i \Delta \delta, \quad (17)$$

where M_1 is the first moment of the gradient sequence. As can be seen, variation of the signal phase is independent of the spin location and proportional to the velocity component (v_i) parallel to the applied gradient g_i .

Flow velocity induced variation of the magnetisation phase must lie between $-\pi$ and π to exclude ambiguity of the dependence between the phase and velocity.²⁵⁹ However, sometimes this limitation is deliberately violated. If the signal-to-noise ratio and the spatial resolution of the experiment are sufficiently high, this ambiguity can be corrected for by adding a value of $\pm 2\pi n$ to the measured phase to eliminate the phase discontinuities ($\pm 2\pi$) between the signals from adjacent pixels.²⁶⁰ At the same time, if the maximum phase variation is much larger than π , the NMR image represents a map of isovelocity lines.²⁶¹

Since the phase of the NMR signal depends on many factors, measuring the molecular velocities requires separation of the flow-related contribution, which can be done in a number of ways.²⁵⁶ Often, an experiment is repeated twice and thus, and in one of the repetitions expression (17) is set to zero by either turning off the flow ($v_i = 0$) or by setting M_1 equal to zero (by *e.g.*, setting $g_i = 0$). Mapping the projection of the velocity vector on the direction of the applied gradient is achieved by calculating the phase difference for each pixel followed by calculating the velocity using expression (17). Phase modulation of the NMR signal can be readily converted into amplitude modulation using the RF pulses; therefore, the NMR signal amplitude is sometimes used as a measure of the velocity.^{261–263} In this case, the Fourier transformation of the experimental data immediately gives the velocity map without performing additional calculations.²⁶² Imaging techniques with the signal amplitude depending on, *e.g.*, flow velocity gradient have been reported.²⁶⁴

Partial outflow of the fluid from the detection coil in the phase contrast experiments does not disturb the observed flow pattern since the phase rather than amplitude of the NMR signal is

measured. At the same time, if a substantial fraction of the fluid leaves the RF coil over the acquisition time, this can lead to loss of the signal against the noise background, thus preventing the determination of the signal phase and, hence, of the flow velocity for a given image pixel.

It should be noted that NMR imaging of a moving object or its parts faces some difficulties, *e.g.*, image distortions due to variation of the spin precession frequency caused by the spin motions in the presence of the field gradient. In addition, dephasing of the magnetisation within the same pixel due to different spin velocities leads to loss of the signal in the NMR image. To avoid these undesired effects, the so-called flow-compensating technique is employed. Namely, the gradient sequence is designed in such a way that the first moment of the sequence, M_1 [see expression (17)], be zero; in this case, the phase of the signal to be acquired is the same for particles moving with different velocities, thus precluding image distortions. The condition $M_1 = 0$ is realised, in particular, for even echo signals at multiple refocussing of the transverse magnetisation in the constant field gradient. Therefore, the even echo partially prevents the loss of the signal intensity even in the case of turbulent flow.²⁶⁵

The phase encoding technique can also be used for measuring higher derivatives of the molecular coordinates with respect to time. For instance, setting M_1 to zero allows the molecular acceleration to be determined. In this case, the phase of the transverse magnetisation is proportional to the product of the projection of the acceleration vector on the direction of the field gradient by the second moment of the gradient sequence

$$M_2 = \int t^2 G(t) dt.$$

The sources of possible difficulties and errors in the phase encoding of flow have been analysed.²²⁸

An image of a fluid flow can be obtained by visualisation of streamlines by creating multiple tags. For steady-state flows the tags in the form of stripes parallel to the streamlines remain unchanged. The tags are created in the form of stripes parallel to streamlines in the upstream regions with respect to the flow region under study. Curved streamlines (if, *e.g.*, a fluid flow in a tube with a diaphragm is studied) inside the flow region under study initially are not in parallel to the straight tag stripes. However, after some time the tags adopt the shape of the streamlines as a result of replacement of the fluid in this region by the fluid from the upstream region.²⁶⁶ Streamline images can also be calculated using information on the three spatial fluid velocity components.²⁶⁷

For non-steady-state flows (*e.g.*, pulsatile intracardiac blood flow), realistic flow patterns can be obtained by visualising the trajectories of the movement of an ensemble of phantom particles that were mentally 'introduced' into the flow at some instant.²⁶⁷ Combining trajectory visualisation technique with animation and with overlay of the trajectory images²⁶⁷ or a colour velocity map²⁴⁶ on the 2D images of anatomic sections gives a complete image of such a flow.

NMR angiography is widely used^{241, 268, 269} in medical evaluation to provide a maximum contrast between the vasculature and surrounding tissues (usually, images of bright vessels against dark background are obtained). This is achieved using various versions of the time-of-flight technique. The most widely used approach involves predominant saturation of immobile spins by imaging at fast repetitions of the gradient echo sequence. The phase techniques and some magnetisation transfer based approaches are also employed in angiography. The quality of angiograms can be improved using some contrast agents that are introduced into blood to shorten the spin relaxation times.^{241, 242} NMR angiography allows studies and characterisation of blood flow and, in particular, establishment of the presence of obstacles and the determination of conditions under which the blood flow favours the appearance of plaque depositions.^{234, 244}

As mentioned above, diffusive molecular displacements can be studied by q -spectroscopy. This method is also widely used in the flow studies. For instance, if isotropic molecular diffusion with the diffusion coefficient D is superimposed on the flow characterised by the velocity $\mathbf{u}$, the expression for the echo amplitude, $E(\mathbf{q}, \Delta)$, has the form

$$E(\mathbf{q}, \Delta) = \exp(-4\pi^2 q^2 D \Delta_{\text{ef}} + i 2\pi \mathbf{q} \mathbf{u} \Delta). \quad (18)$$

As can be seen, diffusion leads to attenuation while flow causes modulation of the NMR signal. By applying the Fourier transformation of the signal one gets

$$\begin{aligned} P(\mathbf{R}, \Delta) &= \frac{1}{\sqrt{4\pi D \Delta_{\text{ef}}}} \exp\left(-\frac{R^2}{4D \Delta_{\text{ef}}}\right) \otimes \delta(\mathbf{R} - \mathbf{u} \Delta) = \\ &= A \exp\left[-\frac{(R - \mathbf{u} \Delta)^2}{4D \Delta_{\text{ef}}}\right]. \end{aligned} \quad (19)$$

Here δ is the delta function, the symbol $\otimes$ denotes convolution and A is a constant. As in the case of diffusion [see expression (13)], the propagator (19) has a Gaussian shape; however, in the presence of a flow the maximum of the propagator is shifted from the point $\mathbf{R} = 0$ to $\mathbf{R} = \mathbf{u} \Delta$.²⁷⁰ If the diffusive molecular displacements over time Δ are small, the propagator $P(\mathbf{R}, \Delta)$ characterises the flow velocity distribution (histogram).^{271, 272} The direction of the displacement component to be measured, $\mathbf{R}_i$, is determined by the direction of the field gradient g_i .

Since measurements of the average propagator are based on measurements of the NMR signal amplitude, outflow of the fluid from the RF coil can lead to underestimation of the measured $P(\mathbf{R}, \Delta)$ value. This underestimation usually increases with an increase in $\mathbf{R}$, since higher flow velocity corresponds to a larger number of spins that have time to escape from the RF coil during the observation time Δ . Partial suppression of this effect can be achieved by measuring the propagator using the slice-selective normal to the direction of the net flow rather than for the entire sample placed in the RF coil. Obtaining reliable results requires detailed analysis of artifacts and measurement errors.¹⁴¹

Similarly to diffusion studies, the use of an extra module in the pulse sequence to encode the spatial information (the so-called dynamic MRI) allows spatially resolved measurements of the average propagator $P(\mathbf{r}, \mathbf{R}, \Delta)$ [see formulae (14) and (15)]. The use of the dynamic MRI is of crucial importance in the presence of a velocity distribution within the same pixel (low spatial resolution, thin capillaries, *etc.*).^{270, 273, 274} In this case other methods for obtaining the flow velocity map only allow the effective velocity for each pixel to be determined, whereas measurements of the spatially resolved propagator make it possible to avoid this undesired averaging. Dynamic MRI with high spatial resolution can be useful in, *e.g.*, obtaining rheological information on non-Newtonian fluids, in studies of dynamic processes in plants and for the determination of the diffusion coefficient and average flow velocity for each image pixel.¹⁴¹

The above-mentioned methods can be used for imaging of the motions characterised by coherence in the measuring time scale, *e.g.*, in studies of steady-state flows. Diffusion, hydrodynamic dispersion and turbulence cause the loss of coherence and attenuation of the NMR signal.²⁷⁵ These processes can be best studied by the methods based on recording the signal amplitude variations (in particular, by measuring the propagator). Nevertheless, in the case of a developed turbulent flow both the phase encoding and the tagging technique can be used to study the average molecular displacements over the measuring time. In principle, the amplitude of the signal in the NMR images allows one to extract information on the incoherent component of the motion (turbulent or periodic pulsations, diffusion, dispersion);^{251, 252, 276} however, this problem is hard to solve. Non-steady-state processes (including aperiodic, transient and turbulent flows) can be studied by fast (10–100 ms) imaging techniques. In the case of periodic

flows the use of synchronisation of the pulsatory flow and the NMR signal acquisition allows relatively slow imaging techniques to be employed to determine the flow pattern at different instants of the pulsation period. Medical experiments concerning blood flow in organisms usually involve synchronisation of the NMR measurements with the electrocardiogram signal.

By measuring the spin echo amplitude with varied pulse sequence parameters one can determine the quantities employed in the statistical description of a random fluid motion^{265, 275, 277–279} including the correlation time of velocity fluctuations, τ :

$$\tau = \int_0^\infty \frac{R_u(t) dt}{R_u(0)}. \quad (20)$$

Here, $R_u(t)$ is the velocity autocorrelation function

$$R_u(\tau) = \langle u(t)u(t+\tau) \rangle, \quad (21)$$

while the particle velocity, $v(t)$, is represented by the sum of the average velocity, U , and the fluctuating component, $u(t)$

$$v(t) = U + u(t). \quad (22)$$

If τ is much longer than the duration of the pulsed field gradients and the time delay between them, a turbulent flow can be correctly described in terms of the mean square of velocity fluctuations, $\langle u^2 \rangle$, or turbulence intensity, I

$$I = \frac{\sqrt{\langle u^2 \rangle}}{U}. \quad (23)$$

Otherwise, in the short correlation time limit, a turbulent flow can be characterised by the eddy diffusivity, D_e

$$D_e = \langle u^2 \rangle \tau. \quad (24)$$

MRI allows measurements of both quantities, I and D_e , as well as studies of spin exchange processes in the coordinate and velocity space.^{280–282} In particular, by independently varying the amplitudes of two gradient pulses one can obtain a 2D NMR spectrum with the axes corresponding to the spatial coordinate of the spin at the instants t and $t + \Delta$ (x_1 and x_2), while the signal amplitude is proportional to the probability density of the spin displacement from x_1 to x_2 over time Δ (position exchange spectroscopy, or POXSY). The 1D sections of such a 2D spectrum characterise the probability distribution of spin migrations over different distances over a specified time. At small spin displacements (*e.g.*, at short times Δ), the 2D POXSY spectrum exhibits a signal (ridge) along its diagonal. As the spin displacements increase, the diagonal ridge is broadened until complete loss of correlation between the initial and final coordinates. It is noteworthy that the diagonals of such a 2D spectrum correspond to the average coordinate ($\langle x \rangle$) and the average velocity ($\langle v \rangle$); therefore, the same 2D spectrum rotated by -45° characterises the correlation between the average particle coordinate and average particle velocity (the probability density for a particle located at position $\langle x \rangle$ to have the velocity $\langle v \rangle$).

Analogously, independent variation of two pairs of gradients in the four-gradient experiments allows exchange studies in the velocity space,^{238, 280, 281} *i.e.*, the probability density for the spin velocity to change from v_1 to v_2 over time Δ irrespective of the spin position (velocity exchange spectroscopy, or VEXSY). The same VEXSY spectrum rotated by -45° characterises the correlation between the average velocity and average acceleration of particles. For unrestricted diffusion the correlation spectrum has a shape of a 2D Gaussian with the standard deviation $\sigma = (2D\Delta)^{0.5}$, where D is the self-diffusion coefficient of water.²³⁸ The SERPENT (sequential rephasing by pulsed field gradients encoding N time intervals) experimental technique^{283, 284} allows studies of the spin velocity or spin displacement correlations for two time intervals measured from a common initial time instant.

3. Fluid flow in various geometries

A developed laminar flow of a Newtonian fluid in a circular cross-section tube or capillary is characterised by a parabolic longitudinal velocity distribution along the tube diameter with a maximum at the tube axis and a zero flow velocity at the tube wall

$$v = v_{\max} \left[1 - \left(\frac{r}{R} \right)^2 \right], \quad (25)$$

where R is the tube radius, r is the distance from the tube axis to the observation point and $\beta = 2$. These distributions were obtained by both MRI tagging technique (see Fig. 3b) and using the maps of longitudinal velocity.^{93, 141, 227, 261, 272, 285–288}

The motion of water flowing through a narrow tube into a cell containing a fragment of a monolithic catalyst with transport channels of different shape and cross section dimensions have been studied.^{8, 20, 93} Mapping the three velocity components at different distances from the inlet edge of the monolith allowed detailed visualisation of a complex flow pattern and a transition to the fully developed flow in the inlet portion of each transport channel. Experiments revealed the presence of counterflows both inside and upstream of the monolith as well as jets flowing out of the transport channels and a vortex motion of water in the immediate vicinity downstream the block.⁹³ A film flow through the channels of a monolithic catalyst at different fluid flow rates has been investigated.²⁸⁹ The flow of a silicon oil film ~ 1 mm thick on the surface of a vertical plate made of poly(methyl methacrylate) has been studied by mapping the velocity and spin density distributions.²⁹⁰ The flow velocity was found to be higher near the plate edges, where the film was thicker due to wetting effects. This velocity increases quadratically with the distance from the plate surface. An increase in the Reynolds number causes the appearance of surface waves on the film surface. The appearance of standing waves was observed with pulsatile supply of silicon oil when the system was isolated from the atmosphere.

Spatially resolved MRI was employed in studies of a developed turbulent flow of water in a tube. The experiments revealed a large average velocity gradient near the tube walls and a nearly planar velocity distribution profile for the rest of the tube cross-section²⁷² (see Fig. 3c).

However, sometimes measuring the velocity for each image pixel is insufficient. Even in the studies with high spatial resolution the molecules within the same image pixel are characterised by different displacements due to, *e.g.*, molecular diffusion. Dynamic NMR microimaging provides a tool for measuring the displacement distribution within each image pixel.^{287, 291} At high spatial resolution, the average propagator for an image pixel is a Gaussian curve [see expression (19)]. The width of the propagator peak is determined by the diffusive molecular displacements while the shift of the maximum position is determined by the average molecular displacement due to the fluid flow.^{141, 270} At small diffusion coefficients (*e.g.*, for polymer solutions), the distribution of the molecular velocities within the same image pixel leads to overestimation of the apparent D value. In the case of a laminar flow this can be avoided by using flow-compensating technique. A feature of flows in thin capillaries is the possibility of overestimating the apparent D values for the near-wall region due to the presence of small air bubbles on the capillary walls, which disturb the flow pattern.

If the spatial resolution is low, the molecular velocity distribution within the same pixel can be rather broad.²⁹² Moreover, for thin capillaries surrounded with a stagnant fluid each image pixel can reflect both the flowing and the stagnant fluid, which leads to incorrect measurement of the average velocity and fluid flow rate in the capillary.²⁹³ In this case, measurements of the propagator for each image pixel allow one to obtain complete information on the fluid flow and to separate the contribution of the stagnant fluid to the NMR signal.^{270, 273}

Fluid flow in a tube can also be studied by measuring the propagator without spatial resolution.^{93, 272, 280} In the case of a

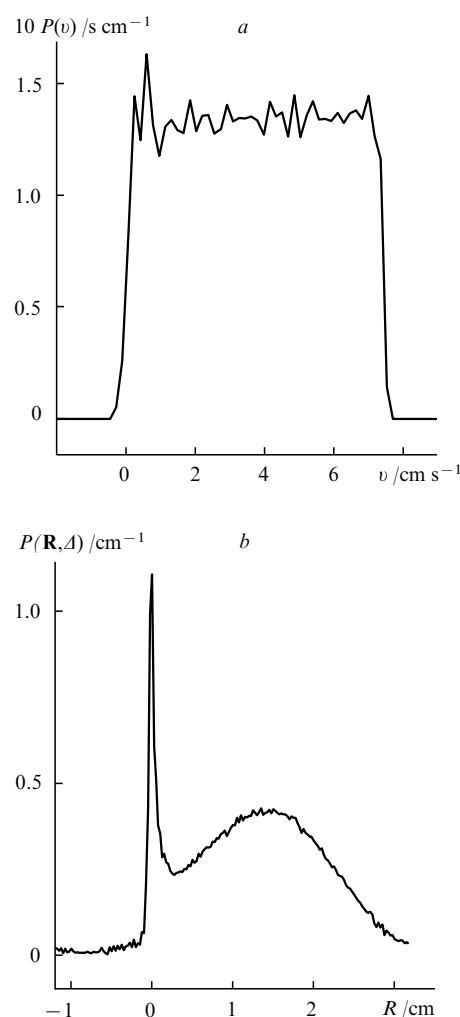


Figure 4. Averaged propagator for axial molecular displacements in flowing water.

Laminar flow ($Re = 285$) in a tube with circular cross-section (a); flow in a cylindrical glass bead pack (b). Bead diameter: 3.2 mm; bead pack diameter: 21 mm; observation time: $\Delta = 306$ ms.

laminar flow of a Newtonian fluid in a cylindrical tube the propagator considered as a flow velocity function is nearly constant in the v range from zero to $v_{\max}$ and equals zero at $v > v_{\max}$ (Fig. 4a). If we go to a turbulent flow at $Re > 2300$, the probability density becomes an increasing function of the flow velocity up to $v = v_{\max}$. Noteworthy is that an analogous propagator can also be observed in the case of a laminar, but not completely developed, flow⁹³ or a laminar flow of non-Newtonian fluid (*e.g.*, blood).²⁷² Studies of spin exchange in the coordinate and velocity space for a laminar²⁸¹ and turbulent²⁸⁰ flow of water in a tube and for a water flow in a converging tube²⁸¹ were carried out using the POXSY and VEXSY techniques.

A feature of a model of a real dialysis cell (artificial kidney) is counterflow of water inside hollow cellulose fibre membranes ('blood') and in the outer jacket ('dialysis solution').^{73, 287} An increase in the cell packing density due to the use of textile fibres leads to a more homogeneous flow distribution of the 'dialysis solution'. The regions near the ends of the dialysis cell are characterised by increased maximum water flow velocity (by a factor of 1.4) compared to the velocity in the bulk of the cell due to swelling of the membranes surrounded by rigid polyurethane shell used for cell hermetisation.²⁸⁷ Unfortunately, the 2D VEXSY spectra revealed no cross-peaks that could be indicative of the reversal of the direction of the molecular motion.²⁸⁰

Considerable attention has been given to the NMR studies of convective motion of various nature. Fluid flow inside a porous hollow-fibre membrane is known to induce slow convective flows in the surrounding fluid. For instance, an NMR imaging study of a reactor with 40 parallel membranes revealed an increased flow velocity in the narrow gaps between adjacent membranes.²³¹

Convection can arise even at relatively small temperature gradients (*e.g.*, 0.05 K cm^{-1} for convection in chloroform). In particular, the temperature gradient in the bore of a magnet of an NMR spectrometer is sufficient to induce a convective flow of water with a velocity of up to 0.5 mm s^{-1} (see Ref. 261). Such a flow in a liquid-containing ampoule 5 mm in diameter was also induced by temperature gradients during thermal regulation or as a result of absorption of the RF radiation. The flow velocity was $\sim 0.5 \text{ mm s}^{-1}$ for water or DMSO and reached up to 5 mm s^{-1} for chloroform.^{262, 294} The 2D NMR images exhibited the presence of numerous convection cells and 'twisting' of the nodal plane in the ampoule.²⁶²

Rayleigh convection with velocities of up to $600 \mu\text{m s}^{-1}$ was observed in a bottom-heated silicon oil layer 1 cm thick.²⁹⁵ The study revealed the presence of four convection cells whose pattern and relative sizes were in agreement with the results of visual observations. A 5% polystyrene solution in cyclohexane in a bottom-heated ampoule exhibited the presence of a convection cell and a steady-state character of convection.²⁹⁶

A convective fluid flow in a freely falling droplet has been studied as a model system with two interacting phases.²⁹⁷ Because of the short residence time of the droplet inside the RF coil recording a 3D NMR image required a total of 33 800 droplets to fall. The droplet size reproducibility was better than 99%. Large-scale water circulation in droplets was mapped and it was shown that the addition of surfactants causes reduction of the droplet diameter, improves reproducibility of the droplet size and shape and shifts the convection pattern towards much smaller length scale.

If a fluid has some regions with locally different concentrations of oppositely charged particles, application of an external electric field induces electro-osmotic transport. For instance, placing a closed capillary with charged walls filled with aqueous KCl solution ($1 \text{ mmol litre}^{-1}$) in an axial electric field causes the fluid in the near-wall region to move, which is due to the increased concentration of the counterions in the near-wall layer.²⁹⁸ This induces a neutral fluid flow with parabolic velocity distribution along the tube diameter; however, in contrast to conventional flow in the tube, the flow velocity on the walls differs from zero and is reversed with respect to the flow velocity direction at the capillary axis.^{235, 298} The characteristic flow velocity was found to be 0.1 mm s^{-1} while the settling time of the steady-state flow with pulsed switching on the electric field was of the order of 100 ms.²⁹⁸ The use of coatings neutralising the surface charge reduces the electro-osmosis effect.²³⁵

A nitrobenzene– C_6D_6 mixture also exhibited electroconvection, which can be due to the appearance of the space charge as a result of association of the polar molecules around the ions.²⁸² In this case, the expression for the effective diffusion coefficient at room temperature has the form

$$D = 1.08 \times 10^{-5} \text{ cm}^2 \text{ s}^{-1} + (3.33 \times 10^{-5} \text{ cm}^4 \text{ kV}^{-2} \text{ s}^{-1}) E^2,$$

where E is the strength of the applied electric field.

The flow of fluids in curved channels is strongly different from the flow in straight tubes. The pressure gradients directed normal to the net flow are responsible for the appearance of complex secondary flows, which lead to significant changes in the flow pattern. A laminar flow of water in a tube with abrupt contraction and/or expansion exhibits large deviations from the parabolic longitudinal velocity distribution and rather high radial velocities. It was found that the flow velocity increases (decreases) as water flows in (flows out of) the narrow region of the tube. Recirculation flow has also been observed in the immediate vicinity downstream

the expansion.^{232, 233} The flow of water in branching tubes has been studied.²⁵⁶

Fluid flow in a tube with an U-shaped bend exhibited parabolic longitudinal velocity profiles before the bend²⁹⁹ and an acceleration of the flow near the inner wall of the tube just after the curved section, which induced a displacement of the rapidly moving molecules and the maximum flow velocity towards the outer wall.^{236, 239, 263, 299} Rather fast flow produced rotating, spiral Dean vortices that were clearly seen in the transverse velocity maps.²⁹⁹

To obtain the velocity distribution maps at different instants of the pulsation period, studies of pulsatile flow in straight²⁴⁰ and U-shaped tubes^{236, 239} were carried out with synchronisation of the pulse sequence with flow pulsations.

Studies of aperiodic flows require the use of fast NMR signal acquisition techniques. For instance, imaging over a period of 20 to 50 ms allowed one to obtain an 'instantaneous' velocity distribution map for a turbulent flow of water in a tube.^{251, 264, 300} In particular, a transition to turbulence with alternation of turbulent and laminar flow regions in the flow pattern was detected in the Re range between 1500 and 3000. The 1D temporal autocorrelation function of the signal amplitude and the 2D spatial autocorrelation function of the signal amplitude corresponding to the transition to turbulent flow were calculated.²⁶⁴ It was found that the correlation time is maximum (0.45 s on the tube wall and 0.8 s at the tube centre) at $\text{Re} = 2000$ and decreases with an increase in the Re value due to the appearance of progressively faster and smaller vortices. The correlation length was maximum (4 mm) at $\text{Re} = 3000$ and also decreased as the Reynolds number increased. Transition to a turbulent flow and recirculation flows in a tube with a contraction have been studied at different Reynolds numbers^{244, 301} and the appearance of a Karman vortex street behind the rod placed in the tube normal to the direction of the net flow ($\text{Re} = 39 - 200$) has been explored.²⁴⁴ At $\text{Re} \geq 82$, the vortices rotating in the opposite direction alternately separated from different sides of the rod at a frequency of 1.7 Hz. The use of fast NMR imaging techniques also allows studies of transient flows, *e.g.*, establishment of a steady-state regime in the system after starting the flow.²³³

Statistical characteristics of a flow at long correlation times, τ , of velocity fluctuations have been measured for a turbulent flow of water in a tube and for grid-generated turbulence using grids of different cell size.²⁷⁷ For the flow in a tube at $\text{Re} > 2000$ the mean square velocity fluctuation rapidly increases as the Re value increases, whereas the flow turbulence intensity remains nearly constant. Measurements in the opposite, short τ limit allowed one to obtain the spatial τ distribution maps and the eddy diffusivity (D_e) distribution maps for the fluid flowing in the region behind the tube contraction/expansion²⁷⁸ and for a jet flowing through a tube into the flat wall of a right liquid-filled cylinder.³⁰² In the last-mentioned experiments the D_e values reached $0.7 \text{ cm}^2 \text{ s}^{-1}$.

The Taylor–Couette flow, *i.e.*, the flow of a viscous fluid in the gap between two coaxial cylinders rotating at different rates, is of great practical value. Mapping the spatial velocity distribution using the NMR imaging technique allows characterisation of the flow of the fluid in the gap.^{226, 303} At low rotation rates, a cylindrical fluid flow occurs, which is employed, in particular, in conventional Couette viscometers. As a critical combination of the cylinder rotation frequencies is reached, a flow instability appears, leading to the appearance of Taylor vortices in the form of toroidal cells in the longitudinal direction.²²⁶ This effect is used in separators and mass transfer reactors. The size and behaviour of the Taylor cells for the spiral Poiseuille flow (a combination of the Couette flow and longitudinal fluid flow) has been studied.²²⁶

Rotational motion including the Couette flow can be studied using the oscillating (rotating) field gradients. Varying the rotation frequency of the field gradient allows selective observation of the signal of a cylindrical fluid volume element for which the rotation frequency coincides with the gradient rotation frequency.³⁰⁴ The 2D correlation spectra of the Couette flow

obtained using the VEXSY exchange spectroscopy exhibit a complex 'ridge' pattern, which is to some extent similar to the Pake structure in the 2D dipolar correlation spectroscopy.²³⁸

Information on the flow of fluids in extruders is useful for optimisation of extrusion process. The velocity distribution maps of a 1.5% aqueous carboxymethylcellulose solution in an extruder with open or closed discharge with immobile cylinder and a rotating straight or tapered screw, obtained using the MRI technique were compared with the results of model calculations.²³⁰

MRI is also widely used in the investigations of multicomponent flow systems; the technique allows studies of the flow of individual components of complex mixtures. The contributions of different components can be separated in a variety of ways.^{1,288} Application of the chemical shift selective NMR imaging was demonstrated taking the oil-in-water emulsions as examples. This type of emulsions is of great importance for food and petrochemical industries.^{288,305} It was found that the radial distribution profiles of the longitudinal velocity²⁸⁸ and the maximum velocity³⁰⁵ for water and oil are identical. At the same time, profile-shape analysis showed that the emulsion viscosity decreases as the shear rate increases.²⁸⁸ Partial separation of the emulsion due to shear-induced migration of the dispersed phase allowed one to observe the flow of neat oil, water and emulsion as well as a recirculation flow in front of the tube contraction.²⁸⁸

Complex fluids, such as polymer solutions and melts, emulsions, suspensions, gels and micellar solutions exhibit viscoelastic properties under mechanical stress. Rheology studies the mechanical properties of such viscoelastic fluids, usually under conditions of a steady-state flow accompanied by shear deformation. The rheological properties of non-Newtonian fluids should be taken into account in the design of various technological processes. Online measurements of the rheological properties of materials in the course of a technological process are of importance for control purposes. MRI can be used as a technique for fast contactless determination of the rheological properties of materials.

In contrast to conventional methods, a single NMR flow imaging experiment with a viscoelastic fluid can provide information on the fluid viscosity over a broad range of shear rates. Information on the shear rate is extracted from the spatial flow velocity distribution maps.^{306,307} For instance, for a laminar fluid flow in a capillary [expression (25)] the shear rate,

$$\dot{\gamma}(r) = \left| \frac{dV(r)}{dr} \right|, \quad (26)$$

continuously changes from zero at the centre of the capillary to the maximum value on the capillary walls. Given the pressure drop, the expression for the shear stress has the form

$$\sigma(r) = -\frac{\Delta P}{2L}r, \quad (27)$$

where r is the current radius and $\Delta P/L$ is the pressure gradient. Shear viscosity can be found as

$$\eta(\dot{\gamma}) = \frac{\sigma(\dot{\gamma})}{\dot{\gamma}}, \quad (28)$$

which allows extraction of information on the shear viscosity for a range of shear rates from one map.³⁰⁶

A number of rheometer designs and features have been reported.^{308,309} These devices can be placed inside the probe of an NMR microimager to perform rheo-NMR microimaging studies of the properties of various fluids. The flow velocity distribution maps of water and polydimethylsiloxane in such rheometers have been obtained.³⁰⁸ Rheometers are small devices and require small amounts of fluids to be studied; hence, one can produce high shear rates.^{308,309} It was found³⁰⁸ that combining rheo-NMR microimaging and NMR spectroscopy allows one to

relate the mechanical properties of fluids to their molecular properties. For instance, the ^2H NMR spectrum of a CTAB/ D_2O micellar solution (CTAB is cetyltrimethylammonium bromide) was studied as function of the radial coordinate in the gap between two cylinders in the Couette geometry. Line splitting in the NMR spectrum measured in the region of the maximum mechanical stress near the internal cylinder walls indicated the formation of a nematic phase in this region of the sample. In a study of polyacrylamide in D_2O it was found that the shear rate correlates with the spin relaxation times of the polymer.

The rheological behaviour of polymer melts, including the shear viscosity, is of great importance in many technological processes. For instance, the molecular mass distribution of linear polymers correlates with the dependence of their shear viscosity on the shear rate.³⁰⁶ Velocity profile measurements for a low density polyethylene melt flowing at 232°C along a cylindrical tube showed that the fluid exhibits a nearly Newtonian behaviour; a slight decrease in viscosity was observed only at shear rates higher than 1 s^{-1} .³⁰⁷

A markedly decreasing dependence of the shear viscosity on the shear rate (the minimum and maximum values differ by two orders of magnitude) was obtained for the flow of a 1% carboxymethylcellulose solution in a tube.³⁰⁶ This dependence is in agreement with the results of conventional measurements performed at shear rates exceeding 10 s^{-1} .

A feature of the motion of suspensions and pastes under conditions of inhomogeneous shear distribution is particle migration towards the region of low shear rate,³¹⁰ which results in strong concentration gradients in the initially well-mixed suspensions and has a negative effect on their heat exchange properties. Simultaneously, this causes essential changes in the rheological properties, since the effective viscosity is strongly dependent on the particle concentration.

A number of studies has been devoted to the investigations of particle migration and its influence on the velocity distribution and concentration profiles for suspensions of microspheres immersed in viscous fluids in different flow geometries. For instance, a suspension of monodispersed spherical particles in a Newtonian fluid of the same density was plunger pumped³¹¹ along a cylindrical tube with abrupt contraction and expansion. The velocity distribution along the diameter was described by the function (25) with $\beta = 2.8$. Analogous experiments were carried out for a suspension of poly(methyl methacrylate) microspheres in polyalkylene glycol in the Couette flow and in a single-screw extruder with a closed outlet.²³⁷

Separation into phases with substantially different viscosities was observed for an aqueous micellar solution and tomato sauce in a plate-and-cone rheometer. Tomato sauce was found to separate into two phases with different rheological properties in Couette geometry.³⁰⁸

Blood can be considered as a complex heterogeneous suspension. Probably, a nonlinear relationship between the mechanical stress, σ , and the shear rate $\dot{\gamma}$

$$\sqrt{\sigma} = 0.33 + 0.16\sqrt{\dot{\gamma}} \quad (29)$$

can be explained by blood erythrocyte migration towards the region with minimum shear stress at the centre of the tube.²⁷² 'Stacking' of erythrocytes at low shear rates equalises the flow velocity along the cross-section of the capillary, thus flattening the maximum of the velocity distribution profile even at small Reynolds numbers (10–50); in addition, some indications of flow disturbance and the presence of the transverse velocity components have been reported. After transition to a turbulent flow (at $\text{Re} \approx 2300$) the experimental blood velocity profile was less flattened than the velocity profile of a water–glycerol mixture of the same viscosity, which can be associated with the elastic properties of erythrocytes.²⁷²

Water flow at the centre of a developing wheat grain¹⁸⁸ and a rising water flow in plant stems^{227,270} (from $45\text{ }\mu\text{m s}^{-1}$ to

3 mm s⁻¹) have been studied. A downflow of nutrients towards the roots of the plant in a castor bean seedling has been reported.²⁷³ Since the pixel size in the NMR images is much larger than the wood tracheid diameters, reliable determination of the velocity in most cases was achieved using the dynamic MRI technique.^{188, 270, 273, 291} This approach permits simultaneous measurements of the velocity distribution maps and the diffusion coefficient. For instance, the experimental diffusion coefficient of water in a wheat grain was found to be 8.3×10^{-6} cm² s⁻¹.¹⁸⁸ In studies of water flow in developing quail and bantam eggs the fluid flow was detected only after a four-day incubation period,²⁵² the maximum flow velocity being 1 mm s⁻¹. In addition, a pulsatile flow at a frequency of 0.4 Hz was detected in the quail egg after a 167 h incubation period.

Studies of other types of motion have been reported, *e.g.*, rotation of a gelatin sample in a tube at rates up to 60 rpm (see Ref. 300) and the transverse expansion of a gel cylinder at axial compression at a constant velocity.²⁸⁶ A combination of static and quasi-static deformation of materials with phase encoding of the molecular displacements can be used for the determination of a material's response to mechanical strain followed by reconstruction of Young's modulus maps by solving the corresponding model equations.³¹²

The distribution of dynamic deformations associated with the propagation of the compression and shear waves in a medium is studied by magnetic resonance elastography.^{313, 314} The technique involves creation of transverse acoustic waves with frequencies ranging from 10 to 2000 Hz in tissues or materials. In this case, the wave attenuation in the medium is much smaller than the ultrasound damping, while the wave propagation velocity is low. In addition, the shear modulus varies over a range of several orders of magnitude.³¹⁵ The waves are created using mechanical or electromechanical (*e.g.*, piezoelectric) devices or a modulated ultrasonic beam. The modulated magnetic field gradients applied synchronously with the oscillations of the medium change the phase of the NMR signal, which is proportional to the spin displacement amplitude and to the amplitude, period and number of the field gradient cycles. This can be used for improving the sensitivity of the experiment to the small-amplitude oscillations of the medium.^{313, 315} The technique allows the detection of displacements smaller than 100 nm. By processing the NMR images one can obtain the spatial molecular displacement amplitude maps, as well as the wave propagation velocity maps in the medium and the elastic modulus maps.³¹⁶ Observation of wave reflection from the boundaries and wave refraction at the interface between the soft and rigid regions of the medium, accompanied by variations of the wave propagation velocity, is also possible.^{314, 315} The wave propagation dynamics can be visualised by combining variation of the phase shift between the magnetic field gradient and the wave with animation.^{315, 317} The possibility of studying single waves or short deformation wave trains in the media³¹⁵ and observing the interference pattern for two point sources have been demonstrated.³¹⁴ Wave propagation velocity and wave attenuation measurements at different temperatures were carried out for phantoms as well as animal and human tissues.³¹⁷

4. Filtration

Fluid flow in porous materials (filtration) often occurs in nature and technology (*e.g.*, in perfusion in biological tissues, petroleum recovery and in catalysis). Dispersive character of the flow is critical to filtration. Flow velocity dispersion is due to several mechanisms.^{157, 318} For a laminar fluid flow in a tube the flow velocity dispersion is due to different particle velocities [see formula (25)]. In this case, the dispersion is to some extent reversible (this can be achieved by reversal of the flow direction). Taylor dispersion is due to random velocity modulation as a result of lateral diffusion. Mechanical dispersion is due to the velocity modulation when moving through a complex system of channels

in the pore space. The presence of stagnant regions (*e.g.*, dead-ended pores) causes dispersion due to partial fluid retention.

Application of the MRI technique to studies of filtration processes has some advantages over other methods, since it allows characterisation of not only the flow properties, but also the medium structure, porosity and saturation level, which can be used for, *e.g.*, estimating the medium permeability and the capillary pressure.³¹⁹ The NMR-porosimetry technique¹ permits the pore size distribution to be determined and even the structure of the pore space to be visualised by recording the 3D images if the pores are relatively large.^{318, 320, 321} The results obtained can then be used in simulation of the fluid flow. Selective detection of the NMR signals of different fluids¹ allows studies of the processes occurring in multicomponent systems.

The MRI techniques employed in the flow studies in porous media have some salient features. When determining the content of a fluid in a porous sample using the NMR imaging technique, one should take into account the fact that the T_1 and T_2 relaxation times of the fluid inside the pores are usually much shorter than those of the bulk liquids, which affects the amplitude of the NMR signal. In addition, the relaxation times depend on the saturation level of the sample.^{322, 323} The relaxation behaviour is complicated in the presence of fluid mixtures. For instance, a surface film of the wetting fluid (water) prevents the T_1 time of oil (in contrast to the T_1 time of water) from 'sensing' the surface, while the transverse relaxation rate can decrease with a decrease in the oil content due to concentration of oil inside larger pores.³²⁴ Therefore, quantitative measurements require analysis of the relaxation behaviour^{322–324} and/or using the calibration curves for the signal amplitude.³²⁴

Placing a sample with numerous interfaces between phases with different magnetic susceptibilities in a magnetic field produces strong local field gradients, which can affect the accuracy of the results obtained, especially if the flow velocities to be measured are low.³²⁵ Fluid flow in an inhomogeneous magnetic field causes further shortening of the decay time of the transverse magnetisation, T_2^* . Therefore, the pulse sequences based on the spin echo or stimulated echo are most often employed, which include the 180°-pulses for refocussing of the transverse magnetisation in the local field gradients.^{326, 327} Usually the condition $T_1 \gg T_2^*$ is met; hence, the stimulated echo technique is preferable. It allows one to perform measurements at the longest observation times, Δ , since in this case the NMR signal decay is determined by the T_1 rather than T_2^* time.

In most cases the pore size of the medium is less than or comparable with the spatial resolution of the NMR images.³²⁶ This leads to a limited use of the imaging techniques involving the averaging of the fluid velocity over the volume element corresponding to a particular pixel of the NMR image.³¹⁸ In particular, calculations of the mass flow rate and the flow velocity distribution should be carried out with inclusion of partial-volume correction.³²⁸ Therefore, often preference is given to the measurements based on the average propagator (corresponding to the number of the molecules with a given velocity, averaged over the measuring time rather than volume)³²⁵ rather than the velocity histogram construction.^{321, 325, 326, 329, 330}

By measuring the propagator one can study the molecular migrations over distances that either are shorter than the characteristic pore size or are of the order of several pore sizes.^{331, 332} At short Δ , the propagator corresponds to the molecular motions inside individual pores³³³ and characterises the instantaneous velocities of a random, steady-state fluid flow^{331, 334} as well as diffusive molecular displacements.¹⁸² In the short-time limit (at $\Delta \rightarrow 0$) the contribution of the diffusive displacements is predominant. In contrast to this, at long Δ , where the fluid flow causes the molecules to be displaced over distances of the order of several pore sizes, measurements of the propagator allow the determination of the average molecular displacements and studies of the hydrodynamic dispersion.³¹⁸

The effective dispersion coefficient can also be defined at short Δ . For an exponential velocity correlation function of the form

$$R_u(t) = \langle u(0)u(t) \rangle = \langle u^2 \rangle \exp\left(-\frac{t}{\tau}\right), \quad (30)$$

the effective dispersion coefficient, D' , is given by the formula

$$D' = \frac{1}{2} \langle u^2 \rangle \Delta \text{ at } \Delta \ll \tau, \quad (31)$$

$$D' = \langle u^2 \rangle \tau \text{ at } \Delta \gg \tau. \quad (32)$$

Thus, the dispersion coefficient D' measured along the direction of the net flow ($D_{||}$) initially increases and then reaches the asymptotic limit as Δ increases.³¹⁸ Generally, there is no need to assume a Gaussian shape of the propagator. The average molecular displacement and the dispersion coefficient only correspond to the two lowest moments of the displacement distribution, whereas the propagator provides a complete displacement distribution.³³⁵

By carrying out experiments with modulation of the field gradient one can determine the frequency spectrum of the fluid velocity autocorrelation function in the frequency range from 10 Hz to 100 kHz. This spectrum is defined as

$$D'(\omega) = \int_0^\infty \langle u(0)u(t) \rangle \exp(i\omega t) dt \quad (33)$$

and describes the dependence of the hydrodynamic dispersion coefficient (tensor) on the fluid particle motion frequency, ω .^{163, 255, 318, 336} The approach allows studies of the frequency spectrum of the particle motions and separation of the contributions of the motions corresponding to different time scales.¹⁶³

The propagator is usually obtained by using the Fourier transform of the echo amplitude, $E(\mathbf{q}, \Delta)$, measured at different $\mathbf{q}$ values [see expression (19)]. However, the dispersion coefficient can also be obtained in another manner, by analysing the $E(\mathbf{q})$ dependence in the small $\mathbf{q}$ region (analogously to the diffusion coefficient).³¹⁸ In contrast to other methods, dispersion measurements with NMR directly provide the necessary information and do not require solving model equations. They also permit the dispersion coefficient to be measured both along the net flow (pressure gradient) and in the transverse direction.

When measuring the propagator, there is no need of introducing any tracers into the flow since their role is played by the phase of the transverse magnetisation. Another approach to the dispersion studies involves the use of paramagnetic compounds (tracers) and recording the relaxation-weighted NMR images.^{137, 337–340} The local concentration of the paramagnetic tracer can be determined from the nuclear spin relaxation time of the fluid.^{337, 339}

The most widely used model of filtration is water flow through a cylindrical bead pack. If the beads are sufficiently large, the NMR images of stagnant water in the bead make it possible to visualise individual pores and the inter-pore channels and to analyse the structure of the pore space.^{320, 321} Mapping different velocity components allowed one to establish the character of the correlation between the average flow rate (F) through the pore 'neck' and the 'neck' surface area (S). All experimental dependences were found to be intermediate between linear $F \sim S$ (plug flow) and quadratic $F \sim S^2$ (viscous flow).³²¹ The maximum flow velocities in bead packs much exceed the average velocity,^{321, 328} while a large fraction of the fluid flow is confined within a small region of the pore space.³²⁰ Transition to a diffuse fluid flow inside the bead pack occurs at a distance of the order of the bead diameter from the inlet edge.³²⁸ Some indications of reverse flows have been reported.³²¹ Peculiarities of water flow in a tube in the regions upstream and downstream the plastic bead pack have been studied.³²⁸

At $d_c/d < 10–15$ (d_c is the diameter of the bead pack and d is the bead diameter), the edge effects play a significant role.³³¹ The dependences of the average bed porosity and the average flow velocity on the distance from the cylinder wall have been plotted based on the experimental data. The porosity is maximum on the cylinder walls (due to ordering of beads), whereas the flow velocity is maximum at a distance approximately one particle radius thick.^{318, 320} Capillary electrochromatography and pressure-driven filtration experiments with bead packs with a small d_c/d ratio confirmed the higher velocity in the near-wall region.³⁴¹ Bead packing inhomogeneities were found to affect the fluid flow.

Both versions of measurements of the average propagator (with or without spatial resolution) are widely used in studies of water flow through bead packs. Judicious choice of the field gradient allows one to obtain the propagator for both longitudinal and transverse molecular displacements, while variation of the observation time permits flow studies in different characteristic length scales. If the average molecular displacements are smaller than the characteristic pore size, the longitudinal propagator is asymmetric, centred at zero displacement^{187, 331} and exhibits an exponentially decaying wing towards larger displacements.^{182, 331} As the observation time increases, the amplitudes of the near-zero peak¹⁸⁷ and of the exponential wing³³¹ decrease; this is accompanied by the formation of a Gaussian propagator centred at the average longitudinal molecular displacement (see Fig. 4b).^{182, 187, 318, 331} At the same time, the average transverse molecular displacements are equal to zero; therefore, the corresponding transverse propagator is centred at zero at any observation time³³¹ and usually has a Gaussian shape, though a propagator represented by the sum of two Gaussians was observed for an bed of glass beads 290 μm in diameter at small molecular displacements.³³¹ The first Gaussian curve corresponded to the hydrodynamic dispersion coefficient, which is four-fold greater than the self-diffusion coefficient of water. The amplitude of this curve decreased with an increase in the observation time. The second curve continuously broadened with increase in the average longitudinal displacement.³³¹ The longitudinal and transverse propagators were also represented as the sums of three curves corresponding to diffusion/dispersion in different length scales and characterised by different diffusion/dispersion coefficients (and different average displacements for axial propagator) and by the observation time dependent relative contributions.¹⁶⁰

The longitudinal ($D_{||}$) and transverse ($D_{\perp}$) dispersion coefficients are much larger³⁴² than the self-diffusion coefficient of the bulk fluid, D_0 , with $D_{||}$ being more than an order of magnitude larger than $D_{\perp}$.¹⁸² For instance, water flow through a pack of glass beads 3 mm in diameter at $\text{Pe} = 1570$ ($\text{Pe} = v l / D_0$ is the Peclet number, where v is the average velocity and l is the characteristic pore size) and $\text{Re} = 3$ is characterised by $D_{||} = 3000 D_0$ and $D_{\perp} = 80 D_0$.¹⁸⁷

The experimentally measured values were found to be dependent on the time³³¹ and spatial³⁴³ averaging scales. The average molecular velocity and $D_{||}$ reach the limiting values at $\Delta \sim 20 d/v_z$, while for $D_{\perp}$ this occurs¹⁶⁰ at $\Delta \sim (5–10) d/v_z$, the D' value increasing with the average velocity.^{125, 318} As the volume (layer thickness) included in the averaging increases, a predicted fluctuation of $D_{||}$ occurs.³⁴³ The calculations also predict a decrease in $D_{||}$ on further increase in the layer thickness. Spatially resolved measurements of the propagator for inhomogeneous samples exhibit the spatial inhomogeneity of the velocity and dispersion distribution.³¹⁸ A number of models for the description of the propagators measured in the filtration experiments have been proposed.^{333, 343, 344}

Slowing down the net mass transfer due to diffusive mass transfer inside porous granules is an important dispersion mechanism for the beds comprised of porous beads.¹⁸² Here, the longitudinal and transverse propagators are described by the sum of two Gaussian curves. One curve is centred at zero displacement and corresponds to diffusion in the bead pores, which allows the determination of the tortuosity factor of the pore

space.^{182, 342, 345} The other curve corresponds to the fluid moving in the intergranular space,^{342, 345} which makes it possible to calculate the average flow velocity (for the longitudinal propagator). With the known fluid flow rate one can find the porosity of the bed if the observation time is not too long.^{182, 345}

In the experiments with beds comprised of porous beads the variations of the average flow velocity and observation time affect variations of the propagator in different manners. An increase in the flow velocity has virtually no effect on the contribution of the fluid confined inside the pores.^{331, 342, 345} At the same time, an increase in the observation time causes the amplitude of the first Gaussian curve to decrease due to water exchange between the pore volume and the intergranular space, thus allowing the exchange dynamics to be studied.^{182, 331, 342, 345, 346} In the long-time limit, the average longitudinal and transverse propagators characterise only the flow contribution; which allows the determination of the overall porosity of the system (layer + beads).¹⁸²

Sometimes, an analogous picture was also observed for water flowing through a non-porous bead (granule) pack (see Fig. 4b).³¹⁸ The component of the propagator centred at zero molecular displacement is thought to correspond to stagnant water present at intergranular contacts. For smaller granules, the characteristic size of these 'pools' is also smaller and the contribution of the immobile fluid decreases faster with increasing the observation time.

Studies of the frequency spectrum $D(\omega)$ of transverse molecular motions for a fluid flowing through a bead pack revealed the presence of three components of the molecular displacements: (i) Brownian motion, (ii) coherent oscillatory motion relative to the bead pack axis due to curvilinear flow around the beads and (iii) random perfusive walks. The experimental spectra, $D(\omega)$, exhibit a characteristic maximum, which is shifted towards higher frequencies with increasing the flow velocity and corresponds to coherent oscillations. A high-frequency plateau $D(\omega) = D_0$ corresponds to diffusive motions, while the low-frequency plateau, which decreases with increasing the flow velocity, corresponds to random perfusive motions.¹⁶³

Measurements of the propagators $P(\mathbf{R}_1, A_1; \mathbf{R}_2, A_2)$ characterising the mutual probability density of a molecular displacement over distance $\mathbf{R}_1$ over time A_1 and over distance $\mathbf{R}_2$ over time A_2 (including the VEXSY and SERPENT experiments) permit studies of the spatial and time correlations of flow velocity fluctuations.^{283, 318, 347} In particular, this approach was employed in comparing fluid flows in disordered and ordered porous media.³⁴⁷ In some instances the spatial velocity correlation can also be calculated from the spatial velocity distribution maps.³³⁷

Molecular motions in a periodic system of identical pores can be accompanied by the appearance of coherence effects. For instance, experiments with water flow through a bead pack revealed flow-dependent diffraction-like effects manifested as a maximum in the plot of the dependence of the echo amplitude, E , on q near $q = 1/d$ (d is the bead diameter). Simulation of the results obtained allowed the determination of the longitudinal hydrodynamic dispersion coefficient, average inter-pore distance and the pore sizes. The peak indicates that the molecular displacements are correlated in the bead-diameter length scale.^{125, 318}

Interest in the flow of gases, fluids and suspensions through porous rocks is first of all related to the gas and oil recovery. For most of rocks mapping the pore space using the MRI technique is impossible. At the same time, the amplitude of the NMR signal from a fluid-filled core depends on the local porosity of the core.³²⁵ The Darcy relation connects the flow velocity to the medium permeability, thus allowing establishment of a correlation between the local porosity and permeability.³³⁰

The flow velocity distribution maps obtained for water, brine^{326, 329, 330} or a mixture of aliphatic hydrocarbons³²⁵ in sandstone cores were converted into corresponding velocity histograms and it was found that the flow velocity increases almost linearly with the medium porosity.³³⁰ The velocity distribution

obtained for a layered core with bimodal pore size distribution was found to be nearly Gaussian.³³⁰ A correlation between the hydrodynamic dispersion coefficient and the average flow velocity has been observed.³²⁹

The flow velocity maps obtained for identical flow rates were shown to be different if the flow rate was altered in between the measurements.³²⁹ To explain this, a stochastic theory of flow through a porous medium has been proposed.³²⁹

Similarly to model bead packs, at short observation times the longitudinal (along the pressure gradient) propagator obtained for the fluid in the sandstone core is centred at zero displacements and exhibits a wing decaying towards larger displacements; as the observation time increases, the propagator approaches a Gaussian curve.^{333, 334} The transverse propagator has a Gaussian shape, is centred at zero displacement and broadens with the delay time.³³³ Measurements of the 2D propagator revealed correlations between the longitudinal and transverse molecular displacements.³³⁴

Filtration of colloidal suspensions are of great practical value for borehole drilling. When using drilling fluids, clay permeates the pores of the surrounding rock, which affects the drilling efficiency and the operating performance of the borehole. Large surface area of suspended clay causes substantial variations of the T_1 time of the fluid, which allows one to follow the clay accumulation in the pores.^{348–350} The maximum penetration depth of clay into the core is less for the cores with lower permeability^{348, 350} and is reached after relatively short times. Further injection of clay suspension has no effect on the penetration depth.^{348–350} For highly permeable limestone the process is accompanied by substantial porosity reduction.³⁵⁰

Filtration is accompanied by deposition of a layer of increased concentration of retained molecules, particles or droplets on the filter surface. Measuring the dependence of the spin relaxation time of the fluid on the pore size allowed the determination of the spatial porosity distribution in the dense deposit layer during pressure-driven filtration of aqueous clay suspension.³⁵¹

Considerable attention has been given to the multicomponent flows and displacement of particular components. These processes occur when cleaning contaminated soils and are of interest from the standpoint of improving the extraction of petroleum content from rocks. By selecting the contribution of a particular component to the NMR signal one can obtain, *e.g.*, the distribution of water (brine) and oil in the sample throughout the displacement process.

A number of studies on the displacement of oil (hydrocarbon) by pumping water through oil-saturated cores^{322, 323, 352–354} or granular beds³⁵⁵ has been reported. Water ingress into cores occurs in the form of jets, the characteristic size of which is much less than the spatial resolution achieved in the experiments.³⁵³ As a result, water rapidly permeates into the sample; however, the process is not accompanied by substantial displacement of oil and the formation of a sharp interface between the two fluids. As time passes, a gradual displacement of oil by water occurs uniformly throughout the sample. A fraction of oil is retained within the sample after pumping a large amount of water, which was confirmed by recording the water and residual oil distribution profiles.^{352, 353, 355} Water poured in a cavity of a porous thimble-shaped ceramic sample pre-saturated with C_6F_6 causes the hydrocarbon to be displaced uniformly across the sample section,⁴⁹ which was confirmed by recording 2D NMR images using the ^{19}F NMR signals.

Displacement of water from various cores^{323, 324, 353, 356} or a granular bed³⁵⁵ by pumping oil has been studied. The process is accompanied by the formation of a clearly visible interface between the two liquids.^{353, 355} The residual water content in the core strongly depends on the oil flow rate.³²⁴ For a sample with the axial bedding planes different porosity and permeability of different layers led to different displacement rates.³²³ Displacement of oil and water by isopropyl alcohol has been studied.³⁵²

The propagators for flowing water or oil at different residual content of oil (water) in the core³³⁴ and for two-phase flow of water and dodecane^{334, 357} have been measured.

The presence of a contaminant (residual content of a poorly soluble fluid) confined inside the pores of a medium can be responsible for prolonged poisoning of water pumped through the medium. Displacement of *n*-hexanol by water from a sand layer was studied by recording the *n*-hexanol distribution profiles.³⁵⁸ The behaviour of individual octanol droplets during the displacement process was followed by using a pack of large beads (3–5 mm).³⁵⁹ Recording the velocity distribution maps showed that a fraction of droplets distant from the fast jet flow is removed very slowly. An increase in the water pumping rate and a decrease in the droplet size led to faster removal of the contaminant. A number of numerical simulations of the process has also been reported.^{358, 359}

Experiments on simultaneous filtration of water and air through a bead pack showed that their distribution in the layer remains inhomogeneous for a rather long time after starting the flow (2 h). It was also found that a nine-fold increase in the water flow rate after establishing the steady-state flow leads to a redistribution of the fluid and gas in the layer, whereas an eight-fold increase in the gas flow rate causes only insignificant changes.^{320, 360}

Filtration induced dispersion can also be studied by introducing paramagnetic tracers into the flow and following the movement of the tracer concentration front in the porous medium. The presence of inhomogeneities in the bead pack or core cause a significant increase in dispersion of the tracer concentration front.^{137, 337, 338} A study of the dispersion coefficient in a pack comprised of large beads showed that the tracer concentration front oscillates with a spatial period equal to the bead size due to the flow velocity fluctuations occurring with the same spatial period. This behaviour was confirmed by model calculations using a 2D grid of cylindrical pores with variable cross-sections.³³⁹

Secondary convective flows due to the gravity force are of significant importance if the bead pack is arranged vertically and the fluids to be mixed have different densities.³⁴⁴ Bottom feed of a more concentrated $\text{Mn}_2(\text{EDTA})$ solution (EDTA is ethylenediaminetetraacetic acid) causes a uniform movement of the concentration front along the flow direction. The injection of the solution from the top leads to a parabolic front accompanied by its convective spreading. Flow direction reversal experiments showed that dispersive spreading of the concentration front is fully irreversible in the former case and partially reversible in the latter (a pack of 2 mm beads was studied). When 8 mm beads were used, a flow instability was observed, accompanied by fast dispersion of the concentration front along the full length of the bead (22 cm).³⁴⁴ It was found that a density gradient causes convection in stagnant fluid. A study of inhomogeneous bead pack with the top part filled with brine and the bottom part filled with water showed that advective fingering is observed first in the region with a higher permeability and later — in the rest of the bead pack.³³⁸

The movement and transformations of the concentration front in chromatographic and ion-exchange columns have been studied.^{340, 361, 362} Because of the high velocity of movement of the concentration bands, investigations of high-pressure chromatography processes require the use of fast NMR imaging techniques. This allowed visualisation^{340, 361} of the movement of $\text{Gd}(\text{DTPA})$ solution (DTPA is diethylenetriaminepentaacetic acid) with a velocity of up to 1 mm s^{-1} at an external pressure of nearly 55 atm. At pH 6 of the liquid phase, a compact concentration band was found to move through a column filled with silica gel without changes in its shape with time. However, an analogous process at pH 7 was accompanied by appreciable band broadening and a change in the shape. NMR images also allow one to assess the packing character of the stationary phase in the column. In particular, in columns with the slurry packed stationary phase the packing gradient of the solid phase induced a gradient of the

spin relaxation times of the fluid throughout the height of the column.

Experiments with a chromatographic column in the form of the bed of polystyrene beads swollen in THF (bead diameter: 100 μm) showed⁴⁹ that a fluoro derivative of glycine poured onto the bead pack surface moves down the column right to the bottom without retention in the polystyrene microcavities.

Processes in a column loaded with ion-exchange resin (Na^+ form) were studied by recording the NMR images using the ^{23}Na NMR signal. The movement of the free Na^+ ion concentration front down the column during successive elution with aqueous HCl solution, aqueous NaCl solution and water was followed.^{340, 361}

5. Motion of granulated materials

The NMR imaging technique is also used in the investigations of the motion of solid granulated materials, when optical methods are inapplicable because of opaqueness of the objects under study. Experiments are carried out with liquid-containing solid particles, such as liquid-containing pharmaceutical pills, mustard and poppy seeds and porous granules partially saturated with liquid. Segregation of granulated materials can be studied using their mixtures with solid particles that are 'invisible' to NMR.

The motion of solid particles in rotating cylinders is widely used in grinding, granulation, mixing and drying of solid granulated materials and in coating processes. When the cylinder is full, rotation of the entire sample allows estimation of the accuracy of the particle concentration and particle velocity distributions obtained in the experiments.²⁵³ The NMR images of a half-filled horizontal cylinder show different regimes of the particle motion depending on the rotation rate.²⁵³ The oblique surface of the granular bed exhibits a clearly visible layer with a reduced average density of the 'flowing' particles, the layer thickness being dependent on the rotation rate. A density gradient due to the dynamic particle packing effects was also observed in other regions of the granular bed.²⁵³ The dynamic angle of repose at different rotation rates was measured²⁵⁴ and the spatial particle velocity distribution maps in the cylinder were obtained.^{253, 254, 265}

Experiments aimed at determining the correlation time of the particle motion, τ , the autocorrelation velocity function [expressions (20) and (21)] and the diffusion coefficient D for the axial motion of particles in a rotating cylinder have been carried out.^{265, 279} It was found that the effective axial diffusivity is maximum near the foot of the sliding particle layer^{254, 279} and is different at different distances from the surface.²⁷⁹ The characteristic τ values lie in the millisecond range, the D are three orders of magnitude higher than the self-diffusion coefficient of water²⁶⁵ and the mean square of velocity fluctuations, $\langle u^2 \rangle$, exceeds $10^{-3} \text{ m}^2 \text{ s}^{-2}$ (see Ref. 279). The experimental values of the dynamic angles of repose, and the spatial maps of concentration, velocity and diffusivity values obtained for solid granules are in good agreement with the results of calculations.²⁵⁴

Often, relative motion of particles with different properties (size, density, shape) causes spontaneous segregation of mixtures. Nearly immediately after a cylinder filled with a well-mixed mixture of particles of different sizes starts to rotate, radial segregation occurs, accompanied by an increase in the concentration of smaller particles near the axis of rotation.³⁶³ As the cylinder continues to rotate, radial segregation evolves into an axial segregation until complete segregation of the mixture into several layers comprised of the particles of different size, which follow one another in the axial direction.³⁶³ For a binary mixture the trends to segregation due to different particle size and density can be mutually compensated.³⁶⁴ If the system is described in the 'particle size' – 'particle density' coordinates, there is a boundary corresponding to good mixing, whereas moving away from the boundary causes greater segregation.

To intensify the motion of solid particles, vibration is often used. For instance, a study has been reported of the motion of beads 2 mm in diameter placed in a container attached to a lever,

the long arm of which was connected to a loudspeaker.³⁶⁵ The amplitude of the oscillations of a specified frequency (20–25 Hz) supplied to the loudspeaker increased until a value at which arching was observed using a stroboscope. The amplitude of container displacements was ~ 0.5 cm. Alternating left-right arching has been studied. The 2D NMR images of the vibrating layer at different instants of the oscillation period exhibited the effect of doubling the oscillation period. The layer edges execute an out-of-phase motion: when one edge is at the top, the other is at the bottom, and *vice versa*. The largest shear deformation was observed in the middle region of the layer, which always moves from the elevated towards the lowered edge of the layer.

Convection in a particle layer placed in a periodically shaken cylindrical container has been studied by recording the NMR images.³⁶⁶ Transformation of the shape of spatial tags illustrated an upward motion of the particles near the axis of the cylinder and a downward motion near the walls, the velocity on the walls being maximum in absolute value. Except for the near-surface region, the velocity of the motion exponentially decreases with increase in the depth.³⁶⁶ The propagators for the vertical particle displacement at different shaking frequencies and amplitudes have been obtained.³³⁵

The gravity driven filtration of a fine-grained granulated material through a pack of larger beads, simulating a catalytic reactor, has been studied.⁸ The 2D NMR flow velocity maps of the material exhibited a flow not only near the walls, but also in the bulk of the bead pack. The propagators characterising the flow velocity distribution of small granules have also been obtained.

6. Gas flow

Gases have large diffusion coefficients as compared to liquids. Because of this, one can expect that the diffusive displacements of gas molecules contribute largely to the net displacement over the observation time. This seems to be the reason for weak interest in the application of the MRI technique to gas flow studies until recently. However, recent advances in this field^{93, 217, 367, 368} are thought to give an impetus to intensive research on gas flow. In particular, visualisation of the flow of gaseous hydrocarbons^{93, 367} can be useful in the MRI studies of heterogeneous catalytic processes.

The potentialities of the NMR imaging technique in the studies of the flow of gases with equilibrium spin polarisation in moderately strong magnetic fields (7 T) have been illustrated taking acetylene, propane and butane flowing in a circular cross-section tube or in transport channels of a monolithic catalyst as examples.^{93, 367} The longitudinal velocity distribution maps obtained for a developed laminar butane flow in a tube exhibit a parabolic radial velocity distribution (Fig. 5a). The propagator measured under the same conditions virtually coincides with the velocity histogram constructed based on the velocity distribution maps. As the observation time becomes sufficiently long for diffusive molecular displacements over a distance of the order of the tube diameter to occur, the rectangular propagator changes into a Gaussian one due to the Taylor dispersion.

It was also found that laminar gas flow can be visualised using the spatial tag technique, which exhibits transformation of a linear tag created normal to the flow direction into a parabolic tag. At the same time, as the Reynolds number approaches the critical value, the NMR signal amplitude rapidly attenuates below the noise level, which precludes investigations of the transition to turbulent flow and a developed gas turbulence.

Nevertheless, the MRI technique can be applied to studies of not only developed laminar flows, but also establishment of a developed gas flow through the entrance region of a tube or channel. The MRI velocity distribution maps for the gases flowing through a tube into a cylinder of a larger diameter, containing a fragment of a monolithic catalyst, at $Re = 190$ –570 have been obtained (see Fig. 5b). In this case the velocity distribution across the transport channels is significantly different from analogous

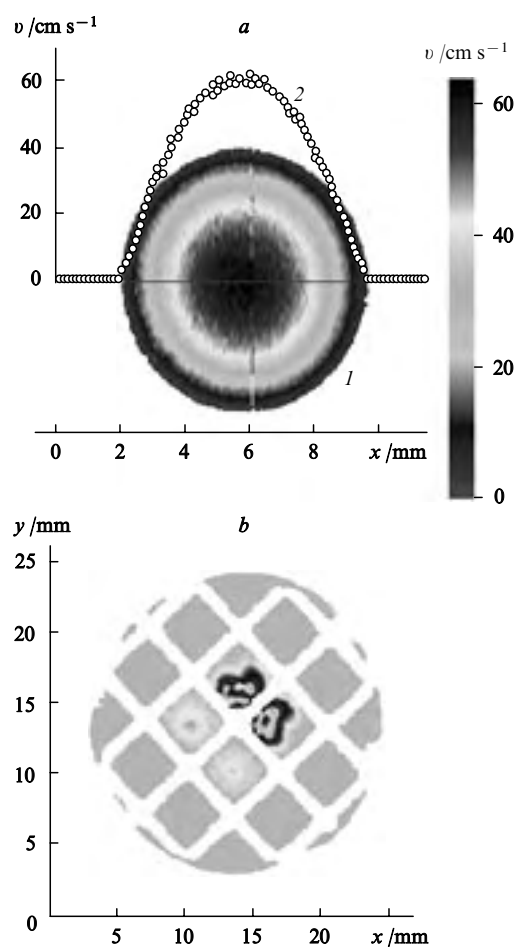


Figure 5. Visualisation of butane flow by the phase contrast technique.² Two-dimensional velocity map (1) and its one-dimensional cross-section (2) for a laminar gas flow in a tube with a circular cross-section; the velocities for the two-dimensional map are given at the right, those for the one-dimensional cross-section are given at the left (a); velocity map for butane flowing into a cell of a monolithic catalyst (cell diameter: 21 mm) with 4 mm square channels (b).

distribution for a completely developed laminar flow. In particular, inhomogeneous shear rate distributions across the channel cross-sections are observed. This is in agreement with the estimates of the entrance length, which exceeded the distance from the inflow edge of the monolith to the NMR image plane.^{93, 367}

Studies of gas filtration through porous materials are of considerable interest. As mentioned above, spatially resolved MRI techniques are of limited use even for liquids. Typical of gases with equilibrium polarisation is a low signal-to-noise ratio, which makes this approach of little promise. In this connection, it is of interest to use the average propagator approach in gas filtration studies. For instance, the propagators for longitudinal and transverse displacements of gas molecules in a porous medium have been obtained for a cylindrical glass bead pack (Fig. 6). By and large, transformation of the propagators with increasing Δ is similar to those observed for the filtration of liquids. At short Δ , a broad (due to high gas diffusion coefficient) Gaussian propagator centred at zero displacement is observed. As Δ increases, a wing appears in the large displacement region and then a Gaussian propagator is formed, which is centred at the average molecular displacement. The width of the propagator is determined by the gasodynamic dispersion coefficient. Despite high gas diffusion rates, the experimental longitudinal and transverse dispersion coefficients are much larger than the self-diffusion coefficient D_0 ($D_0 = 0.03$ cm² s⁻¹ for butane at a pressure of

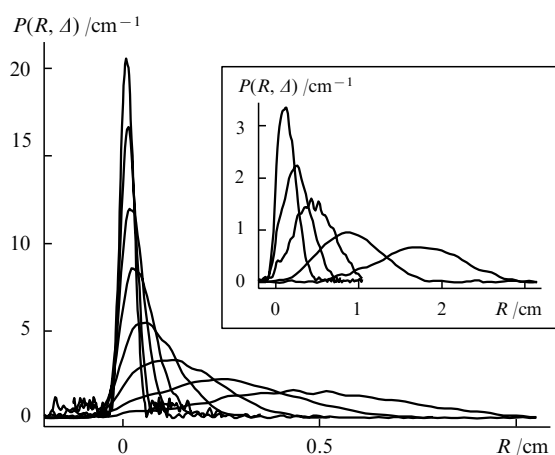


Figure 6. Averaged propagator for axial displacement of butane molecules flowing through a cylindrical glass bead pack (bead diameter: 3.2 mm; bead pack diameter: 21 mm). Observation time: $\Delta = 1, 2, 5, 10, 20, 40, 80, 150$ ms (the corresponding curves are plotted from top to bottom).

The inset presents the data for $\Delta = 40, 80, 150, 300$ and 600 ms.

1 atm and room temperature). The dependence of the dispersion coefficient on the observation time, flow velocity and bead size has been studied. The VEXSY experiments were also carried out, which allowed one to follow the loss of molecular velocity correlation in the pack with increasing the observation time in spite of a rather large diffusive contribution.

Experiments with hyperpolarised gases^{369–372} permit substantial improvement of the signal-to-noise ratio compared to that obtained for gases with equilibrium polarisation. In particular, this makes it possible to achieve a rather high spatial resolution when recording the NMR images using the NMR signal from the gas molecules in macroporous materials. However, acceleration of the spin relaxation of the gas in the pores of the medium can sacrifice the advantages of using hyperpolarised gases in the studies of filtration through many materials.

Xenon flow was investigated using a system with continuous circulation of polarised ^{129}Xe , which allowed enhancement of the magnetisation by more than three orders of magnitude compared to the equilibrium ^{129}Xe polarisation at the same magnetic field (4.2 T).^{217,368} The 2D images in the mixed k, q -space (propagator

with spatial resolution along one coordinate) were obtained in dynamic MRI experiments. Studies of xenon flow in a round tube²¹⁷ at different observation times Δ revealed that Taylor dispersion due to lateral molecular diffusion causes the gasodynamic dispersion coefficient initially to increase with increase in the delay time and then to reach a plateau at delay times that are longer than the characteristic time of molecular diffusion over a distance of the order of tube diameter.

A feature of xenon flow in a tube with a diaphragm having a small opening at the centre is flow acceleration at the tube axis and the reverse flow in the near-wall regions as a result of flow turbulence.³⁶⁸ Analogous studies were also carried out for parallel xenon flow through two polyurethane foam samples with pores 400 and 200 μm in diameter. The velocity distribution maximum was found to be shifted towards higher velocities for the material with a lower density and larger pores.

Application of MRI to gas filtration studies allows the local permeability of porous samples to be determined. If the porous material does not adsorb a gas, the signal amplitude in the NMR image is proportional to the local gas pressure, whereas the viscosity of an ideal gas is pressure independent. Knowledge of the velocity field permits calculations of the spatial distribution of material permeability using the Darcy equation. In this case, carrying out the 1D experiments does not require gas velocity measurements.³⁷³

* * *

When studying various mass transfer processes, a detailed picture of a particular process can be obtained only when using modern physicochemical methods that allow spatially resolved measurements. Numerous examples presented in this review demonstrate that MRI is an efficient tool for studying such processes. The authors hope that this information will be of use to those dealing with mass transfer problems in various fields of science and technology.

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VII. Supplement

In Table S.1 we present additional information on the MRI studies of mass transfer processes.

Table S.1. Applications of the MRI techniques.

Field /T	Object, process	Technique	Dimension	Spatial resolution characteristics	Recording time	Nucleus	Ref.
0.78	water in fired clay	spin echo	1D	0.17–1 mm, a cylinder 20 mm in diameter	—	^1H	2–4
4.7	H_2O or D_2O in concrete of various composition	spin echo or SPI	2D	64×128 ; a slice 25 mm thick (spin echo)	6 min (SPI)	^1H (SPI), ^2H (echo)	5
5.5	5% methanolic solution of alkylalkoxysilane in hardened mortar	STRAFI + dipolar (solid-state) echo	1D	100 μm	—	^1H	6
0.7	water in gypsum, limestone and mortar	—	1D	< 2 mm	5 min	^1H	9
2	water in limestone	spin echo	2D	128×128	40 s	^1H	10
0.8	water in hardened mortar prepared from Portland cement and silica sand	the same	1D	0.9 mm, a cylinder 20 mm in diameter	—	^1H	11

Table S.1 (continued).

Field /T	Object, process	Technique	Dimension	Spatial resolution characteristics	Recording time	Nucleus	Ref.
0.78	aqueous NaCl solution in a calcium silicate brick	spin echo	1D	0.25 mm (2 mm), a cylinder 20 mm in diameter	—	^1H , ^{23}Na	12
2.35	water in hardened cement with clay additive (sodium aluminosilicate) and PVA	—	2D	40 μm , a slice 0.35 mm thick	—	^1H	13
0.7	water in sandstone cores	gradient echo with oscillating gradients	1D	0.4 mm, a cylinder 25 mm in diameter	5.5 s	^1H	14
0.5	decane in peroxide vulcanised natural rubber	the same	2D	250 (400) μm for decane, 600 μm for rubber, a slice 5 mm thick	20 min	^1H	21
2.4	water in zeolite 4A	SPRITE	1D	64 points, 0.55 mm	< 2 min	^1H	22
0.7	the same	gradient echo with oscillating gradients	1D	—	few seconds	^1H	23
2.0	n-hexane in zeolite NaX	stimulated echo	1D	0.3 mm	2 min	^1H	24
1.4	butane in zeolites NaCaA, water in zeolite NaX	FID	1D	0.5 mm	—	^1H	25
2.0	n-Hexane in zeolite NaX	stimulated echo	1D	0.3 mm	2 min	^1H	26
2.35	water in soil (humus)	spin echo	2D	128 $\times$ 128 or 256 $\times$ 256, (0.47 mm) ^{2} or (0.35 mm) ^{2} , a slice 20 mm thick	—	^1H	27
7.05	acetonitrile, benzene, dichloromethane and CCl_4 in carbonaceous adsorbent	FID	—	WSR	—	^1H	28
7.05	water in copolymer of 2-hydroxyethyl methacrylate and tetrahydrofurfuryl methacrylate	spin echo	3D	128 $\times$ 128 $\times$ 8, 78 μm $\times$ 78 μm $\times$ 3.75 mm	35 min	^1H	29
7.05	vulcanised <i>cis</i> -1,4-polybutadiene + cyclohexane- d_{12}	the same	2D	256 $\times$ 256, (37 μm) ^{2} or (58 μm) ^{2} , a slice 1 mm thick	—	—	30
7.05	vulcanised polybutadiene rubber + deuterocyclohexane or cyclohexane- d_{12}	"	2D	256 $\times$ 256, (39 μm) ^{2} or (32 μm) ^{2}	—	—	31
2	acetone in vulcanised rubber	"	1D	128 points, 100 μm a slice of 0.5 cm^2 surface area	32 s	^1H	32
—	hot water (100 $^\circ\text{C}$) in nylon-6,6	steady-state free spin precession (SSFP)	1D	240 μm	—	^1H	33
9.4	1,4-dioxane in PVC	spin echo with inversion – recovery	2D	(70 μm) ^{2} , a slice 4 mm thick	—	^1H	35
9.4	acetone or acetone + methanol in bisphenol A polycarbonate	the same	2D	(70 μm) ^{2} , a slice 4 mm thick	—	^1H	35
2.35	toluene in butadiene rubber, hexafluorobenzene in methylsiloxane rubber, methanol in PEMA, pyridine in bituminous coal	spin echo	2D	128 $\times$ 128, (70 μm) ^{2}	10 min (^1H), 30 min (^{19}F)	^1H , ^{19}F	36

Table S.1 (continued).

Field /T	Object, process	Technique	Dimension	Spatial resolution characteristics	Recording time	Nucleus	Ref.
2.35	pyridine in bituminous coal, methanol in PEMA, toluene in isobutyl rubber	—	2D	$128 \times 128, (40 \mu\text{m})^2$	10 min	^1H	37
7	CH_3OD in PMMA	gradient echo (FLASH)	2D, 3D	$200 \mu\text{m}$	—	^1H	38
7	acetone or CH_3OD in PMMA	spin echo	2D	256×256 , a slice 2 mm thick	—	^1H	39
7	CH_3OD in water-soaked PMMA	gradient echo (FLASH)	2D	$256 \times 256, (100 \mu\text{m})^2$, a slice 1 mm thick	10 min	^1H	40
—	toluene or trichloroethylene in PVC; n-pentane in high-density polyethylene	B_1 -imaging	—	—	—	^1H	41
4.7	toluene in PVC, acetic acid in cellulose, n-pentane in polystyrene	the same	2D	256×128 points (512×512)	2 h	^1H	42
7	acetone or methanol (CH_3OD) in PMMA	spin echo or gradient echo (FLASH)	2D	$256 \times 256, (140 \mu\text{m})^2$, a slice $500 \mu\text{m}$ thick	—	^1H	43
9.4	methanol in PMMA	spin echo	2D	$(70 \mu\text{m})^2$, a slice 4 mm thick	—	^1H	44
4.7	dioxane in polystyrene–divinylbenzene copolymer	gradient echo (FLASH)	2D	$256 \times 256, (115 \mu\text{m})^2$, a slice 1.5 mm thick	2 min	^1H	45
4.7	rubber + benzene- d_6 , cross-linked nematic liquid-crystalline prepolymer + CD_2Cl_2 , poly(<i>N</i> -isopropylacrylamide) + $\text{H}_2\text{O}/\text{D}_2\text{O}$ + CH_3OD	spin echo	1D, 2D	a slice $500 \mu\text{m}$ thick (2D)	—	^1H	46
7	acetone- d_6 + CH_3OD or acetone + CD_3OD in bisphenol A polycarbonate	gradient echo (FLASH)	2D	$256 \times 256, (100 \mu\text{m})^2$, a slice 1 mm thick	25 min	^1H	47
2	acetone + benzene in vulcanised rubber	chemical shift selective spin echo	2D	a slice 4 mm thick	2 min	^1H	48
2	isooctane in vulcanised rubber saturated with cyclohexane	gradient echo for two-quantum coherence	2D	a slice 8 mm thick	8 min	^1H	48
4.7	C_6F_6 or C_6F_6 + C_6H_6 in polystyrene	gradient echo (FLASH)	2D	$256 \times 256, (120 \mu\text{m})^2$, a slice 1.7 mm thick	310 s	^{19}F	49
4.7	C_6F_6 + water in porous ceramics	spin echo	2D	$256 \times 256, (80 \mu\text{m})^2$, a slice 2.8 mm thick	34 min	^{19}F	49
4.7	fluoro derivative of glycine + THF in cross-linked polystyrene bead pack	the same	2D	$256 \times 128, 135 \times 270 \mu\text{m}$	70 s	^{19}F	49
0.5	decane in peroxide vulcanised natural rubber	gradient echo with oscillating field gradients	2D	250 (400) μm for decane, 600 μm for rubber, a slice 5 mm thick	20 min	^1H	50
4.7	H_2O and/or D_2O in PEO	spin echo	1D	512 points, $29.3 \mu\text{m}$	—	^1H	51

Table S.1 (continued).

Field /T	Object, process	Technique	Dimension	Spatial resolution characteristics	Recording time	Nucleus	Ref.
0.1, 2.9	water in sodium polyacrylate	spin echo + STRAFI	1D	—	16 s or 12 min (STRAFI)	¹ H	52
9.4	adsorption of water vapours into M(CF ₃ SO ₃) ₂ (PEO) _n films (M = Pb, Zn; n = 9, 16, 24)	spin echo	1D, 2D	40 μm (50–200 μm), a slice of 400 μm × 9 mm surface area (1D), (40 μm) ² , a slice 400 μm thick	1 min (1D), 20 min (2D)	¹ H	53
9.4	adsorption of acetone vapours into poly(vinyl chloride)	dipolar echo + STRAFI	1D	78 μm, a slice of (10 mm) ² surface area	—	¹ H	54
2	adsorption of CDCl ₃ or CCl ₄ vapours into PMMA or polystyrene	recording FID amplitude after selective pulse	1D	0.5 mm	—	¹ H	56
	sorption of water or water vapours into corn starch amylose	STRAFI	1D	80 points, 50 μm	20 min	¹ H	57
9.4	pyridine-d ₅ or acetone-d ₆ in coal	spin echo	2D	128 × 128, (78 μm) ²	7 min	¹ H	58
0.83	water at 93 °C in glass fibre reinforced epoxy resin based on bisphenol–acetone	PRI	2D	256 × 256, a sample 5–7 cm thick	15 min	¹ H	59
7	1,4-dioxane in polybutadiene rubber	spin echo	2D	a slice 2 mm thick	—	¹ H	60
2	water in natural rubber or in partially epoxidised rubber, cyclohexane in vulcanised rubber	the same	3D	128 × 128 × 8, a slice 2 mm thick	—	¹ H	61
4.7	acetone, DMSO or pyridine in coal	"	2D, 3D	256 × 256, (500 μm) ² , a slice 1 mm thick (2D); 128 × 64 × 64, (200 μm) ³ (3D)	2 min (2D), 15 min (3D)	¹ H	62
2.35	pyridine or pyridine-d ₆ in coal	gradient echo or PRI	3D	128 × 128 × 128, (40 μm) ³ (echo); (80 μm) ³ (PRI)	16 or 42 h (echo); 22 h (PRI)	¹ H	63
7	CH ₃ OD in PMMA	spin echo	2D	256 × 256, (68 μm) ² , a slice 2 mm thick	51 min	¹ H	64
11.7	PVA pellet in water	the same	1D	256, 29 μm	40 s	¹ H	65
9.4	water in hydroxypropyl-methylcellulose	"	1D	128, 156 μm	3 min	¹ H	66
4.7	water in silicone matrix + NH ₄ F	"	2D	(0.25 mm) ² , a slice 0.6 mm thick	3 h	¹ H	68
9.4	polyhydroxyalkanoate film	"	2D	256 × 256, (117 μm) ²	15.5 h	¹ H	69
2.4	water in Portland cement	SPI	—	128 points, 0.7 mm	13 min	¹ H	70
4.7	vulcanised rubber impregnated with aluminium and sodium sulfate crystals, filled phenolic resin or a 72-h tobacco horn worm	spin echo, PRI	—	180 FID, (35 μm) ² (PRI); 128 × 128, a slice 1 mm thick or without slice selection	2–17 h	¹ H	71
2.9	water in Portland cement with gypsum and lime additives	dipolar echo + STRAFI	1D	100 μm	—	¹ H	78

Table S.1 (continued).

Field /T	Object, process	Technique	Dimension	Spatial resolution characteristics	Recording time	Nucleus	Ref.
2.4	water in concrete	SPI	—	128 points, 0.95 mm	12 min	¹ H	79
0.7	layered polymer composite model sample or alkyd resin film with cobalt catalyst	spin echo	1D	256 or 512, 13 or 6.5 μ m	17 min	¹ H	80
0.7	alkyd resin-in-water emulsion	spin echo	1D	128, 8.7 μ m	—	¹ H	81
2	water in sodium silicate film	dipolar echo + STRAFI	1D	100 μ m	1–2 h	¹ H	82
2.4	water in Portland cement	SPI	1D	0.95 mm	—	¹ H	83
2.35	water in concrete	SPRITE	1D	64; 1.6 mm	—	¹ H	84
2.35	agar gel doped with Mn(II), mortar, concrete or polyethylene	SPRITE	2D	64 $\times$ 64, (1.25 mm) ² –(1.5 mm) ²	—	¹ H	85
7.05	water in Portland cement with or without superplastifier	SPI	2D	64 $\times$ 64 or 124 $\times$ 64, 101 μ m $\times$ 140 μ m	—	¹ H	86
0.75	water in clay brick, lime-and-sand brick or gypsum	spin echo	1D	0.15 mm	40 min	¹ H	87
0.1	water in limestone	gradient echo	3D, 1D	128 $\times$ 128 $\times$ 16, 2 $\times$ 2 $\times$ 8 mm (3D); 2 mm, a slice of surface area 10 $\times$ 10 cm (1D)	26 min (3D)	¹ H	88
4.7	water in alumina or silica	the same	2D	a slice 1 mm thick	—	¹ H	89
4.7	water in glass bead pack	spin echo (Hahn echo, EPI or PEPI)	2D, 3D	128 $\times$ 128; (94 μ m) ² , a slice 0.5 mm thick (2D); 128 $\times$ 128 $\times$ 128, (117 μ m) ³ (3D)	51 min or 24 s (2D); 9 h or 15 min (3D)	¹ H	94
2	water or aqueous solution of sodium dodecylsulfate in glass bead pack, sand, silica gel, potato starch	spin echo	1D	a slice 5 mm thick	—	¹ H	95
9.4	dispersion of acryl or polystyrene latex in water	the same	2D	512 $\times$ 512, (43 μ m) ² , a slice 2 mm thick	8.5 min	¹ H	97
9.4	emulsion of alkyd resin in water, aqueous dispersion of acryl latex	"	2D	512 $\times$ 512, (20 μ m) ² , a slice 0.5–1 mm thick	7–51 min	¹ H	98
9.4	water in composite liquid packaging cardboard	"	1D, 2D	128, 15.6 μ m, a slice 2 mm thick (1D); 128 $\times$ 16, 15.6 $\times$ 500 μ m, a slice 8 mm thick	24 s (1D); 2 min (2D)	¹ H	100
0.5	water in white oak wood	"	2D	256 $\times$ 256, (1.2 mm) ² , a slice 8 mm thick	12.8 min	¹ H	101
4.7	water in corn grains	"	2D	(234 μ m) ² , a slice 1.3 mm thick	640 s	¹ H	105
2	brine in sandstone or limestone	stimulated echo	—	WSR	7 h	¹ H	117
2	water in glass bead pack, in limestone, chalk and sandstone cores	inversion–recovery signal or stimulated echo	—	WSR	—	¹ H	118

Table S.1 (continued).

Field /T	Object, process	Technique	Dimension	Spatial resolution characteristics	Recording time	Nucleus	Ref.
2	brine in carbonate rocks and sandstone	stimulated echo	—	WSR	—	^1H	121
1.9	C_2F_6 or C_4F_8 in ceramics (yttrium-stabilised zirconia)	spin echo	3D	—	2 h	^{19}F	122
4.7	^{129}Xe (3 atm) in glass cylinder	stimulated echo	—	WSR	—	^{129}Xe	123
8.5	N_2 in zeolites NaCaA and NaX	spin echo	—	WSR	—	^{15}N	124
—	water in polystyrene bead pack	the same	2D, WSR	$(31.5\text{ }\mu\text{m})^2$, a slice 200 μm thick or WSR	—	^1H	125
1.5	human brain, rat brain <i>in vivo</i>	intermolecular two-quantum coherence + EPI	2D	64×64 ; $(3.8\text{ mm})^2$, a slice 15 mm thick (<i>Homo</i>) or $(0.48\text{ mm})^2$, a slice 4 mm thick (rat)	—	^1H	133
2	copper ions or 4-amino-TEMPO in water-containing gels	spin echo with inversion – recovery	1D	0.1 – 0.2 mm	—	^1H	135
0.2	Fe(II) and Fe(III) ions in agar gel	the same	1D	512, 0.11 mm	28 – 112 s	^1H	136
2	copper ions in water-containing polyacrylamide gel	"	2D	256×256 (128×256), $(0.15\text{ mm})^2$	150 s	^1H	137
2	copper in water-saturated limestone core	"	2D	256×128 , $(0.47\text{ mm})^2$	2.3 min	^1H	137
2.35	D_2O in lyotropic liquid crystal	spin echo	—	WSR	—	^2H	140
1.4	0.1% CuSO_4 + water in capillary	spin echo + PRI	2D	$(20\text{ }\mu\text{m})^2$, a slice 1 mm thick	—	^1H	141
5.9	5% polyacrylamide gel in D_2O	stimulated echo	—	WSR	—	^1H	145
2	water, acetonitrile, DMSO and n-butanol in ampoules; celery stalk	spin echo	2D	128×128 ; $(0.34\text{ mm})^2$, a slice 5 mm thick	—	^1H	147
7.05, 11.7	$\text{H}_2\text{O}/\text{D}_2\text{O}$ or ethanol/ $\text{H}_2\text{O}/\text{D}_2\text{O}$ in ampoule	spin echo or stimulated echo	1D, WSR	—	—	^1H	148
4.7	water in glass or polystyrene bead pack	stimulated echo	—	WSR	—	^1H	149
4.7	water or polyacrylamide gel	spin echo	2D	64×64 ; $(0.63\text{ mm})^2$, a slice 4 mm thick (water) or $(1\text{ mm})^2$, a slice 10 mm thick (gel)	—	^1H	152
4.7	water, pork loin <i>in vitro</i>	the same	—	WSR	—	^1H	153
2.0	water between glass plates	"	—	WSR	—	^1H	155
—	various liquids in rocks or alumina	stimulated echo	—	WSR	—	^1H	156
14.1	yeast cells	the same	—	WSR	—	^1H	159

Table S.1 (continued).

Field /T	Object, process	Technique	Dimension	Spatial resolution characteristics	Recording time	Nucleus	Ref.
2	water + CuSO ₄ in glass bead pack	stimulated echo	—	WSR, a slice 3.6 cm thick	1040–2080 s	¹ H	160
2	water in a polystyrene bead pack or brine in calcium carbonate	the same	—	WSR	—	¹ H	161
4.7, 7	water in kraft cellulose	"	—	WSR	—	¹ H	162
7	water in ampoule or in granular ion-exchange resin pack	spin echo	—	WSR	—	¹ H	163
2	1 mM CuSO ₄ + water in a tube	gradient echo	2D	128 × 64, a slice 5 mm thick	—	¹ H	164
4.7	water or H ₂ O/D ₂ O in alumina or silica	spin echo	2D	128 × 128, (40 μm) ² , a slice 0.3–1 mm thick	—	¹ H	167
1.89	H ₂ O/D ₂ O in zirconia	the same	1D	128 points, 184 μm	17 s	¹ H	174
2.35	H ₂ O/D ₂ O in laponite gel	—	1D	—	—	¹ H	175
—	water in porous polystyrene, natural sponge, pumice stone or glass bead pack	spin echo or gradient echo	3D	—	—	¹ H	176
5	DMSO + NaCl + H ₂ O + D ₂ O in artificial dermal replacement	gradient echo	2D	128 × 128, (67 μm) ² , a slice 2 mm thick	20 or 40 s	¹ H	177
8.5	DMSO, propylene glycol, methanol in fish embryo	spin echo	2D	128 × 128, (40 μm) ² –(17 μm) ² , a slice 100–600 μm thick	—	¹ H	178
6.3	4-hydroxy-TEMPO in water-containing silk fibroin gel	the same	2D	(0.2 mm) ² , a slice 2 mm thick	5 min	¹ H	180
4.7	Ni ²⁺ ions in water-saturated sand pack	—	2D	—	2 min	¹ H	181
4.7	Na ⁺ ions in water-saturated sand pack	spin echo	1D	256 points, 0.5 mm without slice selection	7 min	²³ Na	181
0.5	water in porous silica bead pack	stimulated echo	—	WSR	—	¹ H	182
4.7	water in alumina or silica	the same	—	WSR	—	¹ H	183
9.4	hexadecane in silica bead pack or MgO/n-octanol paste with or without Fe ₂ O ₃ additive	"	—	WSR	—	¹ H	186
2	water or aqueous NaCl solution in glass bead pack or sandstone	"	—	WSR	—	¹ H	187
1.4	water in wheat grain	stimulated echo + PRI	2D	64 × 64, (100 μm) ²	1.6 h	¹ H	188
3	white matter of human brain	spin echo	2D	128 × 128, (2 mm) ² , a slice 5 mm thick	—	¹ H	189
7.5	xylene (or toluene) + non-ionic detergent + water	stimulated echo	—	WSR	—	¹ H	190

Table S.1 (continued).

Field /T	Object, process	Technique	Dimension	Spatial resolution characteristics	Recording time	Nucleus	Ref.
7.05	suspension of human blood erythrocytes	spin or stimulated echo	—	WSR	25 min	^1H	193
7.05	water in glass bead pack	stimulated echo	—	WSR	—	^1H	194
4.7	water and 20% gelatin solution; cat brain <i>in vivo</i>	spin echo	2D	$128 \times 128, (0.55 \text{ mm})^2$	—	^1H	195
0.5	water + CuSO_4 , polyethylene glycol, cyclohexane; apple, seedling of a plant	the same	—	WSR	—	^1H	196
1.5	Xe (0.78 atm) + O_2 (0.15 atm) in glass sphere	FID after selective inversion	1D	1024 points, 0.5 mm (2 mm)	—	^{129}Xe	197
2	^3He (9 atm) + O_2 (2 atm) in glass sphere	spin echo	1D	1024; 0.1 mm, a slice 16 mm thick	—	^3He	198
1.9	^3He (7 atm) in cylinder	gradient echo	1D	0.8 mm	—	$^3\text{He}^*$	199
9.4	Xe (30 atm) and O_2 in aerogel	chemical shift selective spin echo	3D	$(420 \mu\text{m})^2$, a slice 1 mm thick	—	^{129}Xe	200
7	C_2F_6 (5 atm) in ceramic composite	spin echo	2D	$(100 \mu\text{m})^2$, a slice 0.5 mm thick	12 h	^{19}F	201
4.7	Xe (1–3 atm, 90% ^{129}Xe) + O_2 or Xe* (3 atm) in a glass cell or glass bead pack	gradient echo, spin echo or stimulated echo	—	WSR	—	$^{129}\text{Xe}^*, ^{129}\text{Xe}$	202
1.4, 9.4	propane, propene, water, acetone or isopropanol in CsNaX zeolites	spin echo	—	WSR	—	^1H	203
1.4	ethane in NaX and NaCaA zeolites	stimulated echo	—	WSR	—	^1H	204
4.7, 9.4	ethane in zeolite H-ZSM-5	spin echo	—	WSR	—	^1H	205
9.4	n-butane or methane in zeolites	stimulated echo	—	WSR	—	^1H	206
7.05, 9.4	benzene (+ Xe) in zeolite powder, 2,3-dimethylpentane or Xe in zeolite with coke	spin echo	1D, 2D	—	—	$^1\text{H}, ^{129}\text{Xe}$	207
2.1	ethane and ethene in zeolite NaX	the same	—	WSR	—	^1H	208
2.1	cyclopropane and propene in zeolite NaCdX under reaction conditions	"	—	WSR	—	^1H	209
9.4	ethene + CF_4 in silicalite or H-ZSM-5	"	—	WSR	15 min	$^1\text{H}, ^{13}\text{C}$ or ^{19}F	210
—	ethane or methane in AlPO_4^{3-} molecular sieves	stimulated echo	—	WSR	—	^1H	211
9.4	CH_4 or CF_4 in zeolites	spin echo	—	WSR	—	^1H	212
11.75	Xe + He in tris-(<i>o</i> -phenylenedioxy)cyclophosphazene crystallites	broad-line NMR	—	WSR	—	$^{129}\text{Xe}^*$	213

Table S.1 (continued).

Field /T	Object, process	Technique	Dimension	Spatial resolution characteristics	Recording time	Nucleus	Ref.
2.1	water + CuSO ₄ and octanol in glass capillaries	B ₁ -tomography with recording of pseudo-echo and PRI	2D	60 projections, (11 μm) ²	—	¹ H	214
8.5	water in capillaries	spin echo + gradient echo	1D, 2D	128, 9.4 μm, a slice 0.6 mm thick or without slice selection (1D); 128 × 128, (9.4 μm) ² (2D)	2 s (1D)	¹ H	215
3	water in a narrow slit (plastic)	spin echo	1D	512, 25 μm	—	¹ H	216
4.3	Xe flow at 0.8–1.3 atm in a tube 4 mm in diameter	dynamic NMR microscopy (PGSE, PGSTE)	2D in mixed <i>k</i> – <i>q</i> -space	512 × 256(<i>q</i>) (256 × 32) or 1024 × 32(<i>q</i>) (512 × 16), 100 μm, without slice selection	—	¹²⁹ Xe*	217
4.3	Xe (2 atm, 80% ¹²⁹ Xe) in an ampoule with rectangular cross-section	FID gradient echo	1D, 2D 1D	—	—	¹²⁹ Xe*	218
0.0031	Rb (10–100 mg) + N ₂ (10–200 Torr) + ³ He (0.2–2.5 atm) an ampoule with rectangular cross-section	FID	1D	—	—	³ He*	219
—	water in a bent tube with square cross-section	—	—	—	—	—	221
1.5	water in a tube with a cylindrical flow obstruction	gradient echo (EPI)	2D	1.9 × 1.8 mm, a slice 2 mm thick	64 ms	¹ H	224
4.7	water in gap between two coaxial cylinders	gradient echo (FLASH)	2D	512 × 512, 195 × 117 μm or (107 μm) ² , a slice 2 mm thick	0.5 s	¹ H	226
1.4	water + CuSO ₄ in a capillary, water in a plant stem <i>in vivo</i>	stimulated echo + PRI	2D	128 × 128; (12 μm) ² , a slice 1 mm thick (capillary), (75 μm) ² , a slice 3 mm thick (plant)	—	¹ H	227
—	water + 1 mM CuSO ₄ in a tube	gradient echo (FEER)	—	—	—	¹ H	228
—	1.5% solution of carboxymethylcellulose in extruder	spin echo	2D	128 × 128, (0.39 mm) ² , a slice 10 mm thick	—	¹ H	230
2.1	water + CuCl ₂ in membrane bioreactor	the same	2D	—	—	¹ H	231
1.4	water + 0.1% CuSO ₄ in a tube with abrupt contraction (expansion)	spin echo + PRI	2D	64 × 64, a slice 0.33 mm thick	—	¹ H	232
4.7	water + CuSO ₄ in a tube with contraction	spin echo + gradient echo (EPI)	2D	64 × 64, 1.25 × 0.625 mm or 1.5 × 0.5 mm, a slice 2 mm thick	105–115 ms	¹ H	233
1.5	water + glycerol in a tube with branching	gradient echo	2D	256 × 256, (0.5 mm) ² , a slice 4 mm thick	—	¹ H	234
11.9, 14.1	1 mM KCl + water in a tube filled with glass spheres or without glass spheres	spin echo	2D	128 × 128, (78 μm) ² , a slice 100 μm thick	—	¹ H	235
1.5	water in U-shaped tube	gradient echo	2D, 3D	128 × 256 (2D); 192 × 256 × 16, 1 × 0.8 × 1.2 mm (3D)	2 or 10 min (2D)	¹ H	236

Table S.1 (continued).

Field /T	Object, process	Technique	Dimension	Spatial resolution characteristics	Recording time	Nucleus	Ref.
0.6, 2	polyalkylene glycol (PG) or PMMA microspheres in PG	—	2D	128×128 or 256×256 , a sample 1 cm thick	—	^1H	237
7, 1.4	water, water + 0.1% CuSO_4 , or water + 0.5% high-molecular mass PEO	stimulated + spin echo (VEXSY)	—	WSR	140 min or 4.5 h	^1H	238
0.5	water + CuSO_4 in U-shaped tube	—	2D	256×256 , $(0.78 \text{ mm})^2$, a slice 2 or 3 mm thick	36 min	^1H	239
1.9	fluid in tube	gradient echo	2D	256×256 , $(0.5 \text{ mm})^2$, a slice 4.2 mm thick	—	^1H	240
2.35	water in a tube with contraction/expansion	FID + PRI or spin echo	2D	256×256 , $(118 \mu\text{m})^2$, a slice 2 mm thick (echo); 128×32 or 256×64 , 0.7, 0.8 or 1.6 mm, a slice 0.5 cm thick (FID)	8 or 23 ms (FID)	^1H	244
0.5	blood in thoracic aorta	spin echo or gradient echo	2D	256×256 , $(1.6 \text{ mm})^2$, a slice 10 mm thick	15–20 min	^1H	245
1.5	water + MnCl_2 or water + human albumin in tube	spiral trajectories	2D	$(1.46 \text{ mm})^2$ – $(2.4 \text{ mm})^2$, a slice 5–7 mm thick	180 ms (60 ms)	^1H	246
7.05	water + CuSO_4 in a tube or cylinder	spin echo	2D	256×128 , $(0.27 \text{ mm})^2$, a slice 2 mm thick or 1024×64 , $0.078 \text{ mm} \times 0.23 \text{ mm}$, a slice 0.4 mm thick	17 or 2 min	^1H	249
2	water in a tube with partitions	the same	2D, 3D	$128 \times 64 \times 64$ (3D)	137 min	^1H	250
1.0	water + CuSO_4 in a tube	gradient (EPI) or spin echo	2D	64×64 , $(375 \mu\text{m})^2$ (EPI) or 256×256 , $(94 \mu\text{m})^2$ (spin echo); a slice 2.5 mm thick	21.12 ms (EPI)	^1H	251
4.7	fertilised bird eggs	gradient echo	1D, 2D	$(200 \mu\text{m})^2$ or $(300 \mu\text{m})^2$, a slice 2.7 mm thick	—	^1H	252
1.9	mustard seeds in horizontal rotating cylinder	spin echo	2D	128×128 ; $(0.8 \text{ mm})^2$, a slice 8 mm thick	15 min	^1H	253
1.9	the same	the same	2D	a slice 8 mm thick	—	^1H	254
1.9	water in straight tube or a tube with branching	gradient echo or spin echo	1D, 2D	—	—	^1H	256
4.7	water in a tube	spin echo	2D	256×256 , $(78 \mu\text{m})^2$ or $(65 \mu\text{m})^2$, a slice 1 mm or 3 mm thick	6.5, 13 or 80 min	^1H	261
7.05, 14.1	DMSO or water in an ampoule 5 mm in diameter	stimulated echo	2D	32×256 ; a slice 1.4 mm thick	10 min	^1H	262
2.35	water in a tube with U-shaped bend	FID, radial trajectories (RUFIS); spin echo	2D	0.6–1.2 mm (RUFIS)	8–11 ms (RUFIS)	^1H	263
2	water + CuSO_4 , turbulent flow in a tube	spin echo (EPI)	2D	64×64 , $(1.2 \text{ mm})^2$, a slice 3 mm thick	33 ms	^1H	264
1.9	oil-filled plastic beads in horizontal rotating cylinder	spin echo	2D	$(1 \text{ mm})^2$, a slice 20 mm thick	—	^1H	265

Table S.1 (continued).

Field /T	Object, process	Technique	Dimension	Spatial resolution characteristics	Recording time	Nucleus	Ref.
1.9	water + glycerol in a tube with diaphragm (stenosis)	spin echo	2D	128×256 , $(0.39 \text{ mm})^2$	—	^1H	266
1.5	intracardiac blood flow	gradient echo	3D, 2D	$256 \times 256 \times 16$, $1.2 \times 1.2 \times 8 \text{ mm}$ (3D); 256×128 , $1.25 \times 2.5 \text{ mm}$, a slice 7 mm thick	29 min (3D), 2 min/a slice (2D)	^1H	267
0.47	water + CuSO_4 in a tube, water in tomato stem	spin echo (turbo)	2D	128×128 , $(315 \mu\text{m})^2$ or $(117 \mu\text{m})^2$, a slice 3 mm thick	31 or 64 s	^1H	270
7	water + glycerol + CuSO_4 or pig blood in tube	spin echo	1D	$78 \mu\text{m}$ or $23 \mu\text{m}$, a slice 1 mm thick or WSR	20 min (1D)	^1H	272
7.05	0.1% aqueous solution of PEO in tube, water and nutrients in castor-oil plant stem	the same	2D	128×128 , $(54.7 \mu\text{m})^2$; 64×64 , $(469 \mu\text{m})^2$ or $(1.4 \text{ mm})^2$ (tube); 128×128 , $(47 \mu\text{m})^2$ (stem)	—	^1H	273
—	water + CuSO_4 in a coiled tube	gradient echo	2D	64×64	1 min	^1H	274
1	water in a tube	spin echo + gradient echo	2D	32×32 , $(0.75 \text{ mm})^2$, a slice 4 mm thick	20.5 ms	^1H	276
2	water + CuSO_4 in a tube with grid-generated turbulence or without it	gradient echo	1D	256 or 128 , 0.29 or 0.58 mm , a slice 3 mm thick	—	^1H	277
1.5	water + MnCl_2 in a tube with contraction–expansion	the same	2D	256×256 , $(590 \mu\text{m})^2$, a slice 5 mm thick	—	^1H	278
1.9	oil-filled plastic beads in horizontal rotating cylinder	spin echo	2D	$(1 \text{ mm})^2$, a slice 20 mm thick	—	^1H	279
7	water in a tube or in a dialysis cell	spin echo or stimulated echo	—	WSR	—	^1H	280
7.05	water + CuSO_4 in a tube or conical converging tube	spin echo	—	WSR	—	^1H	281
7	$\text{C}_6\text{D}_5\text{NO}_2$	the same	1D	$90 \mu\text{m}$	—	^2H	282
2	water + CuSO_4 in glass bead pack	spin echo + stimulated echo	—	a slice 10 mm thick	—	^1H	283
11.75	water in a tube	spin echo	2D	128×128 , $(39 \mu\text{m})^2$, a slice 500 μm	—	^1H	285
7	water in a tube, gel during compression	spin echo (PEPI)	2D	32×32 , $125 \times 250 \mu\text{m}$	80 ms	^1H	286
7	0.1% CuSO_4 + water in a tube or hemodialysis cell	spin echo	2D	128×64 , $94 \times 190 \mu\text{m}$ a slice 1.6 mm thick	—	^1H	287
2	flow of water, sunflower oil or oil-in-water emulsion in a tube	gradient echo	2D, 3D	64×64 , $(850 \mu\text{m})^2$ or $(780 \mu\text{m})^2$, a slice 2 or 2.5 mm thick; $64 \times 64 \times 64$, $(710 \mu\text{m})^3$ (3D)	20–60 s (2D); 23 min (3D)	^1H	288
0.47	water + MnCl_2 on walls of a monolithic catalyst	—	—	128×128 , $(0.4 \text{ mm})^2$ or 192×192 , $(78 \mu\text{m})^2$, a slice 4 mm thick	13–17 min	^1H	289
4.7	polydimethylsiloxane film on vertical surface	spin echo	2D	—	—	^1H	290
0.7	water + MnCl_2 in a tube, corn stem, tomato pedicel	stimulated echo + (turbo) spin echo	2D	128×128 , $(0.16 \text{ mm})^2$ or $(0.12 \text{ mm})^2$, a slice 3 or 4 mm thick	17–19 min	^1H	291

Table S.1 (continued).

Field /T	Object, process	Technique	Dimension	Spatial resolution characteristics	Recording time	Nucleus	Ref.
1.5	water + MnCl_2 in a tube, blood in human femoral artery	gradient echo or spiral trajectories	2D	256×256 , $(0.63 \text{ mm})^2$ or 205×205 , $(0.88 \text{ mm})^2$, a slice 10 mm thick	—	^1H	292
1.5	water in a tube placed in agar gel	gradient echo	2D	256×256 , $(2.44 \text{ mm})^2$, a slice 5 mm thick	—	^1H	293
7, 11.7	convection in DMSO, water or chloroform	stimulated echo	—	WSR	—	^1H	294
7, 11.7	DMSO, water or chloroform	FID	1D	$170 \mu\text{m}$	—	^1H	294
2	convection in silicon oil	spin echo	2D	256×256 , a slice 1 cm thick	4 min	^1H	295
7.05	5% polystyrene in cyclohexane	the same	2D, WSR	—	—	^1H	296
4.7	falling droplet of water or water + surfactant	—	2D, 3D	—	10 h (3D)	^1H	297
7	1 mM KCl + water in a tube	stimulated echo	2D	128×128 , $(78 \mu\text{m})^2$, a slice 4 mm thick	—	^1H	298
2	water + CuSO_4 in U-shaped tube	spin echo	2D	256 , a slice 5 mm thick	—	^1H	299
1	gelatin in a rotating tube, water in a tube	gradient echo + spin echo	2D	32×32 , $(0.75 \text{ mm})^2$	20.48 ms	^1H	300
2.35	water in a tube with contraction	FID + PRI or spin echo	2D	24 mm FOV (32 projections per 180° sector), a slice 5 mm thick (FID); a slice 2 mm thick (echo)	11 ms (FID)	^1H	301
1.5	water + GdCl_3 (EDTA) in a tube or in a tube with expansion	gradient echo	2D	256×256 , $(1.25 \text{ mm})^2$ or $(0.94 \text{ mm})^2$, a slice 1 cm thick	263 s	^1H	302
2	5 mM CuSO_4 + water in gap between two coaxial cylinders	gradient echo, spin echo	2D 1D	512×512 , $(50 \mu\text{m})^2$, a slice 5 mm thick (2D); 512 , $50 \mu\text{m}$, a slice of surface area $1 \text{ mm} \times 1 \text{ cm}$	2 min (2D); 3.2 s (1D)	^1H	303
4.7	50% $\text{H}_3\text{PO}_4/\text{D}_2\text{O}$ in gap between two coaxial cylinders	spin echo	1D	—	—	^{31}P	304
4.7	oil-in-water emulsion (5% or 20%) + detergent and CuSO_4 in a tube or hollow-fibre membrane filter	spin or stimulated echo	2D	128×128 , $(94 \mu\text{m})^2$ or 256×256 , $(47 \mu\text{m})^2$, a slice 1 mm thick	—	^1H	305
0.6	1% solution of carboxy-methylcellulose in a tube	spin echo	1D	$147 \mu\text{m}$	192 s	^1H	306
0.6	low-density polyethylene melt in a tube	the same	1D	256 ; 0.25 mm	—	^1H	307
7.05	water or polydimethylsiloxane in NMR rheometers of different design	"	2D	128×128 , $(20 \mu\text{m})^2$, $35 \times 78 \mu\text{m}$ or $96 \times 32 \mu\text{m}$, a slice 2 mm thick or without slice selection	30 min	^1H	308
7.05	aqueous solution of cetylpyridinium chloride + sodium salicylate, tomato sauce, CTAB/ D_2O micellar solution, polyacrylamide/ D_2O	"	2D	—	—	^1H , ^2H	309

Table S.1 (continued).

Field /T	Object, process	Technique	Dimension	Spatial resolution characteristics	Recording time	Nucleus	Ref.
1.9	PMMA beads + a mixture of fluids in a tube with contraction and expansion	spin echo	2D	128×128 or 256×128 , $(200 \mu\text{m})^2$, a slice 0.5 cm thick	2 or 4 min	^1H	311
2	urethane rubber based composite or dog kidney in gelatin	stimulated echo	2D	128×128 or 256×256 ; $(0.8 \text{ mm})^2$ or $(0.6 \text{ mm})^2$, a slice 5 or 10 mm thick	—	^1H	312
1.5	agar gel	gradient echo (FLASH)	2D	256×256 ; $(0.55 \text{ mm})^2$	12 s	^1H	313
1.5	agar gel or pig kidney in gel	gradient echo or spin echo	2D	128×128 or 256×256 , a slice 10 mm thick	10–120 s	^1H	314
1.5	agar gel	gradient echo (FLASH)	2D	128×128 or 256×256	20–120 s	^1H	315
1.5	tissues <i>ex vivo</i> , agar gel, female breast	gradient echo or spin echo	2D	256×128 ; $0.63 \times 1.25 \text{ mm}$, a slice 10 mm thick	—	^1H	317
7	water in latex microsphere pack	spin echo	2D	128×128 , $(31.5 \mu\text{m})^2$, a slice 200 μm thick or 64×64 , $(63.5 \mu\text{m})^2$, a slice 1 mm thick	—	^1H	318
2	D ₂ O + hexadecane in limestone	—	1D	—	—	^1H	319
4.7	water or water + air in granular alumina pack	spin echo	3D	$256 \times 256 \times 32$, $(156 \mu\text{m})^3$	—	^1H	320
4.7	water in glass bead pack	the same	2D, 3D	256×256 , $(195 \mu\text{m})^2$, a slice 1 mm thick; $256 \times 256 \times 256$, $(195 \mu\text{m})^3$ (3D)	—	^1H	321
2	water or n-hexadecane + D ₂ O in sandstone or limestone	"	1D	0.6 mm	—	^1H	322
2	water or D ₂ O + n-octadecane or n-hexadecane in sandstone or limestone	"	1D	0.42 or 0.19 mm, a slice 4 mm thick	2 min or 16 s	^1H	323
2	D ₂ O and n-dodecane in limestone	"	1D, 2D	128 points, 783 μm (1D)	—	^1H	324
1.9	mixture of aliphatic hydrocarbons in sandstone	stimulated echo	2D	$(1.2 \text{ mm})^2$, a slice 14 mm thick	—	^1H	325
0.5	water in a tube, water or 3% brine in sandstone	spin echo	2D	$(1 \text{ mm})^2$ or $(3 \text{ mm})^2$, a slice 1 cm thick	—	^1H	326
0.5	water in a tube or water in glass bead pack	stimulated echo	—	WSR	—	^1H	327
1.9	water + contrast agent in plastic bead pack	spin echo	2D	128×128 or 128×256 , $(0.4 \text{ mm})^2$, a slice 5 or 20 mm thick	4 min	^1H	328
—	water in sandstone	spin echo (PEPI)	2D	a slice 18 mm thick	—	^1H	329
2	1% KCl + water in sandstone	spin echo	3D	$64 \times 64 \times 16$, $1 \times 1 \times 8 \text{ mm}$	—	^1H	330
0.5	water in bead pack	spin echo or stimulated echo	—	WSR	—	^1H	331

Table S.1 (continued).

Field /T	Object, process	Technique	Dimension	Spatial resolution characteristics	Recording time	Nucleus	Ref.
2	3% aqueous NaCl solution in sandstone	stimulated echo	—	WSR	—	^1H	333
2	water or 3% NaCl + dodecane solution in sandstone	the same	—	WSR	—	^1H	334
—	water in polystyrene bead pack	spin echo	—	WSR	—	^1H	336
1.89	water + Gd-based contrast agent in glass bead pack	spin echo, modified stimulated echo	1D 2D	128 (1D), 1.39 mm; 128 × 128, 0.91 mm × 1.16 mm, a slice 5 mm thick	300 ms (1D)	^1H	337
1.5	water + CuSO_4 or water + CuSO_4 + NaCl in fused quartz bead pack	spin echo	2D	128 × 128, (2.36 mm) ² , a slice 5 or 10 mm thick	0.5–3 min	^1H	338
5	GdCl_3 in glass bead pack filled with water	spin echo, stimulated echo	2D	128 × 16, 1 × 3 mm, a slice 4 mm thick	—	^1H	339
1.5, 4.7	aqueous Gd(DTPA) solution in chromatographic column (^1H); free Na^+ ions in ion-exchange column	gradient echo (FLASH)	2D (^1H), 3D (^{23}Na)	256 × 256 or 128 × 128, (300–1000) × (300–1000) μm , a slice 2–5 mm thick (^1H)	0.4–6 s (^1H), 4 min (^{23}Na)	^1H , ^{23}Na	340
0.5	water in porous silica bead pack	stimulated echo	—	WSR	—	^1H	342
—	water in glass bead pack	spin echo (PEPI)	2D	16 × 32, a slice 10–50 mm thick	—	^1H	343
0.1	$\text{Mn}_2(\text{EDTA})$ complex in glass bead pack filled with water	spin echo	3D, 1D	256 × 128 × 32, 1 × 2 × 3 mm (3D); 256 points, 1 mm (1D)	13 min (3D), 9 s (1D)	^1H	344
0.5	water in porous silica bead pack	—	—	WSR	—	^1H	345
2	3% brine or water + CuSO_4 in glass bead pack, glass or polyamide fibres or in sandstone	stimulated echo	—	WSR	—	^1H	347
348	drilling fluid (suspension of bentonite in water with additives) in limestone or sandstone	spin echo	1D	128; 0.48–2.4 mm	—	^1H	2
2	aqueous clay suspension (bentonite) in limestone	gradient echo (FLASH) or spin echo	2D	128 × 64 or 128 × 128, a slice 5 or 10 mm thick	1.9 s (FLASH)	^1H	349
2	bentonite + water + NaOH + lignosulfonate dispersant (+ barite) in sandstone or limestone	spin echo	1D	128	—	^1H	350
2	clay suspension in water	spin echo with inversion – recovery	1D	0.54 mm	—	^1H	351
1.5	oil + aqueous CaCl_2 solution + isopropanol- d_8 in sandstone, oil + aqueous NaI solution in dolomite	chemical shift selective spin echo	2D	128 × 256, (0.5 mm) ² , a slice 5 mm thick	20 min	^1H	352

Table S.1 (continued).

Field /T	Object, process	Technique	Dimension	Spatial resolution characteristics	Recording time	Nucleus	Ref.
1.89	oil + water in dolomite	chemical shift selective spin echo	1D, 2D	128 points, 0.8 mm (1D), 128 × 128, 0.3 × 0.8 mm (2D)	5 min (1D), 2.5 h (2D)	¹ H	353
2	n-octadecane + D ₂ O in limestone	spin echo	1D	—	7.5 s	¹ H	354
1.9	water + NiSO ₄ or mixture of hydrocarbons in crushed glass pack	the same	2D	256 × 256, (0.45 mm) ² , a slice 1.7 mm thick	26.5 min	¹ H	355
—	hexadecane and D ₂ O in sandstone	—	1D	—	—	¹ H	356
4.7	n-hexanol and water in sand	spin echo	1D	400 μm	—	¹ H	358
4.7	octanol and water in glass bead pack	the same	2D, 3D	256 × 256 × 256, 195 × 195 × 195 μm or 128 × 128 × 128, (390 μm) ³ (3D), 256 × 256, (195 μm) ² , a slice 1 mm thick	—	¹ H	359
1.9	water + Cu(II) in ion-exchange column	gradient echo	3D	16 × 16 × 512, a slice 0.13 mm thick	20 min	¹ H	362
1.9	pharmaceutical granules in horizontal rotating cylinder	spin echo	2D	(0.8 mm) ² , a slice 8 mm thick	—	¹ H	363
2	mustard seeds + glass or sugar beads in rotating cylinder or narrow cylinder	—	3D	128 × 128 × 128	—	¹ H	364
1.9	oil-filled plastic beads rotated in a container	gradient echo	1D (2D)	a slice 4 × 2.5 mm	—	¹ H	365
2	poppy grains in shaken vertical cylinder	—	2D	a slice 1 or 2 mm thick	—	¹ H	366
4.2	Xe (0.4 atm) + N ₂ (0.27 atm) + He (total pressure of the gas mixture 4 atm) in capillaries, in a tube, flow through a tube with diaphragm or polyurethane foam	gradient echo (PGSE)	2D 2D in mixed <i>k-q</i> -space	256 × 128, 110 × 340 μm, a slice 5 mm thick 256 × 32, a slice 4 mm thick	51 min —	¹²⁹ Xe* ¹²⁹ Xe*	368 368
4.3	Xe (1–3 atm, 80% ¹²⁹ Xe) in coaxial tubes or in capillary bundle	gradient echo (FLASH)	2D	128 × 64, 0.1 mm	—	¹²⁹ Xe*	370
4.3	Xe (1–3 atm, 80% ¹²⁹ Xe) in aerogel	the same	1D	0.1 mm	—	¹²⁹ Xe*	370
9.4	Xe (10 ¹⁹ cm ^{−3} , 70% ¹²⁹ Xe) in mice lungs <i>in vitro</i> in an ampoule	"	2D	128 × 128, (0.37 mm) ²	600 ms	¹²⁹ Xe*	371
2.35	C ₃ F ₇ H (2 atm) in phantom or sandstone	gradient echo	1D	0.5 mm	21 min	—	373

Notes: PVA is poly(vinyl alcohol), PVC is poly(vinyl chloride), PEMA is poly(ethyl methacrylate), PMMA is poly(methyl methacrylate), PEO is poly(ethylene oxide), DMSO is dimethyl sulfoxide; PRI is projection reconstructed imaging, WSR is without spatial resolution, FID is free induction decay; EPI is echo-planar imaging, PEPI is echo-planar imaging with PI-pulses, STRAFI is stray field imaging and FLASH is fast low-angle shot.

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Electrocatalysis on polymer-modified electrodes

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Abstract. The procedures for applying polymeric films onto conductive supports and doping them with active microparticles of metal-catalysts or functional redox groups are considered. General principles of the electrocatalytic action of these systems are discussed. Experimental results on the electrocatalysis on electrodes modified by polymeric films are analysed. Attention is drawn to systems involving particles of platinum-group metals incorporated into polymeric matrices. The properties of electrodes modified by ion-conducting and electron-conducting polymers are compared. Certain problems to be solved in future studies of the electrode systems under discussion are formulated. The bibliography includes 265 references.

I. Introduction

The development of new types of electrode materials pertains to important problems of electrochemistry. The electrodes the surfaces of which have been formed with involvement of polymeric films are the promising subject of studies aimed at solving this problem.[†] The attention of scientists to these electrode materials is determined by the fact that their adsorption, electrochemical, photoelectrochemical, corrosion and electrocatalytic properties can be changed by varying their surface composition and structure. The progress in solving this problem requires the knowledge of the structure and electrochemical properties of the support-modifying layer system and an insight into the mechanisms of the processes in this system.

Polymers used in electrochemical systems may be divided into two groups, *viz.*, ion-exchange (without electron conduction) and electron-conducting polymers. The polymeric films with solely ionic conduction applied onto conductive supports should be, as a rule, functionalised by redox groups to find catalytic (electrocatalytic) applications (this is the reason for the frequently used term 'redox polymers'). The latter act as mediators, so that the

polymer-support system can accelerate certain electrode processes.

The structures of electron-conducting organic polymers are characterised by the presence of conjugated bonds between electroactive groups in the chains, which is the reason for their high electron conductance in a certain potential range. The possibilities of the mediator catalysis by electron-conducting polymers can substantially be widened by additional introduction in them of functional groups through chemical bonding or Coulomb interaction between multicharge ions sorbed from a solution and charges of the polymeric matrix.

The use of polymeric films as the matrices for classical electrocatalysts, *viz.*, platinum-group metals, opens up wide prospects. The development of such systems increases substantially the number of electrode processes where the use of polymers can be very effective. Particularly, this will allow the use of M-polymer-support systems (M is the metal-catalyst) in the electrooxidation of hydrogen and simple organic compounds, electroreduction of oxygen, *etc.*, which attracts the keenest attention in the context of the fuel cell problem. It is those chemical reactions, which are accompanied by strong adsorption (chemisorption) of initial and/or intermediate species, that are frequently called 'electrocatalytic' in the electrochemical literature.^{1,2} At the same time, in many studies, the term 'electrocatalysis' is used in a more broad sense, embracing acceleration of electrode reactions and/or enhancement of their selectivity due to the mediator catalysis.

This review surveys the current directions of research in the field of using polymers for fabricating highly active electrodes. The main advances and problems in this field of electrochemistry are considered. Despite the abundance of reviews on electrochemistry of polymers (*e.g.*, see Refs 3–16), quite a limited number of publications generalising the results on electrocatalysis on polymer-coated electrodes are available: certain reports comprehensively discussed the problems of synthesis, structure and physicochemical and electrocatalytic properties of a single polymer or a group of polymers similar in composition (*e.g.*, Refs 9, 11, 12), other reviews delving deeply into the theory of electrochemistry of polymers and the principles of their use for electrocatalysis merely listed the electrode systems and electrocatalytic processes studied (*e.g.*, see Refs 6, 13, 16).

[†] In the scientific literature, these electrode systems are shortly called the polymer-modified electrodes, because it is by the polymeric coatings that their electrochemical behaviour is often determined virtually totally. It is not without purpose that along with the term 'polyaniline-modified electrodes', the term 'polyaniline electrode' is frequently used.

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This review cannot also pretend to comprehensively cover all the problems on the subject and give an exhaustive bibliography, otherwise this would contain over thousand references. The questions concerned with the main procedures of the preparation of electrodes with polymeric coatings, the principles of using them for the catalysis of electrochemical processes, the specific and/or general features of the behaviour of systems with ion-exchange and electron-conducting coatings, the main developments and problems in the promotion of a number of important electrode reactions are considered. Among the latter reactions, preference is given to the processes occurring in aqueous solutions and vital for the development of fuel cells and electrosynthesis. Nafion and poly(vinylpyridine) are chosen as the typical representatives of ion-exchange polymers, and polyaniline and polypyrrole represent the electron-conducting polymers. Attention is drawn to the systems with electrocatalytically active surfaces formed by incorporation of microparticles of noble metals into polymeric matrices. An attempt is undertaken to analyse the reasons for such a wide scatter and discrepancy in the experimental results on the electrocatalytic activity of these systems.

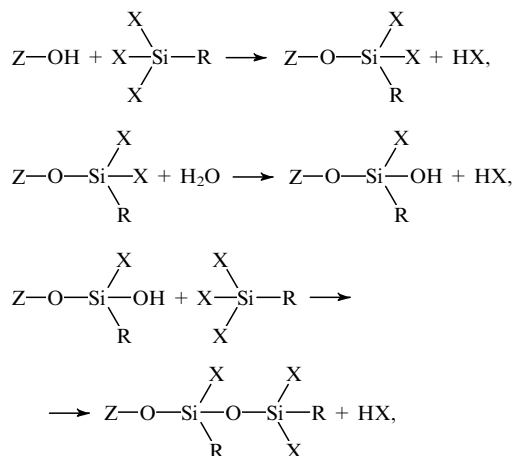
II. Modification of electrode surfaces by polymers

Of the various methods for applying polymeric coatings onto conductive supports, here we consider only those used most frequently in fundamental studies for fabricating the support–polymeric matrix systems. As a rule, films of ion-exchange polymers are ‘attached’ to the surface by chemical bonding or through adsorption interaction.^{17–32} Both chemical and electrochemical methods are used for synthesising conducting polymeric films on the surfaces of solid supports.^{3, 7, 9, 14, 33} Solubility of the polymer is the important factor determining the adhesion of the film.

1. Methods of application of modifying polymeric coatings

a. The immersion method

The immersion method is based on the exposure of an electrode (support) to a polymer solution for a certain time sufficient for the adsorption of molecules and the formation of a film on the surface.^{17–21} Due to chemisorption and low solubility of coatings formed in the solutions used, the films obtained by this method well adhere to the surface. The formation of coatings can proceed as a result of chemical reactions of the polycondensation type. A typical example is the formation of polymeric layers from organosilanes X_3SiR ($X = Cl, OCH_3$, etc., R is the substituent involving a certain functional group) on oxidised surfaces.^{14, 20, 21} The formation of molecular networks occurs due to a sequence of reactions presented by the following scheme:



where Z is the supporting surface.

b. ‘Drop evaporation’

The method of drop evaporation was used for modifying electrodes of small areas. Dropwise application of several microlitres of a polymer solution of a given concentration followed by evaporation of the solvent allowed one to obtain films well characterised with respect to both the amount of the polymer and its composition.^{22–25} The structural uniformity of the films depended to the greater extent on the evaporation procedure, namely, the latter should occur sufficiently slowly. The composition of the original film (including its functional groups) can be changed by treating it with the corresponding reagent using the same method of ‘drop evaporation’. Thus the stability of a poly(ethylene imine) film in acidic solutions is increased upon treatment with a solution of dibromobutane in propan-2-ol, which resulted in cross-linking of the polymer^{26–28} and a decrease in its solubility in aqueous solutions with low pH.

c. Oxidative and reductive deposition

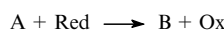
Solubilities of certain compounds in their oxidised and reduced forms are different. This can be used for the deposition of modifying (including polymeric) films on electrodes.^{29–32} For example, it was found^{29, 30} that viologens with more than four carbon atoms in the alkyl substituent and certain polymeric viologens form stable films of radical cations upon their chemical or electrochemical reduction. The same principle was also applied for the deposition of poly(vinylferrocene) films.^{31, 32}

The methods discussed of deposition of polymeric coatings and their versions were used for the deposition of redox polymers and, in certain cases, for modifying electrodes by electron-conducting polymers. However, the common practice for the preparation of electron-conducting polymeric films is electrochemical polymerisation.

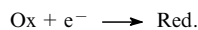
2. Redox polymers as the mediators of redox processes

Ion-conducting polymeric films with incorporated redox groups were used as the charge carriers from the substrates in a solution to the support.^{7, 10, 14, 17–20} If the substrate is oxidised or reduced faster on electrodes modified by redox polymers as compared with unmodified electrodes (support), one can speak of the catalytic effect of the film. A scheme in Fig. 1 illustrates the process of charge transfer in the reduction of species A to species B ($A + e^- \rightarrow B$) through redox centres (Red/Ox) in the polymeric film.

In the general case, the reduction rate is determined by the rates of the following processes: diffusion of species A from the solution bulk to the film surface, the reaction



in the film surface layer, the charge transfer in the film and the reaction



A specific and the most important process in the systems of the type discussed above is the charge transport in the film, which is characterised by the formal diffusion coefficient D_f . Despite the absence of the self-conduction of the polymer, the charge transfer through the film is possible by either physical diffusion of Red and/or Ox in the film or the step-by-step electron exchange between neighbouring redox centres (see Fig. 1).^{34–41} These processes are accompanied by the motion of polymeric chains, the solvent and counter-ions. The redox centres frequently represented polycharge ions [$Fe(CN)_6^{3-/4-}$, $Mo(CN)_8^{3-/4-}$, $IrCl_6^{2-/3-}$, etc.] which are strongly bound to ion-exchange polymers due to the Coulomb interaction.

Figure 2 exemplifies the voltammograms of a smooth platinum electrode and the electrode modified by a poly(ethylene

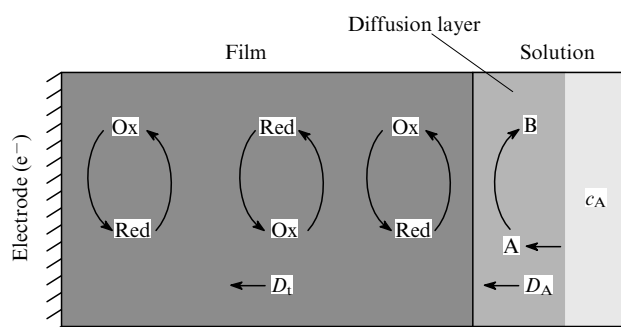


Figure 1. A scheme of reduction of a substance on the electrode modified by a redox-polymer film.

D_A is the diffusion coefficient of A particles in solution; c_A is the concentration of A in the solution bulk; D_i is the formal coefficient of charge diffusion in the polymeric film.

imine) film.[‡] It is seen that before the introduction of a redox group into the ion-exchange polymer (curves 1), the system was characterised by a very low polarisation capacity I/v (lower than that of the support, *i.e.*, smooth platinum). With the accumulation of $\text{Fe}(\text{CN})_6^{3-/4-}$ ions in the film, the system acquires the gradually increasing redox activity due to the following reaction:

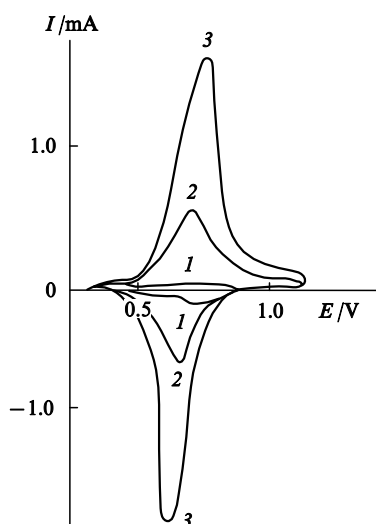
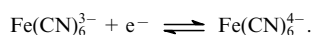


Figure 2. Cyclic voltammograms of a platinum electrode modified by a poly(ethylene imine) film.

Measured in solutions: (1) 0.5 M H_2SO_4 ; (2) 0.2 mM $\text{K}_3\text{Fe}(\text{CN})_6$ + 0.5 M H_2SO_4 every 5 min (2) and 60 min (3) after the immersion of the electrode into solution. The potential scan rate $v = 50 \text{ mV s}^{-1}$.

3. Electrochemical polymerisation

Synthesis of polymeric films by electrochemical polymerisation shows a number of advantages over the method of chemical polymerisation. First, the films are formed directly on the electrode surface, and the reaction product, *viz.*, an electroactive film, exhibits a high conductivity. Second, the electrosynthesis provides a good current efficiency and a strict stoichiometry of the process; hence, the films of desired masses and thicknesses can be obtained. Third, the properties of the polymeric film can be controlled in the course of the synthesis. Possible electrochemical and chemical

reactions occurring during the syntheses of polyaniline^{3, 4, 42, 43} and polypyrrole^{11, 12, 43–46} were described in detail in the literature.

Electrochemical properties of the support–electron-conducting polymer system depend strongly on the conditions of the polymer synthesis. Below, we consider the effects of some of these conditions.^{3–9, 11, 42, 43, 47, 48}

a. The effect of the support material

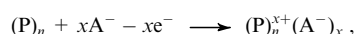
In the synthesis of electron-conducting polymers, different materials were used as the supports, *viz.*, platinum,^{49–53} gold,^{53–55} metal oxides,^{49, 55, 56} glassy carbon,^{51, 52} pyrographite,⁵³ stainless steel^{49, 57} and iron^{58–61} for polyaniline; noble metals,⁶² conductive glass,^{43, 62} carbon materials,^{11, 63} aluminium, tantalum and copper,^{62–66} steels^{63–67} and semiconductors⁶⁸ for polypyrrole. From these studies, it can be concluded that the nature of the support material had virtually no effect on the synthesis and properties of conductive polymeric films with the thicknesses exceeding tens of monolayers. The exception is provided by the metals with surface oxide films.^{11, 45}

On the other hand, the formation of first layers initiated by the formation of radical cations^{3, 47} is determined largely by the nature and the structure of the support. However, in such systems the electrochemical effects caused, on the one hand, by the adsorption-induced surface modification and, on the other hand, directly by the polymeric film can hardly be separated.

The process of film formation was shown to be ‘sensitive’ to the solution composition (see below); hence, to obtain reproducible results, it is desirable that the synthesis (not too lengthy) is carried out in a three-electrode cell with separate anodic and cathodic compartments.

b. The effect of the polarisation mode

Films of conducting polymers used in electrocatalysis are mainly prepared by electrooxidation of monomers (the anodic synthesis). This synthesis always proceeds at a potential exceeding those of anodic doping of polymers. The anodic doping is the reversible oxidation of a polymer resulting in its transition from the state of an insulator or semiconductor into the conductive state.^{3–11, 13, 47, 69} The electroneutrality of the oxidised polymer with positive charges on certain parts of its chain is achieved by incorporation of counterions, *i.e.*, anions into the polymeric matrix (P)



where n is the degree of polymerisation. The x/n ratio characterises the degree of doping of the polymer. Dedoping (cathodic reduction) of an anodically doped polymer results in the elimination of charges in its chains and the dissociation of the anions to the solution. The doping–dedoping processes are accompanied by

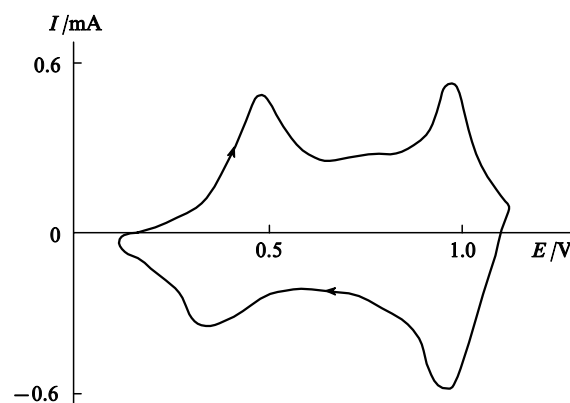


Figure 3. A cyclic voltammogram of a glassy carbon electrode modified by a polyaniline film.

[‡] Hereinafter, the potential values E are shown with respect to the reversible hydrogen electrode in the same solution, unless otherwise specified.

redox reactions, which determine the redox activity of electron-conducting polymers. The intrinsic redox activity of a polyaniline film (Fig. 3) is manifesting itself in the vicinity of two pairs of anodic–cathodic peaks in the cyclic voltammogram (at ~ 0.45 and ~ 0.95 V). In the potential range between these peaks, the film exhibited a high electron conductivity (up to 10^5 S cm $^{-1}$).

The films can be synthesised using different modes, *viz.*, potentiostatic, galvanostatic, potentiodynamic and pulsed modes. These modes were used in the synthesis of electron-conducting films of polyaniline^{43, 50, 70–78} and polypyrrole.^{11, 70, 79–82} An analysis of the experimental results obtained allowed the following conclusions to be drawn.

The number of aniline molecules incorporated into the polymeric film was roughly proportional to the charge passed through the system during the synthesis.

The mass of the polymeric film on the electrode, as a rule, was proportional to the charge consumed in its doping. However, the slopes of the corresponding linear dependences vary depending on the synthetic mode.

The results of measurements of these dependences for polyaniline have shown that, for a galvanostatic synthesis, the degree of doping decreases with a decrease in the current density. Under potentiostatic conditions, the maximum degree of doping was reached at the potential of 0.9 V. In the potential cycling mode, the dependence of the degree of doping on the potential scan rate also demonstrated a maximum.⁵⁰

The following explanation to the regularities observed was proposed.⁵⁰ At low current densities, the film growth involves a small number of nuclei, which can result in a polymeric structure with a low redox activity. Probably this is the reason for the decrease in the redox activity observed for the films synthesised at the potentials below 0.9 V. As the potential increased above 0.9 V, the redox activity of films decreased probably due to the degradation processes⁸ in the polymeric films.^{51, 83–85} The decrease in the redox activity of polyaniline at high potential scan rates was probably due to either the finite rate of recombination of radical cations or the adsorption of the monomer on the polymer.⁴⁷ Syntheses under galvanostatic (the current density > 0.1 mA cm $^{-2}$) and potentiostatic (the potential > 1.0 V) conditions were accompanied by noticeable exfoliation of polymeric films formed.

Of different deposition modes used, the cyclic potential scanning allowed polyaniline of the maximum redox activity to be obtained.^{50, 51} Films synthesised under such conditions also exhibited better adhesion to the electrode. The foregoing mainly concerns the films with thicknesses of ~ 300 – 400 nm.

c. The effect of solution composition ¶

Physicochemical properties of polypyrrole^{43, 46, 80, 81, 86, 87} and polyaniline^{88–114} films were shown to depend on the solution composition. This can be illustrated by several examples.

The polymerisation rate of aniline depends on the nature of an acid (supporting electrolyte) in the order $\text{HCl} < \text{HClO}_4 < \text{HBF}_4 < \text{HF} < \text{H}_3\text{PO}_4 < \text{H}_2\text{SO}_4$.⁴⁷

The effect of organic additives, benzene and its derivatives serving as examples,^{99–101} is defined by the character of their interactions with the polymer during the film growth, *viz.*, on the possibilities of formation of chemical bonds with elements of the polymer chain and of co-polymerisation. Thus in the presence of phenol, the synthesis of polyaniline decelerated and, for a certain phenol/aniline concentration ratio (1 : 2) in solution, the synthesis stopped. The presence of phenol in the deposition solution enhanced by 15% the susceptibility of polyaniline to doping and

prevented its degradation. The presence of phthalic acid in solution increased the porosity of the polymeric film, which was accompanied, on the one hand, by the increase in its susceptibility to doping and, on the other hand, a decrease in its stability towards degradation. The additions of salicylic acid had the opposite effect.

According to the results of other studies,^{50, 51} no polymeric chains were formed in a two-dimensional adsorption layer at the polymerisation potential. For a polymer to form, its monomer should be present in solution in a certain concentration. For example, for polyaniline, this concentration was $\geq 10^{-4}$ mol litre $^{-1}$ (see Refs 75, 76). Probably, the monomer can be adsorbed on the polymer and get incorporated into it under certain conditions.

d. Stability of film characteristics

Keen attention was drawn to the problem of stability of electrochemical parameters of modified electrodes.^{70, 72, 73, 84, 85, 94, 95, 99–101, 115}

For acidic media, cyclic voltammograms measured on films synthesised on supports by the electrochemical polymerisation method were shown to be stable only in a certain potential range. The extension of the potential cycling range into anodic and cathodic directions entailed a decrease in the area under the peak of polymer doping in the voltammogram and caused irreversible changes in certain characteristics of the polymer, *e.g.*, its conductivity. The limits of the potential range where a film exhibited stable electrochemical properties depended of many factors, *e.g.*, on the electrolyte composition.

These changes in the film characteristics were caused by the degradation of polymers. According to the features of the changes occurring in the polymeric film, two main types of degradation could be singled out.^{96, 97} For one of them, the specific doping ability of the polymer tended to decrease, whereas its mass remained constant; for the other, both the specific doping ability and the polymer mass decreased. Such processes of severe degradation resulting in disintegration of the film were also observed in the course of the polymer synthesis. For high potentials of the synthesis, the growth of the film bulk was accompanied by its exfoliation.

The radioactive tracer technique proved to be effective for studying polymer degradation.^{94, 96, 115} Using this method, it became possible to confirm the existence of the degradation types mentioned above and show that different electrochemical synthetic modes produced polyaniline films with different stabilities towards oxidative degradation.

The differential radioactive tracer method has shown that the processes of oxidative degradation of polyaniline films with thicknesses < 500 nm involve the whole mass of the polymer on the electrode. At the potentials of 0.7–0.75 V in 0.5 M H_2SO_4 , the third degradation type named ‘mild degradation’ was observed.⁹⁷ It was shown that under these conditions, the polymer mass and its susceptibility to doping (the area under doping peaks) remained constant, chemical bonds of certain polymer molecules with the surface were broken with retention of the electrochemical bonding due to the interaction between polymeric chains.

e. Composite polymeric films

Composite materials containing nonconducting and ion-conducting polymers along with electron-conducting ones were proposed to improve unsatisfactory mechanical characteristics of conducting polymeric films (polyaniline, polypyrrole). Many studies are aimed at the development of such composite materials.^{43, 105, 112, 116–129} These were synthesised in one or two steps. In one-step method, the electrode is immersed into a solution containing a matrix polymer and the monomer of a conducting polymer, and the electrosynthesis is carried out in this solution. Alternatively, a layer of an inert ‘matrix’ polymer which usually represents a nonconducting (ion-conducting) polymer with good mechanical properties, *e.g.*, Nafion, is formed in the first step. In

§ Irreversible redox processes which occur during potential cycling.

¶ This review considers the systems using water as the solvent. Hence, the term ‘solution composition’ means the monomer concentration and concentrations and compositions of the supporting electrolyte and different additives.

the second step, the electrode covered with the matrix polymer layer is immersed into a monomer solution, and the conducting polymer is synthesised. In the course of electropolymerisation, particles of the matrix polymer become incorporated into the conducting polymer. For the details of the syntheses of composite materials see Ref. 43.

It should be borne in mind that, in many cases, the formation of a composite implies the appearance of new qualities rather than simple 'summation' of the properties of its components. An illustration to the issues mentioned above is provided by the results obtained using radioactive-tracer and electrochemical methods for the formation of polyaniline–Nafion composite films on platinum and glassy carbon.^{128, 129} Particularly, for Nafion-covered electrodes, it was shown that aniline is first accumulated in the porous matrix polymer and only later transformed into polyaniline (the template synthesis^{130, 131}). The degradation of such a film proceeds more slowly; hence, a substantially smaller amount of polyaniline fragments is removed from the electrode. This can be associated with the complex and branched structure of the polyaniline formed in the porous Nafion matrix.

III. Electrochemical reactions on polymer-modified electrodes

1. Films of nonconducting polymers

Ion-exchange polymeric films with incorporated redox systems are promising for electrochemistry of organic substances. Their use often made it possible not only to decrease the electrolysis overvoltage but also to enhance the selectivity of the main electrode reaction.^{132, 133}

Thus manganese dioxide is known to selectively oxidise allyl alcohol to the corresponding aldehyde leaving the double bond intact. It was shown that the introduction of the $\text{Mn}^{2+}/\text{MnO}_2$ pair into the Nafion film provides the efficient electrolysis of cinnamyl alcohol to β -phenylacrolein.¹³⁴ The current efficiency in aldehyde increased from $\sim 70\%$ to $\sim 82\%$ with the changeover from the Pt–Nafion system to the Mn, Pt–Nafion one.

Figure 4 shows voltammograms of a glassy carbon electrode in an aqueous cysteine solution in the absence and in the presence of the Nafion– $\text{Os}(\text{bipy})_3^{2+/3+}$ (bipy is bipyridyl) film on the surface. As can be seen, the diffusion current of cysteine electro-oxidation reached its limiting value in the second case.¹³⁵

Dimethylferrocene immobilised together with glucose oxidase in an ion-exchange film on a graphite support was used as the charge-carrier from the reduced enzyme (obtained as a result of glucose oxidation) to the conducting support.¹³⁶ In this system too, the limiting diffusion currents of glucose oxidation were reached, which allowed an amperometric sensor for glucose to be developed.

The oxidation of Fe^{2+} cations to Fe^{3+} carried out on a cross-linked poly(4-vinylpyridine) (PVP) and PVP-poly(α -lysine) films containing the $\text{IrCl}_6^{3-}/\text{IrCl}_6^{2-}$ pair^{137, 138} can be cited as the

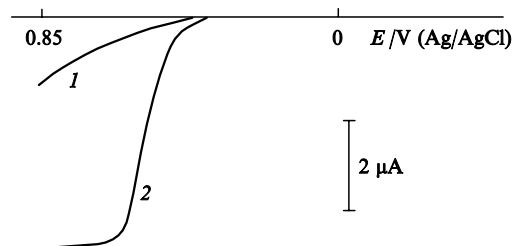


Figure 4. Voltammograms of cysteine oxidation on a rotating disk electrode of glassy carbon (1) in the absence and (2) in the presence of the surface of a Nafion film with the $\text{Os}(\text{bipy})_3^{2+/3+}$ redox system;¹³⁵ $v = 1 \text{ mV s}^{-1}$; cysteine concentration is $1.28 \text{ mol litre}^{-1}$, pH 4.

example of the mediator catalysis for inorganic reactions. These studies have also theoretically discussed the possibility of estimating the contributions by the mass transfer, the kinetics of interactions of particles and the charge transport in the films into the general mechanism of the electrode process involving a mediator.

2. Electron-conducting polymeric coatings

To date, a considerable number of electrochemical reactions which occur on electrodes with electron-conducting films were studied. However, the occurrence or the absence of the catalytic (electrocatalytic) effect for a particular process was debated more often than in the case of ion-exchange polymers. Apparently, this is largely caused by different conditions of film preparation and different compositions of supporting electrolytes used, because, as was shown above (see Section II.3), these factors strongly affect the physicochemical and electrochemical properties of electron-conducting coatings. The ambiguous interpretation of these results was due to the lack of a theory of electrocatalytic effects by such coatings, which would encompass the whole diversity of the occurring processes.^{6, 10}

A typical electrocatalytic reaction studied on electrodes modified by conducting polymers is the oxygen electroreduction. Studies of this process on a gold electrode covered with a polypyrrole film have established the promoting effect by the polymer.^{139, 140} Using the method of the rotating ring–disc electrode, the authors of these studies have shown that this effect is due to an increase in the selectivity to the oxygen electroreduction to give water.

It was also concluded^{139, 140} that polypyrrole films are permeable to oxygen and the reaction mainly proceeds at the metal/polymer interface. In another study,¹⁴¹ no promoting effect was observed for polypyrrole doped with perchlorate anions.

The promoting effect of polyaniline films on the oxygen electroreduction on glassy carbon electrodes in dilute acidic solutions was observed.^{142, 143} It was noted that in the course of this process the electrochemical characteristics of polyaniline remained stable for a long time, *i.e.*, the polymer did not degrade.

Studies of oxygen reduction on polyaniline and Nafion films have revealed the promoting effects of polymers on the electrochemical reaction.¹²⁴

The problems of organic reactions on electrodes modified by polymeric films were discussed.^{144–152} Particularly, the electro-oxidation of formic acid on polymer-modified platinum and gold electrodes was described in most detail.^{144–147, 152} The promoting effect of a platinum-supported polyaniline film on this process in the potential range below 0.5 V was found.¹⁴⁶ Presumably, the polymer prevented accumulation of the products of strong adsorption of formic acid on the electrode, which thus increases the number of active sites for the oxidation reaction.

By combining radioactive-tracer and electrochemical methods, the promoting effect of polyaniline films on the steady-state oxidation of formic acid on platinum and gold electrodes was also confirmed.^{144, 145} It was shown experimentally that the amount of products of strongly adsorbed formic acid on a polyaniline-film modified electrode was higher as compared with unmodified electrodes (Fig. 5). This result qualitatively agrees with the conclusions made earlier.¹⁴⁶ However, it was found^{144, 145} that an eightfold increase in the polymer-film thickness did not change the amount of strong-adsorption products accumulated on the electrode, which contradicts the conclusions drawn in Ref. 146. At the same time, the authors of these studies^{144–146} have agreed on the location of the oxidation process, *viz.*, that the reaction occurs on platinum areas unoccupied by the polymeric film. This conclusion was confirmed experimentally.^{144, 145} It was shown that if the polyaniline-free platinum areas are filled with CO adsorption products, then virtually no HCOOH oxidation occurs.

The promoting effect was explained^{144, 145} by assuming that polymers catalyse the oxidation of weakly bound adsorption products of formic acid just as it was shown in earlier studies

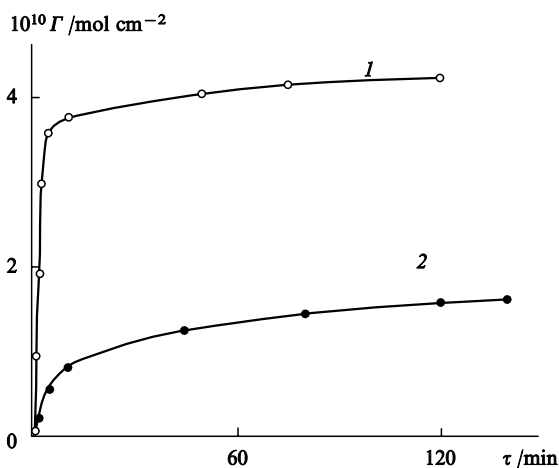


Figure 5. Kinetics of HCOOH adsorption at a potential of 0.2 V from a 10^{-2} M HCOOH + 0.5 M H₂SO₄ solution on (1) platinum electrode and (2) platinum electrode modified by a polyaniline film. Measurements were carried out by a radioactive tracer method.¹⁴⁴

(*e.g.*, see Ref. 153) dealing with oxidation of organic substances on platinum modified by thallium adatoms.

The electrooxidation of methanol on polyaniline-modified platinum was also shown to be accompanied by a substantial decrease in the amount of products of strongly adsorbed methanol on the electrode; however, in this case, the polymer inhibited the electrooxidation.¹⁵⁴ Thus, as would be expected, the nature of the polymer effect (promotion, inhibition) on the oxidation process depends on the nature of the organic substance to be oxidised.

Polyaniline films were shown¹⁴⁹ to catalyse the electrooxidation of hydroquinone in a wide potential range. This effect was also confirmed later.^{155–162} Figure 6 shows polarisation curves of electrooxidation of hydroquinone and reduction of benzoquinone on a film-free gold electrode and that covered with a polyaniline film. The half-wave potentials of these processes were shown to shift in the cathodic direction for the hydroquinone oxidation and in the anodic direction for the benzoquinone reduction. It was found¹⁶¹ that the exchange current of hydroquinone oxidation increased by two orders of magnitude on freshly prepared polyaniline films (supported on platinum). Most scientists associated the

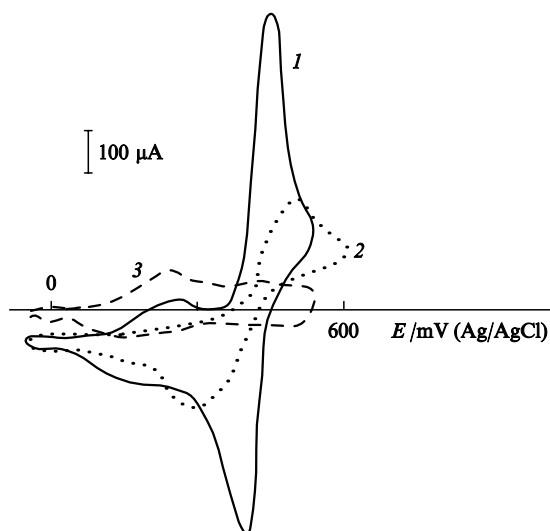


Figure 6. Cyclic voltammogram of (2) Au and (1, 3) Au–polyaniline system in (3) 0.5 M H₂SO₄ and (1, 2) *p*-benzoquinone solution (10^{-2} mol litre⁻¹) in 0.5 M H₂SO₄.¹⁵⁹ Potential scan rate is 50 mV s⁻¹.

catalytic effect with the adsorption interaction between the polyaniline film and these compounds.^{159–161} Some convincing evidence (based on experimental results) for the specific adsorption of hydroquinone on the emeraldine form of polyaniline has been obtained.¹⁶² This case allows us to speak of ‘classical’ electrocatalysis directly by the conducting polymer. The effect of the polyaniline film morphology on the rate of hydroquinone oxidation was assumed¹⁶² to be associated with the changes in the film surface areas involved in the adsorption and oxidation of the substrate. Alkyl derivatives of polyaniline behaved like polyaniline in the benzoquinone–hydroquinone reaction.^{163–166} The differences in the kinetics of the hydroquinone–benzoquinone reaction on polyaniline and poly(*ortho*-phenylenediamine) films were explained¹⁵⁹ by the different distribution of equilibrium potentials at the polyaniline/solution interfaces.

The processes discussed above occurred in the potential range where the film was the electron conductor. In earlier studies (*e.g.*, see Ref. 167), it was assumed that in the ‘nonconduction’ potential range, electrode reactions should be entirely inhibited. However, this assumption turned out to be incorrect. Thus the reactions of hydrogen oxidation and oxygen reduction were shown to proceed (even if at much slower rates) in the potential region of ‘nonconducting’ films as well.¹⁶⁸ These processes were found to be strongly affected by the support nature. On nonconducting polyaniline films, the processes of reduction of oxygen¹⁶⁹ and naphthoquinonesulfonate¹⁶³ were observed to occur. To explain the occurrence of these processes, their rate-determining steps were assumed to be located at the metal/solution (due to porous structures of the films) and/or metal/polymer (for the mediator catalysis) interfaces¹⁶⁸ and the oxidant was supposed to inject positive charges into the polymeric matrix.^{6,163} Moreover, it should be borne in mind that sufficiently thin films (≤ 500 nm) across which the potential drop is small were used most often,¹⁷⁰ and that the relaxation from the conducting state to the nonconducting one is sufficiently slow.¹⁷¹

As is seen from the above examples, to date there is no agreement on the reasons for the appearance of catalytic effects in the systems containing electron-conducting films.^{6,172} Some authors favoured the mediator mechanism, the other (without any strong evidence) assumed the potential change in such systems to be associated only with the potential drop across the polymer/electrolyte interface. An analysis of thermodynamic equilibria in the metal–polymer–electrolyte system at different interfaces has shown¹⁷² that in the general case the potential drops across all the interfaces involved should be taken into account. For a more accurate elucidation of the role the polymer plays, additional information is required, particularly, on the exact location of the reaction and its rate-determining step. However, it is very difficult to obtain this information for electrodes with polymeric coatings.

Considerable progress has been achieved in modifying electron-conducting polymers by different redox groups and catalytic centres such as porphyrins, phthalocyanines, transition-metal complexes, biological molecules, *etc.*^{6,169,173–182} In most of such systems, the mechanism of mediator catalysis was realised. Thus it was found¹⁵² that electroreduction of oxygen on glassy carbon can be accelerated by covering it with a polyaniline film containing anions of heteropolyacids (SiW₁₂O₄₀)⁴⁻ and (PW₁₂O₄₀)³⁻. The possibility of using polythiophene and polypyrrole films modified by heteropolyacid anions for catalysing this process was also considered.^{183–187} On a polyaniline + cobalt tetra-2,3-pyridineporphyrin (CoTPP) composite film, the oxygen reduction potential shifted to more positive values as compared with its reduction potential on the electrosorbed CoTPP.¹⁶⁹ It is of note that even an increase in the currents was observed in the transition of polyaniline into the reduced state.

It was shown^{186,187} that modification of a glassy-carbon electrode surface by an [Os(bipy)(PVP)Cl]Cl coating [PVP is poly(vinylpyridine)] allowed the limiting diffusion currents of nitrite electroreduction to be reached. This makes this system promising for the development of a sensor for nitrite anions.

IV. Electrodes coated with polymeric films with incorporated metal-catalyst particles

From the foregoing it follows that modifying polymeric films play the role of charge carriers in electrocatalysis, and their catalytic activities manifest themselves in the processes free from destruction of substrate molecules. Platinum-group metals are the best electrocatalysts (catalysts) for the processes which involve cleavage of interatomic bonds (*e.g.*, oxidation of hydrogen, organic substances, *etc.*). It is possible to prepare highly dispersed deposits of these metals by incorporating them into polymeric matrices.

A specific feature of the systems thus obtained is that the polymeric matrix determines the conditions for the metal phase development. The properties of the matrix (film) itself can be changed by choosing a particular polymer and varying the conditions of the surface film formation.

Keen attention was drawn to the processes of deposition of platinum-group metals in ion-exchange polymeric matrices,^{188–201} because the latter are stable in different media and can be used as the solid polymeric electrolytes in electrochemical reactors. It was proposed in many studies to prepare deposits of platinum-group metals using electron-conducting polymers where the formation conditions and the behaviour of metal particles can differ substantially from those in ion-exchange films.^{54, 154, 202–222} This can result in a three-dimensional structure representing a conducting matrix with sufficiently uniformly distributed catalyst microparticles. The porous structure of such a matrix can make the metal-catalyst accessible for reactants and provide the exit of the products to solution.

For these systems, the practically important effect of the increase in the electrocatalytic activity calculated either per the geometrical surface of the electrode or per a mass unit of the noble metal could be achieved mainly due to an increase in the surface area of the deposit. However, of prime scientific interest is to increase the activity per the surface unit of the metal catalyst as compared with the compact metal. This can be associated with the structural peculiarities of microdeposits (*e.g.*, the size effect¹), the interaction of metal particles with the polymeric matrix and the changes in the reactant activities in the porous space of the matrix.

In theoretical studies, great attention was drawn to the electronic structure of microdeposits. Due to the high work function values for metals of the platinum group²²³ as compared with other materials, it could be expected that the electrons would be partially transferred from the matrix to the microdeposit and, as a consequence, the mean electron density in the deposit would increase. However, such an effect was detectable only where the sizes of microdeposit particles were commensurable with the thickness of the electrical double layer. According to the estimates,^{224, 225} even in the absence of their interaction with the matrix, the Fermi energy in small particles (the size $d \leq 3$ nm) should substantially differ from that in the compact metal.

1. Dispersion of particles of platinum-group metals in polymeric matrices

Different chemical procedures were developed for introducing metal particles into polymeric matrices.^{194, 226–231} For example, deposits of Pt, Pt + Ru, and Pt + Sn were obtained by reducing the corresponding salt solutions by reactants diffused from the other side of a membrane.^{226, 227} Membranes were often impregnated with solutions of platinum-group metal salts and then immersed into the reducing solution.^{228, 229}

However, those methods which use the electrodeposition of metals are most convenient (especially, for films) for incorporating metal particles into polymeric matrices.^{188–193, 195–222} By varying the potential, current and deposition time, one can control the accumulation rate and the amount of the metal deposited. Such methods can be divided into two groups, *viz.*, with single- and two-step deposition. In the former case, the film is first formed (by a chemical or electrochemical method), and then the metal is electrodeposited in it (often on it). In the latter method, the film is

formed electrochemically from a solution containing both a monomer capable of electropolymerisation and a salt of a metal-catalyst. By varying the electrodeposition conditions (supporting electrolyte concentration, components concentrations, modes of current and potential variations, *etc.*) it is possible to prepare films with diverse morphologies and various contents and depth-distributions of metal particles.

Two-step deposition was used for both ion-exchange and electron-conducting films. In the films devoid of intrinsic electron conduction [*e.g.*, Nafion and poly(vinylpyridine)], the formation of metal particles begins from the support, and their further growth occurs along the pores 'from one particle to another' with retention of contacts between the particles (Fig. 7). Gradually, the electrodeposition process reaches the film surface (this stage is not shown in the figure), which can occur before the whole porous space is filled, as a result of the difference in the rates of formation and growth of films in different pores. Later, the metal layers are deposited on the film surface, and this process is only indirectly controlled by the film. Evidently, the specific behaviour of metal particles incorporated into the polymeric matrix should be judged based on the analysis of the behaviour of systems in which the metal deposit, at least, its greatest part, has not yet 'escaped' to the film surface. According to the literature data, as might be expected, the mechanism of deposit growth and the sizes of metal particles formed strongly depend on the modes of the support polarisation.

During the formation of metal particles in electron-conducting polymers, the metal-catalyst can be deposited directly onto the polymer. Though it was suggested²²⁰ that during the deposition of metals on an electron-conducting polymer in the potential range where the polymer is dedoped and assumed^{9, 13} to become 'non-conducting', the mechanism of metal deposition in the films remains virtually the same as for ion-exchange polymers (see Fig. 7a). However, it was found^{211, 222} that the deposition of a metal directly on the polymer can also occur in the potential range of its 'nonconducting' state. Using the AFM method for the

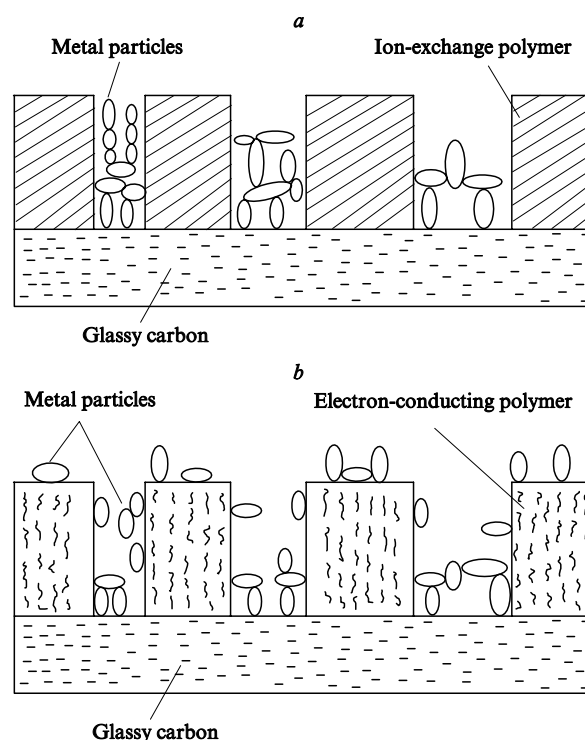


Figure 7. A scheme of accumulation of metal particles in a polymeric matrix formed on a glassy carbon support for (a) ion-exchange and (b) electron-conducting polymers.

palladium deposition in sufficiently thick polymeric matrices where the metal volume was an order of magnitude lower than that of the porous space (estimated from the results of Ref. 232), palladium particles were observed on the film surface at the deposition potential of 0.14 V, *i.e.*, in the range where polyaniline is nonconducting. The appearance of metal particles was explained by the 'residual' conductivity which is retained after the polymer is dedoped²³³ and ensures sufficiently small potential drops across thin (~ 500 nm) polymeric films. The results of layer-by-layer Auger-spectroscopic studies²¹¹ of a polyaniline film[†] with palladium particles have shown that deposition of palladium preferentially occurs in the external regions of the film. Figure 7b shows the model for deposition of metal particles into an electron-conducting film. In this case, the contact between metal particles is not necessary: the most pronounced manifestation of the catalytic activity can be expected at the potentials of high conductivity of the polymer (especially, for thick films).

A single-step method of preparation of composite M – electron-conducting polymer films was used less frequently. Potential cycling in the range from sufficiently high positive values at which the monomer is preferentially polymerised, to the potentials close to that of the reversible hydrogen electrode, at which the metal is preferentially deposited, made it possible to provide a largely uniform distribution of metal-catalyst particles throughout the film.^{211, 222} Moreover, the formation of substantial amounts of metal on the film was ruled out. However, the single-step synthesis by periodic application of sufficiently high potential values to the electrode led to noticeable degradation of the polymer even during the formation of the electrocatalytic system,²²⁰ and the degradation became more pronounced in the presence of particles of platinum-group metals.²²²

The use of polymeric matrices (especially those of ion-exchange polymers) made it possible to obtain ultradispersed deposits of platinum-group metals (with the grain diameter of 3–5 nm) with larger specific surface areas. As a rule, the most dispersed deposits were formed at small metal-to-polymer mass ratios, *i.e.*, where the deposit fraction remained within the polymeric matrix is substantial.^{195, 200} For large amounts of deposited metals and/or small film thicknesses, the specific surfaces substantially decreased and, as would be expected, often approached those of individual metal deposits.^{200, 201, 203, 219, 233–235}

At attempt was made to deposit platinum in preformed polyaniline films from aqueous H_2PtCl_6 solutions.¹⁵⁴ The form in which platinum is accumulated in the film was concluded to be strongly dependent on the lower limit of the potential cycling interval, *viz.*, in the 0.1–0.7 V range, it was accumulated as two- and four-charged ions, whereas in the 0–0.7 V interval, platinum metal particles prevailed.

A comparison of the data shown in Table 1 allows one to assess the possibilities of increasing the catalyst surface area by using polymeric matrices. The table shows the maximum values of specific surface areas for several metals of the platinum group electrodeposited into Nafion and poly(vinylpyridine) (the results^{196–199, 220} were averaged) and similar values for electrodeposits of these metals on platinum. The greatest effect was observed for palladium. It is important that the polymeric matrix also favoured the stabilisation of particles. This made it possible, for example, to observe the size effect, *viz.*, a sharp decrease in the amount of absorbed hydrogen, for palladium particles of sizes < 7 nm [poly(vinylpyridine) matrix].¹⁹⁸

The attempts to achieve such a great development of the metal-catalyst surface area for electron-conducting polymeric films have failed.^{219, 120, 222} This indirectly confirmed that the metal deposit can grow on the film surface even for small metal-to-polymer mass ratios.

[†] The film was deposited by the two-step method, and palladium was deposited in the potential range of 'nonconducting' polyaniline.

Table 1. Maximum specific real surface areas ($\text{m}^2 \text{g}^{-1}$) for deposits obtained for metal–polymer–glassy carbon systems (S_1) and metal electrodeposits on platinum (S_2).^{196–199, 220}

Metal	Polymer	S_1	S_2
Pt	poly(vinylpyridine)	100	18–25
	Nafion	80	
Pd	poly(vinylpyridine)	100	10–15
	Nafion	90	
Rh	poly(vinylpyridine)	60	30–40

However, for palladium microdeposits in polyaniline, the specific surface areas of $35\text{--}45 \text{ m}^2 \text{g}^{-1}$ were reached (see Refs 220, 222).

2. Determination of the real surface area of metal-catalyst particles in polymeric matrices

The determination of the real surface area of metal-catalyst particles incorporated into polymeric matrices presented a serious problem for comparing correctly the specific electrocatalytic activities of deposits. Unfortunately, many studies of the electrocatalytic activity of metal-catalyst–polymeric matrix systems did not pay due attention to this problem and did not separate the contributions to the electrocatalytic activity into those caused by the surface development and by the changes in the intrinsic specific activity of the incorporated particles.^{54, 154, 212–218}

Determination of specific surface areas of metal deposits in polymeric films S ($\text{m}^2 \text{g}^{-1}$) also presented independent interest for estimating the degree of dispersion of the metal-catalyst. The use of a certain model allows the average sizes of metal particles to be calculated roughly from the S values. The modern physical methods such as the scanning tunnelling microscopy and atomic force spectroscopy made it possible not only to assess more accurately the average size of particles but also to determine their size distribution.²³⁶ However, the use of these methods for characterising the particles located inside the polymeric matrix is associated with considerable experimental difficulties.

The method for estimating the real surface areas from the hydrogen adsorption, which is commonly accepted for platinum group metals,^{237, 238} often gave insufficiently correct results and in many cases could not be used at all. Thus the 'hydrogen regions' of metal particles in polymeric matrices can be deformed due to the small sizes of these particles, their adsorption interaction with the polymeric matrix and the changes in the pseudo-capacity of the support.^{197, 239, 240} In systems with electron-conducting polymeric matrices such as polyaniline and polypyrrole, additional difficulties arose due to the severe overlapping of the potential ranges of hydrogen adsorption–desorption and those of the intrinsic redox activity of the polymer.^{154, 219, 220} The method for determination of the surface area by hydrogen adsorption cannot be used in principle for palladium particles, because the hydrogen absorption in the Pd(H) α -phase substantially exceeds the hydrogen adsorption.^{241, 242} Many of the difficulties noted above could be avoided if the real surface area was estimated by the underpotential deposition (upd) of copper.^{196, 220, 241–243} In the Pt–poly(vinylpyridine) system (a glassy carbon support), a 10% deviation between the specific surface areas of platinum determined from hydrogen adsorption and upd of copper appeared only for $S > 80 \text{ m}^2 \text{g}^{-1}$. The use of copper adatoms for determination of the real surface area of palladium particles deposited into poly(vinylpyridine) and Nafion films proved to be effective.^{198, 199} At present, this is the most correct electrochemical method for determination of real surface areas of palladium particles incorporated into polymeric matrices. Calculations of real surface areas of palladium electrodes by the oxygen adsorption^{241, 243} proved to be useless, because the polarisation of electrodes to high anodic potentials often caused irreversible changes in the M–polymer–support systems.^{83, 85, 98, 115, 196}

It was found²¹⁹ that due to many similar charges being consumed in the removal of hydrogen adatoms from incorporated platinum particles and in the polyaniline film oxidation, the real surface areas estimated in parallel experiments from the hydrogen adsorption differed twofold even for the platinum-to-polymer mass ratio of ~ 70 . According to experimental results,²²⁰ well reproducible real surface areas estimated from upd of copper could be obtained for platinum and palladium particles incorporated into polyaniline when the metal-to-polymer mass ratio was ~ 0.2 .

The formation of monolayer coverages by adatoms (Cu, Ag, *etc.*) with the subsequent removal of their ions from the solution bulk, allowed the surface areas of metal-catalysts to be determined by suppressing the hydrogen adsorption.

To determine the surface area of platinum particles in a polyaniline matrix, it was proposed¹⁷⁷ to use the CO adsorption. However, depending on the structures formed by adsorbed CO (bridge or linear), the real surface areas estimated can differ twofold. Moreover, carbon monoxide can be sorbed by the polyaniline film itself.²²¹

The possibilities of using physical methods for the estimation of the sizes of particles incorporated into polymeric matrices could be remarkably increased, if the film could be separated from the support. Thus composite films of polypyrrole with palladium particles were deposited on plates of In–Ti oxides and then separated from them and analysed using a transmission electron microscope.²⁴⁴ The average size of palladium particles was found to be ~ 5 nm.

3. Electrode processes on polymeric films with incorporated particles of metal-catalysts

The results on the electrode processes on polymeric films with incorporated metal-catalyst particles are discrepant and unequal with respect to their quality and scientific importance.^{245–265} This often means not only the quantitative discrepancies, but also concerns qualitative deviations in experimentally observed effects. This was caused by a number of factors, the main of which are as follows:

- (1) the difference in the procedures used for synthesising the metal-catalyst–polymeric matrix systems;
- (2) the wide scatter in the metal-to-polymer mass ratios; this can cause substantial differences in the behaviour of electrodes with essentially similar metal-catalysts and polymers (see Section IV.1);
- (3) different conditions of measuring polarisation curves;[‡]
- (4) uncertainty associated with the steady-state criteria;
- (5) the low ‘sample-to-sample’ reproducibility of the electrochemical reaction rates (like electrooxidation of organic substances) even for individual electrodes of platinum-group metals;[§]
- (6) in most studies, the specific currents were expressed per the geometrical surface area of the electrode, which dramatically reduced the fundamental importance of the results (see Section IV.2).

The difficulties mentioned above were caused by the complicated nature of both the electrode systems themselves and the electrocatalytic processes on them, as well as by different factors which could promote or inhibit the electrode reactions. Hence, the attempts to explain the results obtained for the modified electrodes under consideration have yet involved only phenomenological

interpretations. In connection with the aforesaid, when choosing the data for the discussion, we focused attention on the results of those studies in which the measurements were carried out under steady-state conditions on electrodes with small metal-to-polymer mass ratios and which provided the estimates of the metal-phase surface area. The literature data on the methanol and formic acid electrooxidation and oxygen electroreduction in acidic solutions well illustrate the variety of experimental results on the electrocatalysis by particles of platinum-group metals deposited in/on polymeric coatings (Table 2).

Most of the studies in which the promotion of the methanol electrooxidation was detected, measured non-steady-state currents calculated per unit of the geometrical surface area (with several exceptions^{196, 200, 201, 213, 219, 222, 247}), *i.e.*, considered the gross effect. (Sometimes, the oxidation rate increased only two- to three-fold, *e.g.*, in Refs 219 and 247.)

When the effect of Nafion and poly(vinylpyridine) matrices on the behaviour of platinum particles was studied for extremely small amounts of the metal deposited (no more than $21 \mu\text{g cm}^{-2}$), it was found^{196, 200} that the specific rates of CH_3OH electrooxidation (under steady-state conditions) decreased as compared with the oxidation rate on platinised platinum (Pt/Pt). A similar effect of the Nafion matrix for the platinum mass $< 60 \mu\text{g cm}^{-2}$ was mentioned.²⁰¹ In the Pt–poly(vinylpyridine)–glassy carbon system, with an increase in the metal-phase dispersion, the rate of CH_3OH electrooxidation decreased.^{196, 200}

At the same time, for platinum deposits incorporated into Nafion films with the platinum mass $< 60 \mu\text{g cm}^{-2}$, higher steady-state specific currents of CH_3OH electrooxidation as compared with the currents on Pt/Pt were found.²⁰⁰ The increase was explained by the changes in the binding energy of the products of CH_3OH adsorption with the surface due to the changes in the deposit structure. Inasmuch as small-mass deposits are much more dispersed as compared with large-mass ones, one can speak of the qualitative agreement between different estimates^{196, 200, 201} of the effect of the degree of platinum dispersion on the methanol electrooxidation rate.

For the electrooxidation of formic acid on platinum particles incorporated into poly(vinylpyridine) and Nafion, it was found that the specific rates increased with an increase in the degree of metal-phase dispersion.^{196, 200} Moreover, the activity of highly dispersed platinum deposits ($\geq 30 \text{ m}^2 \text{ g}^{-1}$) was higher as compared with electrodeposits of platinum on platinum. A similar effect was greater for the Pt–Nafion–glassy carbon system (Fig. 8).¹⁹⁹

The results discussed above show that the changes in the activity of metal particles incorporated into polymeric matrices largely depended on the nature of the substrate. Thus the effects of the degree of dispersion were found to be opposite for the

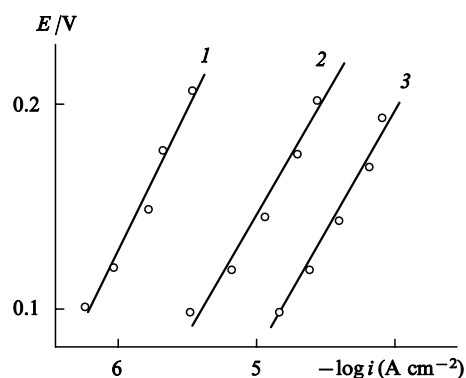


Figure 8. Stationary polarisation curves for electrooxidation of formic acid in the Pd/Pt (1), Pd–Nafion–glassy carbon (2) and Pd–polyaniline–glassy carbon (3) systems in a 0.5 M HCOOH + 0.5 M H_2SO_4 solution.^{199, 222}

‡ Unfortunately, the authors of the overwhelming majority of studies used the potentiodynamic method for recording relatively fast polarisation curves. As a rule, this involved measuring non-steady-state currents, the interpretation of which was especially difficult due to the uncertainty in the surface coverages by original particles, their products, solution ions, *etc.*

§ Naturally, as one passes to more complicated M–polymeric matrix systems, the reproducibility of the results is reduced. Hence, the comparative estimates of the activity based only on the experimentally observed two- to three-fold change in the currents should be considered with caution.

Table 2. Results on the electrooxidation of methanol and formic acid and electroreduction of oxygen in the M – polymer – support systems.

M – polymer – support system ^a	Film thickness / μm	M content / $\mu\text{g cm}^{-2}$	Substrate	Polarisation curves	Catalytic effect ^b	Ref.
Pt – polyaniline – glassy carbon	3–4	2–51	CH ₃ OH	non-steady-state	+ (geometrical)	202
Pt – polypyrrole – platinum	—	—	O ₂	steady-state	+ (geometrical)	129
Pt – polypyrrole – glassy carbon	—	—	O ₂	non-steady-state		129
Pt – polypyrrole – gold	—	—	O ₂	"	+ (geometrical)	129
Pt – Nafion/polyaniline – glassy carbon ^c	1.4–9.3	11–31	O ₂	steady-state, non-steady-state	— (geometrical)	126
Pt – polyaniline – platinum	—	—	HCOOH	the same	+	213
Pt – Nafion – glassy carbon	0.5	4–55	CH ₃ OH	"	+ (geometrical)	265
Pt – polyaniline – glassy carbon	—	25–750	CH ₃ OH	steady-state	+ (real)	219
(Pt + Pb) – polyaniline – glassy carbon	—	—	CH ₃ OH	"	+ (real)	219
Pt – polyaniline – platinum	—	—	HCOOH	non-steady-state	+ (geometrical)	252
Pt – polypyrrole – platinum	≤ 7	—	HCOOH	"	+ (geometrical)	252
Pt – polypyrrole – glassy carbon	—	45–131	CH ₃ OH	non-steady-state, steady-state	+ (geometrical)	255
Pt – polypyrrole – gold	—	57	CH ₃ OH	the same	+ (geometrical)	264
Pt – Nafion – glassy carbon	5	2–1000	CH ₃ OH	steady-state, non-steady-state	+ (real)	201
Pt – polyaniline – glassy carbon	0.3	—	CH ₃ OH	the same	+ (geometrical)	154
	0.3	—	HCOOH		+ (geometrical)	
Pt – polyaniline – gold	—	—	CH ₃ OH	"	+ (geometrical)	54
Pt – polypyrrole – SnO ₂ /glassy carbon ^c	0.08–0.16	13.1	O ₂	"	+ (geometrical)	263
Pt – Nafion – glassy carbon	1.0	4–21	CH ₃ OH	steady-state	— (real)	200
	1.0	4–21	HCOOH	"	+ (real)	200
Pt – poly(vinylpyridine) – glassy carbon	1.0	5–20	CH ₃ OH	"	— (real)	200
			HCOOH		+ (real)	
Pt – polypyrrole – glassy carbon ^d	0.5–10	200–1000	CH ₃ OH	non-steady-state	+ (geometrical)	246
Pt – poly(vinylpyridine) – glassy carbon	1.0	5–120	CH ₃ OH	steady-state	— (real)	196
	1.0	5–120	HCOOH	"	+ (real)	196
Pd – Nafion – glassy carbon	4–6	1.6–6.5	HCOOH	"	+ (real)	199
Pt – polyaniline – glassy carbon ^e	0.25–0.3	62–76	CH ₃ OH	"	+ (real)	222
	0.25–0.3	62–76	CO		+ (real)	
	0.25–0.3	62–76	HCOOH		+ (real)	
Pd – polyaniline – glassy carbon ^e	0.25–0.3	5–30	HCOOH	"	+ (real)	222
Pd – polyaniline – glassy carbon	0.25–1.5	8–30	HCOOH	"	+ (real)	170
Pt – polypyrrole – (Pt, Ni)	1.0	100	CH ₃ OH	non-steady-state	+ (geometrical)	247

^a Electrodeposition was used for incorporating metal into polymers unless otherwise specified. ^b Signs 'plus' and 'minus' designate the presence or absence (as assessed by the authors of the cited paper) of the catalytic effect; in the parenthesis, the surface area type (geometrical or real) used for calculating the currents is shown. ^c Chemical deposition was also used. ^d Three methods were used. ^e One-step method.

methanol and formic acid electrooxidation processes. A similar phenomenon was also mentioned for other catalytic systems, viz., not only for systems containing Pt particles, but also for those with Rh, Pd and Ir (see references in Ref. 240). This can be explained by assuming that particles involved in methanol electrooxidation occupy the greater number of surface sites than the sites required for the adsorption of HCOOH or CH₃OH.²⁴⁰

On the whole, the specific steady-state currents of methanol electrooxidation on platinum particles deposited in/on polyaniline films were found to be higher than the currents of its oxidation on Pt/Pt particles.^{219, 222} However, a substantial catalytic effect was observed²¹⁹ only for the platinum mass $> 60 \mu\text{g cm}^{-2}$. Inasmuch as only very thin films were studied (35–50 nm), it can be assumed that the effect was caused by the peculiarities of the structures of

platinum deposits formed on the surface of a polyaniline film (see Section IV.1).

The higher electrocatalytic activity of platinum particles in a polyaniline matrix as compared with Pt/Pt particles was also found²²² for the electrooxidation of formic acid and carbon monoxide. For CO, the effect was explained by the growth of its concentration in the polymeric film. The fact that CO is sorbed by the film was confirmed by a special study.²²¹ For platinum dispersed in polyaniline, the effect of promotion of formic acid electrooxidation was apparently of the same nature as for the aforementioned (see Section III.2) increase in its electrooxidation rate on platinum electrodes observed upon covering them with polyaniline films.

The greatest increase in the specific rates of formic acid electrooxidation was found for palladium particles incorporated into polyaniline (see Fig. 8). Moreover, the steady-state currents increased more than by an order of magnitude when both single-²²² and two-step¹⁷⁰ methods were used for synthesising Pd–polyaniline–glassy carbon systems. It is remarkable that the slope of polarisation curves remained virtually unchanged, although the process occurred in the potential range of polyaniline ‘nonconduction’. This suggests, first, that the mechanism of HCOOH electrooxidation of palladium remains unchanged²⁴⁸ and, second, that the electrode reaction rate can remain virtually unaffected by the ohmic potential drops in sufficiently thin films of electron-conducting polymers in the potential ranges of their ‘nonconduction’ (see also Section III.2).

According to the literature data, electrodes modified by composite Pt–polyaniline coatings can also be used for the oxidation of propan-2-ol,²⁴⁹ ethylene glycol,^{178,250} and D-glucose²⁵¹ (the latter can also be oxidised on a Pr–polypyrrole coating²¹⁸) at moderate anodic potentials. However, the authors of these studies have used the potentiodynamic method for measuring voltammograms and have not estimated the real surface area of the metal phase. Hence, even if certain ‘electrocatalytic effects’ were found in these studies, this is more likely to be attributed to the surface development of the metal-catalyst. A minor increase in the specific steady-state currents was found for ethanol electrooxidation on platinum particles incorporated into a polyaniline matrix by the chemical deposition procedure.²²⁹

Most authors associated the promoting effect of polymeric matrices on the electrooxidation of simple organic substances at moderate potentials (before the onset of oxygen adsorption) either with the deceleration of the appearance on the surface of metal-catalyst of strongly chemisorbed species, which are the ‘poison’ for the current-controlling reaction, or/and with an increase in the amount of weakly bound species.²⁴⁵ The ‘parallel mechanism’ of electrooxidation of organic compounds, which was first proposed in Refs 253, 254 for the reaction of methanol electrooxidation have gained substantial recognition.

Inasmuch as, as a rule, the sizes of metal-catalyst particles in polymeric matrices exceed 5 nm, the ‘pure’ size effect can hardly be considered. It is most probable that the catalytic effect is caused by the changes in the structure and/or the composition of the surface. Moreover, the changes in the latter can be caused not only by the adsorption of polymeric molecules and their fragments but also by the adsorbed impurities which could get into the metal phase from the deposition solution.^{197,222} The surface composition was shown to strongly affect the formation of adsorbed OH groups, which play an important role in electrooxidation of organic compounds.²⁴⁵

Only few interpretations of the results took into account that the activities of water and substrate molecules in the pores of the M–polymer–support system can differ from those in the solution bulk.^{194,222} However, the difference in these characteristics is quite probable, because, according to experimental results, *e.g.*, for Nafion¹⁹⁴ and polyaniline,²³² the polymers have channels with the mean size of ~ 1 nm, *i.e.*, approaching the thickness of the electrical double layer. Evidently, the effect of the triple metal/polymer/solution interface on the kinetics of electrocatalytic processes should also be taken into account.

A new in principle interpretation of the promotion of formic acid electrooxidation in the Pt–polyaniline–glassy carbon system was given for the case where the incorporation of platinum into the film was accomplished by the potential cycling in the 0.1–0.7 V range.¹⁵⁴ It was assumed¹⁵⁴ that under these conditions platinum is preferentially accumulated as complex ions (Pt^{2+} and Pt^{4+}) which catalyse the process. The effect was unsteady and decreased in time very quickly, because the complex ions were removed from the film being exchanged for solution ions. Methanol was not electrooxidised on such platinum complexes which confirms again the substantial differences between the electrooxidation mechanisms of methanol and formic acid.

The electrocatalytic activity of M–polymeric matrix systems in electrooxidation of organic compounds could be enhanced (as in the case of individual metal-catalysts^{240,245}) by the deposition of adatoms of foreign metals (*e.g.*, see Refs 251, 256, 257).

The high currents of hydrogen evolution on composite electrodes Pt–polymer [poly(vinylpyridine), Nafion, polyaniline]–glassy carbon and Rh–poly(vinylpyridine)–glassy carbon could be obtained for very small amounts of metal-catalysts ($\sim 20 \mu\text{g cm}^{-2}$).^{200,222,234} For small overvoltages, the parameters of polarisation curves with the currents calculated per 1 cm^2 of the geometrical surface area turned out to be similar to those for compact metal electrodes for which the hydrogen evolution was controlled by diffusion.^{258,259}

Some of these results^{200,222} correlated well with the results of studies^{189,202} which showed that the ‘hydrogen reaction exchange currents’ in the Pt–polyaniline and Pt–Nafion systems virtually coincide with those on smooth platinum. However, it is more likely that the currents measured in the latter studies^{189,202} were also of the diffusion nature rather than of the kinetic nature.

It was found^{200,222,234} that with an increase in the overvoltage, the hydrogen evolution current on Pt–polymer–glassy carbon electrodes became smaller than those observed on smooth platinum. This was explained by the earlier transition to the mixed-kinetics region. The potentials of the transition depended on the polymer structure; for the polymers under consideration they changed in the following order: polyaniline > poly(vinylpyridine) > Nafion. Indeed, this points to the decrease in the real exchange currents of the hydrogen reaction in composite electrodes due to the adsorption interaction between the metal-catalyst particles and the polymer and/or its destruction products.^{200,222} The results obtained for the Pt–Nafion–glassy carbon system, namely, that the diffusion currents estimated per 1 cm^2 of the geometrical surface area exceeded the specific currents on smooth platinum, are of special interest.²⁰⁰ This was explained by the more effective stirring of the near-electrode layer by hydrogen bubbles on the hydrophobised surface.

A number of studies^{126,260–263} have mentioned a possibility in principle of oxygen electroreduction on platinum particles incorporated into polyaniline or polypyrrole, but did not provide any correct comparison with the activity of platinum in this reaction. A lower activity was reported¹²⁶ for platinum deposited on a mixed polyaniline–Nafion film as compared with compact platinum. This was explained by the peculiarities of the formation of metal-catalyst deposits on such a film. Other scientists assumed the oxygen electroreduction rate to be largely controlled by the oxygen diffusion in the polymeric matrix. On the whole, the sufficiently fast degradation of electron-conducting polymers in the presence of oxygen and the catalysis of this process by incorporated particles of platinum-group metals were shown^{96,97,115,200,222} to have an adverse effect on the stability of properties of electrocatalytic systems involving these polymers and used in the oxygen electrode.

V. Conclusion

The results shown above suggest that the research carried out to date with polymer-modified electrodes is largely aimed at the elucidation of interrelations between the properties of support materials, polymeric coatings and incorporated metal-catalyst particles and/or certain functional groups. The fact that polymeric materials cannot provide the destructive chemisorption of substrate molecules gives the grounds to expect that the systems with polymeric matrices containing microparticles of catalytically active metals are more promising for a number of electrode reactions (particularly, those in fuel cells).

Inasmuch as the properties of polymeric matrices and microparticles are interrelated, the theoretical concepts describing the dependence of fine particles on the properties of phases in contact with them are of special importance. These studies are directly connected with the development of concepts on the structure of

different interfaces in the systems studied, including the three-phase interfaces, viz., support/polymer/solution and polymer/metal-catalyst/solution. Taking into account the polymer–solvent interaction and possible changes in the activities of solvent and substrate molecules in the polymeric matrix also appears to be very important.

The cited examples of polymer-containing electrode systems comprise only a small fraction of those available in the literature. However, at present, the development of theoretical concepts should be aimed at more comprehensive and deep experimental research to reveal more distinctly the catalytic effects for electrode reactions rather than at the increase in the number of systems studied. For this purpose, not only the complex use of modern experimental techniques (physical, physicochemical, analytical, etc.) but also the modernisation of experimental methods (see Section IV.3) are necessary.

This review only mentions certain examples of the use of polymer-covered electrodes in practice. Great interest to the new type of electrode systems was associated, first of all, with the great diversity of their practical applications, namely, the modernisation of present-day electrolyzers and electrochemical generators and development of their new types, synthesis of effective anti-corrosion coatings, the development of biosensors, the extension of the possibilities of electrocatalysis, the development of electrochromic devices, applications in micro- and nanoelectronics, etc.

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Thermal stability of nanomaterials

R A Andrievskii

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Abstract. The main processes and phenomena (grain growth, phase transformations, relaxation, diffusion, and so on) in nanomaterials subjected to heat treatment are considered. Experimental data and theoretical views on the thermal stability of nanomaterials are analysed and generalised. Attention is drawn to unsolved problems. The bibliography includes 152 references.

I. Introduction

At present, the concept of nanomaterials (NM), the development of which has been substantially stimulated by a number of publications,^{1–3} is widely known. This is indicated, for example, by the fact that representative all-Russian and international conferences and seminars dealing with nanomaterials have been regularly held for many years; this subject is also actively discussed at the Symposia of the American Materials Research Society (MRS) and the NATO Advanced Study Institute (NATO ASI); monographs, collections of works, and reviews have been published (see, for example, Refs 4–24).

The main emphasis in the above-mentioned studies^{1–3} was put on the crucial role of numerous interfaces existing in NM. The properties of solids containing such interfaces can be changed appreciably both by structural and electronic modification and by using new doping resources irrespective of the type of bond, size factors, etc. When the grain or crystallite size (L) is several nanometers, the proportion of interfaces in the total bulk of the material is at least $\sim 50\%$. This value was approximately estimated from the $3s/L$ ratio, where s is the width of the near-boundary region; for a reasonable value $s \approx 1$ nm, a proportion of 50% is attained when $L \approx 6$ nm. Gleiter and coworkers^{1–3} proposed a method for producing nanomaterials, which included preparation of ultradisperse powders by vaporisation–condensation and subsequent *in situ* compaction at high pressures. This procedure gave disk-like specimens 10–20 mm in diameter with a height of up to 0.1–0.5 mm. In order to obtain high-purity specimens, it is necessary to eliminate contact of the highly reactive powders with the environment (although these specimens

usually contain up to 10%–20% of residual porosity). However, initially, this fact was ignored and gave rise to some erroneous inferences (see, for example, Ref. 21).

This method for the preparation of NM was assimilated by researchers in many countries, first of all, in the USA (Siegel's group in the Argonne National laboratory²⁵ and research groups in some other universities); this triggered an avalanche-like accumulation of data concerning the properties of NM.

The first Russian session devoted to the research of properties of consolidated NM was held in 1984 and called the first All-Union Conference on the Physical Chemistry of Ultradisperse Systems.[†]

In an earlier study of NM published in 1983,²⁷ it was shown that compaction of ultradisperse nickel powders at high pressures and moderate temperatures furnishes NM with a crystallite size of about ~ 60 nm with a hardness exceeding that of usual polycrystalline nickel by a large factor. Unfortunately, the publications cited^{26,27} have passed almost unnoticed by both Russian and foreign specialists. Meanwhile, these studies²⁷ demonstrated one more time, independently of the results obtained by Gleiter and coworkers,^{1–3} the validity of the known Hall–Petch relationship, which relates strength (hardness) to the grain size ($H \sim L^{-1/2}$) in the nano-size range, and the expediency of extending this relationship to NM. At present, the greatest L value is taken to be ~ 100 nm.^{17,20,21}

In view of the relatively small dimensions of NM crystallites (and, correspondingly, the numerous interfaces they contain), it becomes clear why it is important to study the nanostructure evolution, which is accompanied by changes in the properties of NM, upon heat treatment or other types of treatment. Naturally, these items attract attention of researchers; various aspects of the problem of NM stability have been considered in a number of papers, reviews, and monographs (see, for example publications^{14,18,20–22,28–31}); however, generally, this item does not appear to be adequately studied.

In terms of the fields of application, one can distinguish the following main functional types of NM for which thermal stability is especially significant: tool materials and materials for high-temperature friction units; thermal and diffusion barrier components; high-temperature semiconductors, catalysts, and sensors; porous, emission and filter component parts; and refractory materials of various types. The knowledge of thermal stability patterns is also important for NM manufacture technology. In particular, when selecting the optimal conditions for superplas-

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[†] Proceedings of this conference were published only in 1987.²⁶

ticity and when developing the conditions for controlled crystallisation from the amorphous state and for plasma sputtering of nanostructured coatings and high-energy methods for consolidation of ultradisperse powders, specialists should take into account conditions for nanostructure maintenance. The information outlined above accounts for both the theoretical and practical interest in the problems of thermal stability of NM.

II. The key types, structure, and general characteristics of nanomaterials

The concept of NM introduced by Gleiter and coworkers,^{1–3} mainly in relation to metal-like materials, has now substantially expanded. Twenty years later, Gleiter²² considered a broader spectrum of NM, apart from the above-mentioned objects, namely, semiconductors, polymers, diamond-like and supramo-

lecular structures, and biomaterials. This can be supplemented by ceramics, catalysts, nanoporous materials, and a large number of nanocarbon and, generally, nanotubular structures; the scope of investigations of these materials is swiftly extending.

The NM listed above have been prepared by different methods and have different types of microstructure. Table 1 and Fig. 1 present data concerning compact and nonpolymeric NM.^{21,22} Classification according to the composition, distribution, and the shape of structural components implies three kinds of structural shapes (layer-shaped, rod-shaped, and equiaxed forms) and four sorts regarding the chemical composition and component distribution, namely, single-phase compositions, statistical multiphase compositions with either identical or non-identical interfaces (*i.e.*, the possibility of segregation is taken into account), and matrix compositions. The number of structural types can be greater due to mixed variants, the presence of porosity and so on. One should

Table 1. Key methods for the preparation of compact NM.

Preparation technique	Main types	Objects
Powder technology	Gleiter method (gas-phase deposition and compaction) electric-discharge sintering hot pressure treatment high static and dynamic pressures at ambient and high temperatures	elements, alloys, compounds
Severe plastic deformation	equal-channel angular pressing high-pressure torsion pressure treatment of multilayer composites phase cold hardening	metals and alloys
Controlled crystallisation from the amorphous state	normal and high pressures	amorphous materials
Film technology	chemical vapour deposition (CVD) physical vapour deposition (PVD) electrodeposition sol–gel processes	elements, alloys, compounds

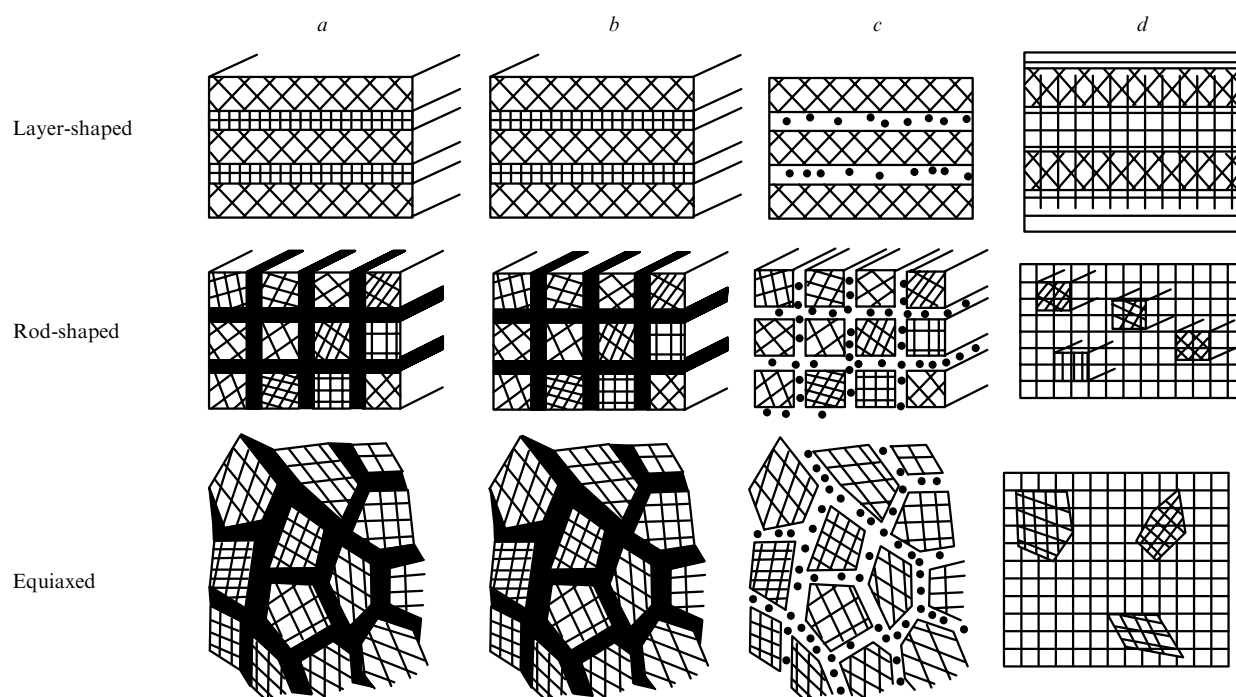


Figure 1. Sketch of single-phase (*a*) and multiphase NM with a statistical (*b*, *c*) and matrix (*d*) distribution of structural components.²² (*b*) identical interfaces; (*c*) non-identical interfaces.

also take into account the conditional character of the classification of production processes because the borders between particular technological expedients are often blurred. When comparing the thermal stability of different NM, one must bear in mind that the diversity of production techniques and types of macro- and microstructures has an influence on the NM behaviour during heating.

The most frequently encountered structural types are single-phase and multiphase matrix and statistical objects, rod-shaped and multilayer structures (so-called superlattices); the latter type is

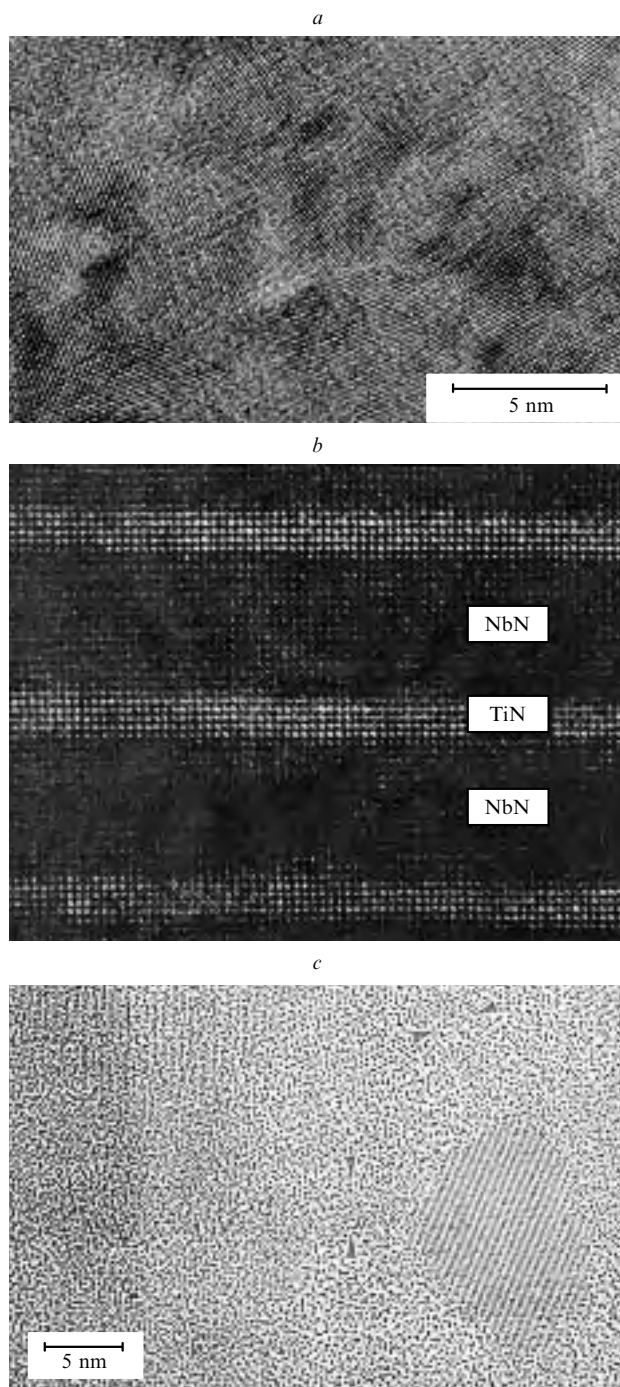


Figure 2. Photomicrographs of the NM structure: (a) Ti(N,B) film prepared by magnetron sputtering;³² (b) multilayer TiN/NbN film prepared by magnetron sputtering (the overall thickness of individual monolayers is 4.6 nm);³³ (c) 'Finemet' magnetic alloy prepared by crystallisation from the amorphous state followed by annealing at 500 °C ($t = 1$ h); the arrows mark the grain boundaries.³⁴

typical of films. Figure 2 shows examples of some typical structures. High-resolution transmission electron microscopy is especially effective for elucidating the NM structure.^{32–34} Attention is drawn by the difference between the structures and thicknesses of interfaces for NM prepared by different procedures (see, for example, Figs 2 a and 2 c). Various opinions have been expressed concerning the nature of interfaces in NM (see, for example, Ref. 21); however, it is clear that the diversity of production methods also leaves a mark on the nature of the interfaces. X-Ray diffraction methods, which allow one to estimate the anisotropy of grain size and to obtain information on structure distortion, are also widely used to study nanostructure (this has been done most comprehensively in investigating the effect of annealing on the rutile nanostructure³⁵).

It is evident that the vast majority of NM, except for supramolecular structures (which was first noticed in the review by Gleiter²²), are non-equilibrium in their nature. A system can move away from equilibrium for several reasons. As regards NM, the most important of these reasons is the abundance of interfaces (grain and phase boundaries and triple junctions), which gives rise to excess free surface energy. Figure 3 sketches a triple junction and Fig. 4 shows the dependences of the overall fraction of interfaces and the fractions of proper grain boundaries and triple junctions on the grain size.[‡]

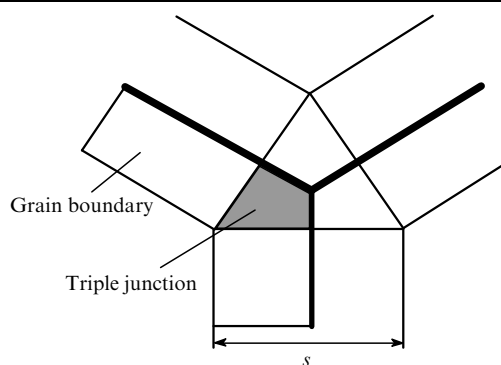


Figure 3. Triple junction formed by grains shaped like tetrahedral dodecahedra.

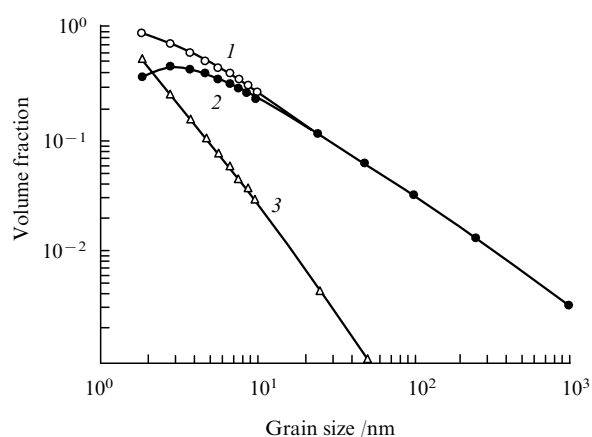


Figure 4. Effect of the grain size on the overall fraction of interfaces (1) and on the fractions of grain boundaries (2) and triple junctions (3) (boundary width 1 nm).³⁶

[‡] According to estimates,³⁶ the overall fraction of interfaces amounts to $V_1 = 1 - [(L-s)/L]^3 \sim 3s/L$, the fraction of proper grain boundaries is $V_2 = [3s(L-s)^2]/L^3$ and the fraction of triple junctions is, correspondingly, $V_3 = V_1 - V_2$.

As noted above, for grain sizes of less than 5–6 nm, these fractions are rather high and, hence, the excess free surface energy is also rather high; the fraction of boundary segregations also increases.

Note that the values of the interfacial and boundary surface energy can differ from those for usual coarse-crystalline materials; however, reliable experimental data are scarce (see, for example, Ref. 21). It is worth noting that the presence of free space in virtually non-porous NM has been noted in many publications. For example, this was found in densimetric measurements for nanocrystalline nickel³⁷ and gold³⁸ specimens (Table 2) and in a study of positron annihilation in palladium.³⁹ A possible constituent of the free space is the discontinuity of the grain boundaries.

The NM structure often contains non-equilibrium phases; therefore, phase equilibrium diagrams can markedly vary. Nanomaterials produced using film technology and high-energy treatment (static and dynamic high pressures, intensive plastic flow, *etc.*, see Table 1) occur inevitably under residual stress and contain crystal structure defects; this also influences their energy state.

Table 2. Density of nanocrystalline nickel³⁷ and gold³⁸ specimens (γ_t is the theoretical density).

Specimen	Preparation method	L /nm	γ_t /g cm ⁻³	γ /g cm ⁻³
Nickel	pulse electrodeposition	11 ± 1	8.897	8.34 ± 0.02
Gold	magnetron sputtering	18 ± 2	19.299	19.0 ± 0.5

Thus, heat treatment, exposure to force fields or radiation, or long-term operation of NM even at usual temperatures induce recrystallisation, segregation, homogenisation and relaxation processes; phase transitions; phase formation and destruction; amorphisation, sintering, and nanopore (nanocapillary) closing. For a long period, these processes have been the subjects of numerous studies related to material science and the physics and chemistry of solids. For example, the theoretical views on the stability of colloids and thin films have been surveyed in a monograph.⁴⁰ However, the mechanisms of many of these processes as applied to NM have not been adequately studied. Currently, it is still difficult to differentiate between them and to evaluate their role but, generally, almost all of the above phenomena have an appreciable effect on the properties and the service performance of NM. In the limiting case, degradation of NM is possible, although in many cases, an additional heat treatment of NM proves useful for stabilising their properties.

III. The main processes in nanomaterials during heat treatment

1. Grain growth
a. Experimental data

The experimental curves that illustrate the effect of temperature and duration of the annealing on grain growth in various types of NM are shown in Figs 5–12.^{41–53} The general regularities based on the data presented here and other data on grain growth in nanocrystalline specimens are outlined below.

1. The lognormal or normal grain size distributions remain virtually the same for the initial and annealed specimens. Numerous kinetic studies gave diverse results. For example, in the general case, a power law holds for grain growth (see Fig. 5) but it is often rather difficult to prefer either a relation like $L^2 \sim t$ or some other ($L^{1.3;4} \sim t$).⁴¹ Using experimental results (isothermal annealing) for NbAl₃ nanocrystals prepared by mechanical doping⁴⁷ and for Fe₃₃Zr₆₇ and (Fe,Co)₃₃Zr₆₇ alloys prepared by crystallisation from the amorphous state,⁴⁸ the relationship $L^3 \sim t$ was found.

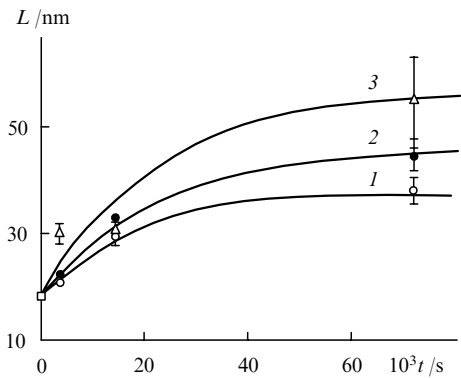


Figure 5. Kinetics of the grain growth in nanocrystalline copper prepared with sliding friction.⁴¹ T/K: (1) 575, (2) 625, (3) 675.

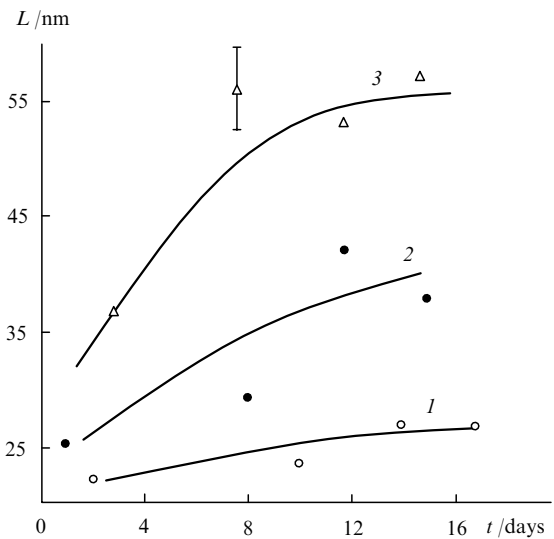


Figure 6. Kinetics of the grain growth in nanocrystalline copper prepared by compacting an ultradisperse powder in a vacuum.⁴² Porosity (%): (1) 7, (2) 4, (3) 3; T = 298 K.

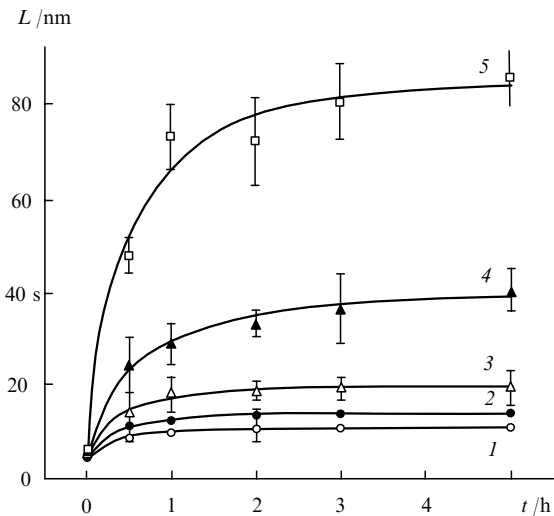


Figure 7. Kinetics of nanograin growth during annealing of RuAl powders prepared by mechanosynthesis.⁴³ T/K: (1) 873, (2) 973, (3) 1073, (4) 1173, (5) 1273.

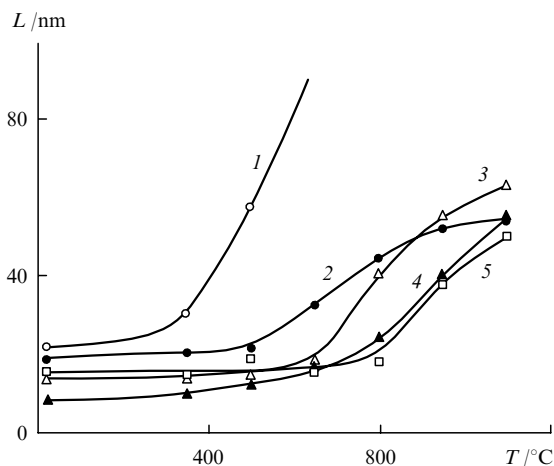


Figure 8. Effect of temperature ($t = 1$ h) on the nanograin growth in iron (1) and iron–aluminium alloy (2–5) powders prepared by mechano-synthesis with attritor milling under nitrogen (1–4) or argon (5) at low temperatures.⁴⁴

Aluminium content in the alloy (mass %): (2) 2.6; (3) 10; (4) 10 (milling for a longer period); (5) 10.

The exponential quantity n can depend not only on the object of investigation but also on the temperature range ($1/n = 0.05–0.5$).^{20,22} The experimental data obtained in kinetic measurements of the growth of nanograins during annealing of ruthenium monoaluminide powders were found to be in good correspondence with the following expression:

$$\frac{L^2(t) - L_{\max}^2}{L^2(0) - L_{\max}^2} = \exp\left(-\frac{2qt}{L_{\max}^2}\right), \quad (1)$$

where indices t and 0 refer to the current and initial time, $L_{\max}$ is the maximum grain size at the given annealing temperature dictated by factors restricting the grain growth (for example, boundary segregations) (see Fig. 7), and q is a kinetic constant.⁴³

In a study of the grain growth ($L_0 \sim 8$ nm) in iron powders treated in a high-energy attritor and annealed at $350–600$ °C in a dynamic vacuum ($\sim 10^{-3}$ Pa, annealing time from 5 min to 142 h), a dependence of the exponential quantity on temperature was found and the correspondence of the experimental kinetic data to both the dependence of the $\sim t^n$ type and relation of type (1) was established.²⁹

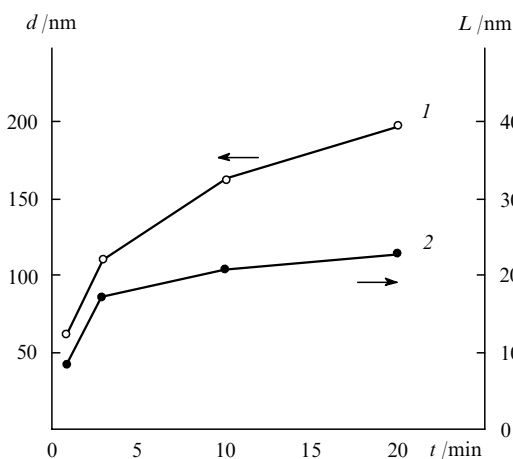


Figure 9. Effect of the duration of deposition from a $[\text{Cd}(\text{CH}_3\text{COO})_2 \cdot 2\text{H}_2\text{O} + \text{H}_2\text{NCSNH}_2 + (\text{HOCH}_2\text{CH}_2)_3\text{N} + \text{NH}_4\text{OH}]$ solution at 75 °C on the CdS film thickness (1) and crystallite size (2).⁴⁵

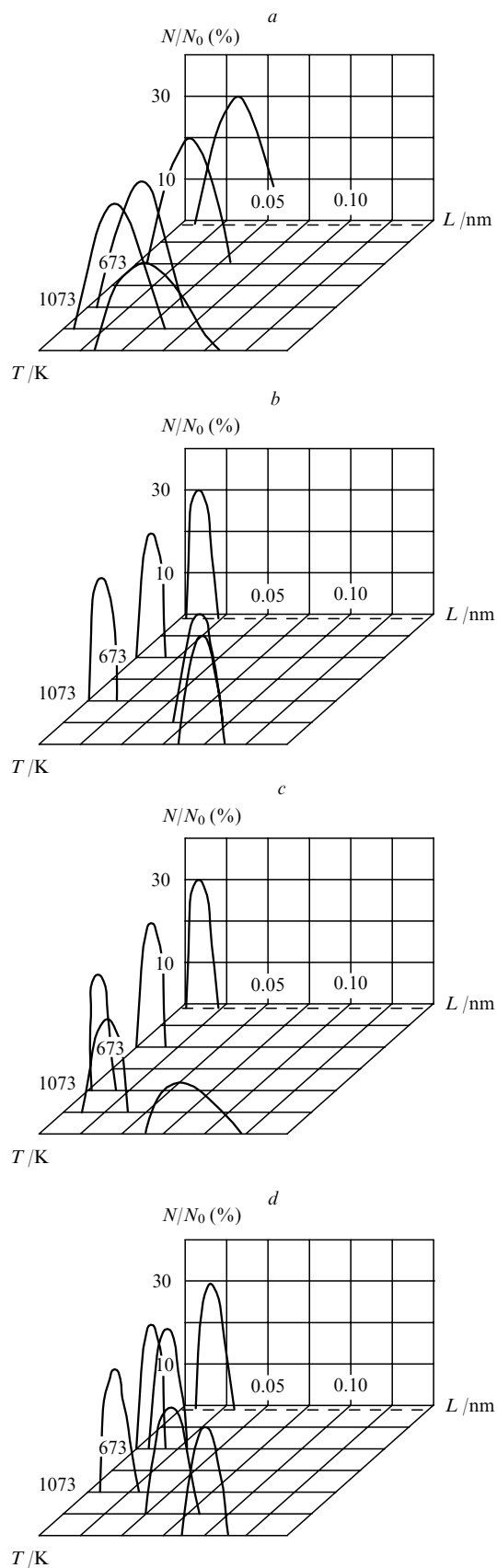


Figure 10. Statistical size distributions of crystallites in ZrN films (a, b), a ZrN + TiN 20-layer film (c) and a doped (Zr,Ti)N film (d) annealed at different temperatures.⁴⁶ Film thickness μm : (a, c) 2, (b) 0.1, (d) 1.

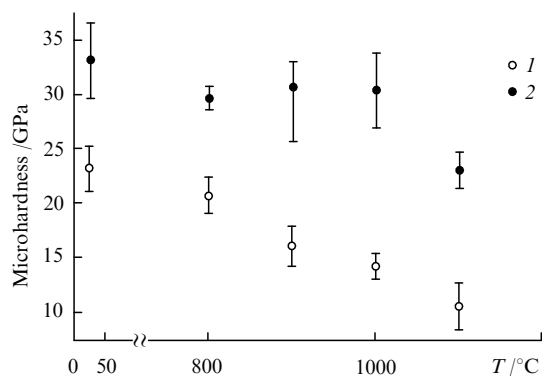


Figure 11. Change in the microhardness of TiN/AlN multilayer films after annealing in an argon atmosphere for 2 h.⁵³ The total thicknesses of TiN and AlN individual layers are 16 (1) and 2.9 nm (2); the total film thickness is 300 nm.

2. When NM are kept for a long time even at room temperature, growth of grains takes place.^{22, 42, 49, 50} This so-called anomalous growth of grains occurs if the grain size distribution is inhomogeneous (in this case, large grains serve as seeds for the anomalous growth).²² The activation energies for grain growth in NM and for the grain-boundary diffusion are close.^{21, 22} Measurements over a broad temperature range showed an increase in the activation energy for boundary growth with temperature rise; for example, for RuAl nanocrystals, the activation energies were found to be 39, ~72 and 213.5 kJ mol⁻¹ for temperatures of 873–1073, 1073–1173 and 1073–1273 K, respectively. This dependence could be due to the progressive effect of the boundary segregation temperature on the retardation of grain growth.⁴³ The activation energy for grain growth in iron at low temperatures is 125 kJ mol⁻¹ (which is close to the activation energy of the boundary self-diffusion in iron), while at higher temperatures, this value is 248 kJ mol⁻¹ (which is approximately equal to the activation energy of bulk self-diffusion).²⁹ These results can be

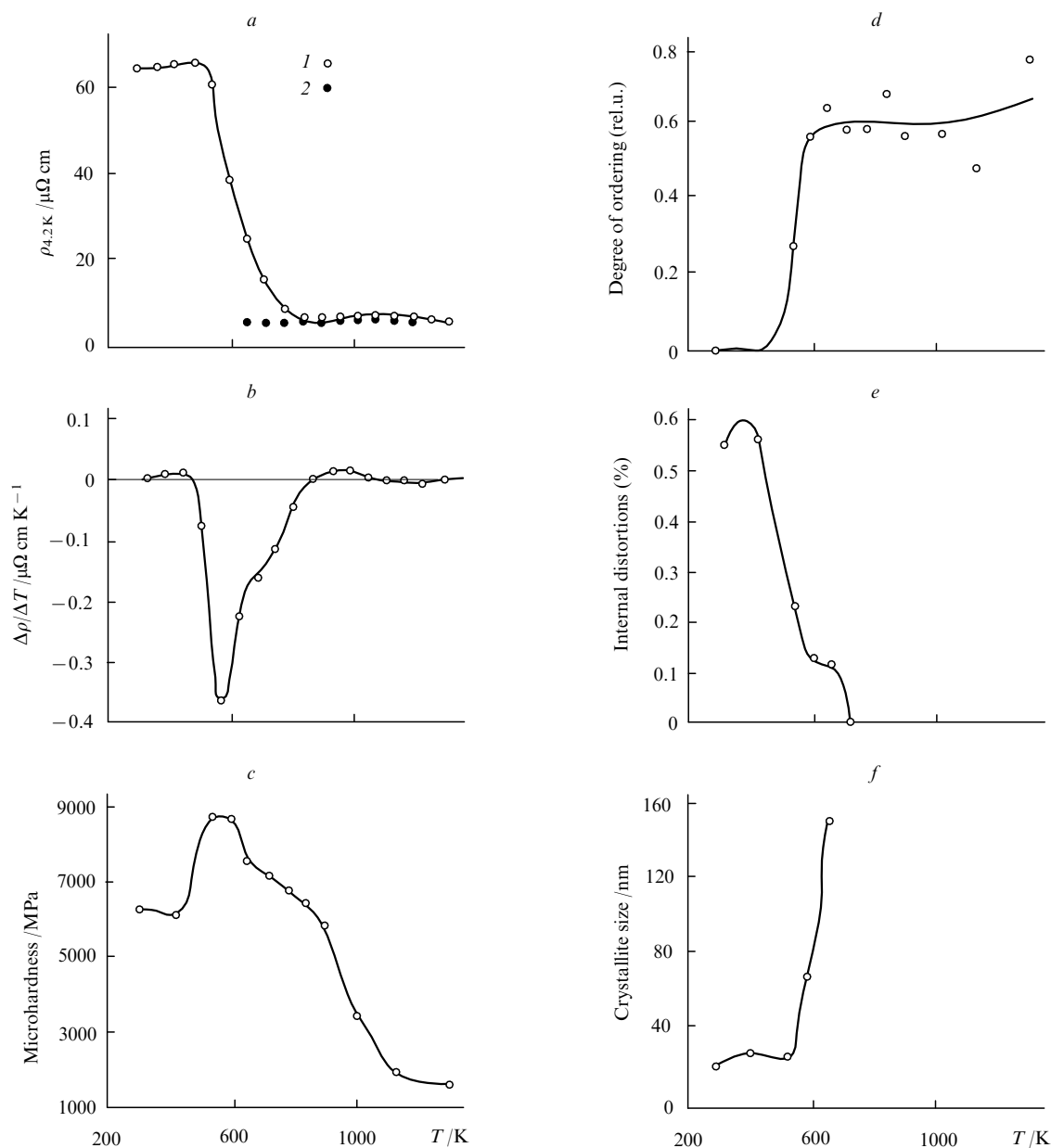


Figure 12. Effect of the annealing temperature on the electrical resistivity at 4.2 K $\rho_{4.2K}$ (a) during temperature increase (1) and decrease (2); temperature gradient $\Delta\rho/\Delta T$ (b); microhardness (c); degree of ordering (d), internal distortions (e); and crystallite size (f) of nanocrystalline Ni₃Al.¹⁸

explained by assuming different growth mechanisms for low- and high-temperature ranges.

3. The low-temperature milling of Fe–Al alloys reduces the tendency of the resulting NM for recrystallisation, which is attributed to the formation of fine FeAl_2O_4 particles and boundary segregations (see Fig. 8). The temperatures of the onset of active grain growth are mainly correlated with the melting points. In the presence of interstitial impurities (oxygen, nitrogen, *etc.*) and with formation of oxides and nitrides in the system, the grain growth starts at higher temperatures. This was confirmed for the Ag–O,⁴⁹ Ti–N⁵⁰ and Mo–N⁵¹ systems. Their thermal stability was demonstrated in relation to two-phase nanosystems, Cu–Ag and TiN– Si_3N_4 .^{49, 52}

4. In film specimens, the size of crystallites is much smaller than the film thickness but is correlated with the latter (see Figs 9, 10). A decrease in the film thickness promotes the growth of grains (see Fig. 10); in multilayer films, thermal stability increases with a decrease in the thickness of layers (Fig. 11).⁵³

5. It was noted in several publications (see, for example, the studies^{21, 22, 53, 54}) that the thermal stability of grains increases as the grain size diminishes.

6. The growth of grains is accompanied by not only changes in structural parameters such as microdistortions, the degree of ordering, *etc.*, but also by changes in physicochemical properties of NM (Fig. 12).¹⁸

The features noted above were established using electron microscopy, diffraction and calorimetric techniques.

b. The models and theoretical concepts

The problem of maintenance of the nanostructure of NM has been discussed in several reviews and original studies (see, for example, the publications^{20–22, 28, 30, 31, 50–56}). The main factors considered to favour the production of thermally stable NM include the presence of nano- and micropores, boundary segregations and two- or multi-phase nanostructures, a decrease in the grain-boundary surface energy, the formation of supersaturated solid solutions, an appropriate grain morphology, and homogeneity of the grain size distribution. The stagnation of grain growth in nanocrystalline films and ultradisperse powders has been discussed in the literature.⁵⁷

The research into grain boundaries and, generally, interfaces has been the subject of numerous publications (including monographs, see for example, Refs 58–62). However, these works barely touch upon the specificity of nano-objects. In recent years, the structures of grain boundaries have been calculated and the NM properties and the probability of vacancy generation during boundary migration have been predicted using molecular dynamics techniques (see for example, the studies^{21, 22, 28, 63–69}). In particular, it was shown that one-component NM can be simulated by two-phase models (the grain body and grain boundaries). In estimating the properties that depend little on the structure, this approach provided satisfactory results.^{21, 22} The contribution of triple junctions to the excess energy of NM was found to be rather weighty.⁶⁷

The molecular dynamics simulation proved to be useful for confirming the generation of vacancies upon grain boundary migration.⁶⁶ This process is related to elimination of the free space existing as interface discontinuity; the 'injection' of vacancies inside the grain body should increase the free energy of the system and hamper the boundary migration. An increase in the vacancy concentration during recrystallisation of ultradisperse powders has been recorded experimentally by positron-annihilation analysis.⁶⁸

The following relation was obtained for the critical size of crystallites:^{69, 70}

$$\frac{L_c}{2} = \left[24NkTZ(\beta sd)^2 \frac{m}{D} \right]^{1/3}, \quad (2)$$

where N is the number of atoms in unit volume; k is the Boltzmann constant; Z is the coordination number; β is the excess relative free

volume of the grain boundaries; d is the distance between the vacancy sources and sinks; m is the boundary mobility; and D is the self-diffusion coefficient. When $L_0 < L_c$, excessive vacancies retard the migration of grain boundaries, and when $L_0 > L_c$, the grains grow in the usual way, for example, in conformity with the law ($L^2 \sim t$). If the number of dislocations as vacancy sinks is relatively low, the grain boundaries or film surfaces mainly act as the sinks. In this case,

$$\frac{L_c}{2} = 24NkTZ(\beta s)^2 \frac{m}{D}, \quad (3)$$

where $L_c/2 \approx d$. For example, for aluminium ($m = 2 \times 10^{-14} \text{ m}^4 \text{ J}^{-1} \text{ s}^{-1}$; $T = 273 \text{ K}$; $D = 1.3 \times 10^{-17} \text{ m}^2 \text{ s}^{-1}$), the L_c value amounts to $\sim 100 \text{ nm}$, *i.e.*, this is a typical value for an NM structure.⁷⁰

When using relation (2) [or (3)], one should take into account the estimates of the typical grain sizes in NM made in a publication.⁷¹ In crystallites with dimensions of less than L^* ,

$$L^* = \frac{\alpha E b}{2\tau_{PN}}, \quad (4)$$

where α is a coefficient dependent on the dislocation geometry and ranging from 0.1 to 10, E is the shear modulus, b is Burgers vector, and τ_{PN} is the Peierls–Nabarro stress, the existence of dislocations is unlikely. For example, for linear edge dislocations, the following L^* values (nm) were found for some metals⁷¹ and for titanium nitride:³²

Cu	Al	Ni	Fe	TiN
25	10	10	2	~ 1

When $L_c < L^*$, relation (2) should be used, while for $L_c > L^*$, the use of formula (3) is preferred. However in both cases, one should bear in mind that these relations are approximations.

Yet another interesting conclusion concerning triple junctions has been drawn in a study of grain boundary migration. Triple junctions can be considered as a sort of impurity at interfaces but they mainly play an important role at relatively low temperatures. It has been shown for zinc and aluminium^{72–74} that the migration velocity of grain boundaries with triple junctions is lower than that for grain boundaries without the junctions at low temperatures. This is due to different activation energies for migration of these boundaries. A temperature rise entails an inversion: the boundaries with junctions become more mobile and the grain growth is controlled by the grain boundary migration. In the case of 99.995% pure zinc, the upper limit of the predominant influence of triple junctions is $\sim 380^\circ \text{C}$ (tilt boundary grains in the $\langle 10\bar{1}0 \rangle$ system) and $\sim 430^\circ \text{C}$ (tilt boundary grains in the $\langle 10\bar{2}0 \rangle$ system). For 99.999% pure aluminium, these temperatures were found to be $\sim 400^\circ \text{C}$ (tilt boundary grains in the $\langle 111 \rangle$ system) and $\sim 510^\circ \text{C}$ (tilt boundary grains in the $\langle 110 \rangle$ system).

The retarding role of triple junctions should be enhanced by a decrease in the grain size (see Fig. 4). Analysis of the variation of the areas of two-dimensional grains showed that, with allowance made for triple junctions, the velocity of grain boundary migration is proportional to the grain perimeter, but the pattern of dependence on topological parameters would be more complex.^{8, 75} However, the general features of switching of the mechanism of the triple junction effect on grain growth and the temperature ranges in which each particular mechanism is effective have not yet been adequately studied.

In investigating the grain growth in metallic films, a thermodynamic approach taking into account tensile stresses has proved to be useful.⁷⁶ According to estimates, the boundary migration and injection of vacancies inside the grains create conditions

§ Number of triple junctions per grain (m); when $m = 6$, grains exist in an equilibrium form; when $m < 6$, smaller grains disappear and when $m > 6$, larger grains grow (anomalous growth situation).

where recrystallisation is thermodynamically unfavourable and the grain growth is retarded. The incubation period depends on the grain size (or the distance between the sinks) and on the temperature

$$t_{\text{inc}} = \frac{(\beta s d)^2 N k T}{\gamma D L_0 c_{\text{eq}}}, \quad (5)$$

where γ is the grain-boundary surface energy, L_0 is the initial grain size, c_{eq} is the equilibrium concentration of vacancies. For example, for $T/T_M \approx 0.3$ and $L_0 = d \approx 10$ nm, the t_{inc} value would be $\sim 10^7$ s, i.e., ~ 150 days. From general considerations, this appears reasonable, although somewhat overestimated. One should bear in mind that relations (2)–(5) are approximations and also the fact that the residual stresses in the crystalline films are not necessarily tensile but can also be compressive.

The thermodynamic aspects of the segregation effects have been considered in several studies (see, for example, the publications^{21, 22, 28, 56, 77, 78}). The patterns of adsorption at crystallite boundaries have been studied since long ago. It is noted in monograph⁵⁹ that a thermodynamic theory that regards the interfacial areas as a separate phase was proposed by Zhukhovitskii back in 1944. The same study presents the thermodynamic relations determining the activity of a component in the interfacial layer as a function of its bulk concentration. Well-known are also Arkharov's studies in which the attention is focused on the role of boundary segregations in the formation of the properties of metal alloys.

The general thermodynamic aspects of boundary segregations in metallic and ceramic alloys have been considered by Ishida;⁷⁹ as applied to NM, this topic was discussed in a number of publications.^{55, 56, 77, 78, 80} An important result obtained in these works is as follows: calculations performed in different approximations (Langmuir–McLean and Fowler–Guggenheim) showed that the free Gibbs energy (G) varies non-monotonically[¶] as a function of the crystallite size, the minimum G being located in the nano-size region (Fig. 13). Hence, the temperature rise in doped nanocrystals may produce situations where further increase in the grain size becomes thermodynamically unfavourable.

Nanocrystalline nickel alloys with a minor content of phosphorus (2 at.%–5 at.%) were used to demonstrate the possibility

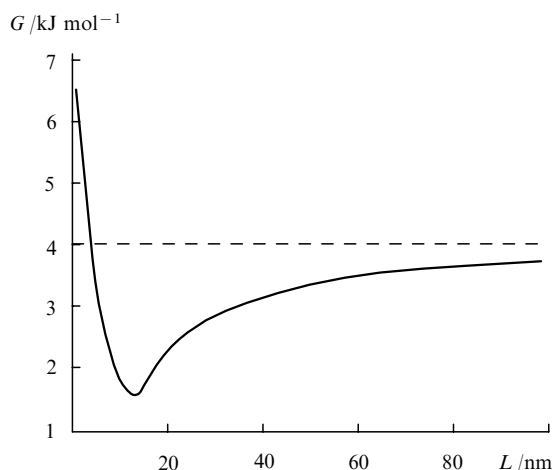


Figure 13. Gibbs free energy for a binary nanostructured alloy with an average concentration of 5 at.% at $T = 600$ K vs. crystallite size (for a standard polycrystal, $G = 4$ kJ mol^{−1}).⁷⁷

[¶] We would like to note incidentally that this non-monotonic variation is correlated with the views⁸¹ of singular points reflecting the topological transitions in the nanocrystalline state.

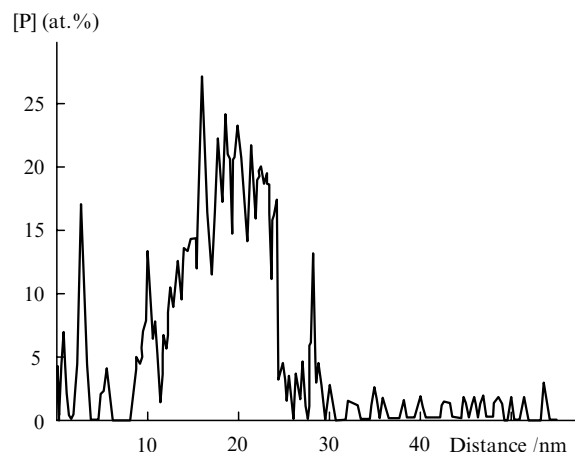


Figure 14. Concentration profile of phosphorus in a triple junction for a nickel–phosphorus alloy (3.6 at.% P) after heating to 400 °C at a rate of 5 K min^{−1} (see Ref. 82).

The alloy containing 25 at.% P corresponds to nickel phosphide (Ni₃P).

of Ni₃P crystallisation *via* boundary segregations (Fig. 14).^{56, 82} It was found^{55, 83} that during the annealing of palladium–zirconium alloys (grain size 10–25 nm), the grain boundaries became enriched in zirconium.^{55, 83} In the Pd₉₀Zr₁₀ alloy, the grain size increased after annealing at 350 °C, whereas in the Pd₈₀Zr₂₀ alloy, no increase in the grain size was noted even after annealing at 500 °C, which was attributed to greater enrichment of grain boundaries in zirconium in this alloy. This fact was determined based on the change in the lattice spacing.

Experimental investigations of the boundary segregations in NM make use of unique analytical equipment (such as atomic tomograph, atomic force microscope) as well as advanced investigation methods (for example, electron energy loss spectroscopy and so on).⁸² Interesting features of iron segregation in nanocrystalline iron–yttrium alloys have been followed.^{14, 28}

The possibility of crystallisation at compound boundaries due to the inflow of surface active elements has been considered theoretically by Rabkin,⁸⁴ who noted the retarding effect of particles (so-called pinning effect) and pointed to low probability of complete stoppage of boundary migration. Nevertheless, stabilisation of the nanograin growth has been observed by many researchers [for example, during annealing of RuAl (see Fig. 7), iron or aluminium powders after milling in an attritor^{29, 43, 85}]. Evidently, to take into account numerous factors that govern the evolution of grain ensembles [such as boundary migration, diffusional segregation, phase crystallisation,⁸⁴ vacancy injection by moving grains, the possible relaxation of the residual stresses, size effects as applied to the intergrain surface energy and integral free energy (see Fig. 13), and so on], it is necessary to perform a versatile computer simulation of the main processes occurring during heat treatment of NM. An attempt at Monte Carlo simulation of some of these factors has been reported.⁸⁶

2. Phase transformations

The presence in NM of a nanocrystalline structure, supersaturated solid solutions or unusual crystalline phases is due to non-equilibrium conditions of NM preparation.

Experimental and theoretical studies of the thermal stability of these objects are few, although thermodynamic characteristics and the features of phase diagrams as applied to nanoparticles have been the subject of investigation of many researchers (see, for example, Refs 87–89). However, phase transitions in compact NM (diffusiveness, shifts, *etc.*) have not been studied systematically.

Several attempts have been undertaken to carry out rough calculations of state diagrams with allowance for the component

dispersity (see, for example, Refs 87, 90–93). Using the relations for the partial free energies of the system in the liquid and solid states (for the latter, the excess component of the boundary surface energy was taken into account), in the simple approximation of regular solutions, relations were derived that reflect the influence of the component dispersity on, for example, the decrease in the eutectic temperature ΔT_E :

$$\Delta T_E = \frac{\Delta G_2}{R \ln x}, \quad (6)$$

$$\Delta T_E = \frac{\Delta G_2}{R \ln x_E - \Delta S_{M2}}, \quad (7)$$

$$\Delta T_E = \frac{\Delta G_1}{R \ln[(1 - x_E)/(1 - x)] - \Delta S_{M1}}, \quad (8)$$

where G_i is the contribution of the excess boundary surface energy per mole, $\Delta G_i = 6V_i\sigma_i/L_i$ (V_i is the molar volume), σ_i is the grain-boundary surface tension, x and x_E are the limiting solubility and eutectic concentrations; ΔS_{M_i} is the melting entropy.⁹²

These relations are equivalent, their practical value being dependent on the presence of particular data for components 1 and 2.

Expressions (6)–(8) lead to a size dependence of the type $\Delta T_E \sim 1/L$. The calculated ΔT_E and T_E values for the TiC–TiB₂, TiN–TiB₂ and TiN–AlN systems are summarised in Tables 3 and 4. It can be seen that a tangible decrease in T_E can start when the dimensions of the dispersed component are several tens of nanometers, although one should remember that the calculations are rough. With more complicated approximations, the estimates cannot be brought to a numerical solution. The available thermodynamic information is inadequate for determining the solubility regions in the phase diagrams.

The phase stability in multilayer films has been considered in terms of various statistical thermodynamic approaches.^{94,95}

The presence of metastable structures is especially typical of NM prepared by mechanosynthesis or by film techniques. The

Table 3. ΔT_E values in TiC(TiN)–TiB₂ and TiB₂–TiC(TiN) pseudo-binary systems with different degrees of dispersity of one of the components.⁹²

L /nm	ΔT_E /K	
	TiC(TiN)–TiB ₂	TiB ₂ –TiC(TiN)
200	~45	~35
100	~90	~70
20	~450	~350
10	~900	~700

Note. In the polycrystalline state, T_E for the TiC–TiB₂ system is 2790 K; for the TiN–TiB₂ system, 2870 K.

Table 4. T_E values for the TiN–AlN pseudo-binary systems with different degrees of component dispersity (for macrodisperse specimens, $T_E = 2715$ K).⁹¹

Dispersed component	L /nm	T_E /K
TiN	200	2660
	100	2610
	20	2160
AlN	200	2710
	100	2690
	20	2565
TiN, AlN	200	2650
	100	2590
	20	2110

formation of supersaturated solid solutions and compounds was detected in the Fe–Cu, Fe–Ni, Fe–Ti, Fe–Al, W–Cu, Ni–Al, TiN–TiB₂, and TiN–AlN systems, *etc.*^{14,44,50,95–104} Detailed study of the Fe–Cu and Fe–Ni systems (crystallite size 3–50 nm)^{96,98,99,104} showed a pronounced increase in the solubility of the components in each other. Whereas iron dissolution in copper increases the thermal stability, the reverse process has virtually no influence on the grain growth parameters; two-phase Fe + Cu compositions were found to be less stable than single-phase ones.

In multilayer films (superlattices), cubic structures are often formed instead of hexagonal ones due to epitaxy (examples are aluminium and niobium nitrides with the NaCl structure in combination with cubic titanium and zirconium nitrides;^{30,50} and titanium with FCC structure in multilayer titanium–aluminium films¹⁰⁵).

Magnetron sputtering with both single-phase and two-phase TiB₂ + (0%, 25%, 50%, 75% or 100%) TiN targets at moderate deposition temperatures ($\sim 150^\circ\text{C}$) resulted in the synthesis of single-phase nanostructured boride–nitride films of the following composition: Ti(B_{0.73}N_{0.2}O_{0.05}C_{0.02})_{1.56} and Ti(B_{0.56}N_{0.29}O_{0.05}.C_{0.1})_{1.32} with a hexagonal structure and Ti(B_{0.34}N_{0.49}.O_{0.12}C_{0.05})_{1.49} and Ti(N_{0.6}O_{0.2}C_{0.2})_{1.58} with a cubic structure. The composition formulae were determined using Auger analysis. Judging by these formulae, these films were essentially non-stoichiometric because the homogeneity regions of titanium diboride and nitride in the equilibrium state differ from these values (TiB_{1.89–2.0} and TiN_{0.7–1.2}). However, the solubility of interstitial elements in films is rather high; therefore, fairly broad homogeneity regions appear in the state diagram of the TiB₂–TiN system.^{102,103} The equilibrium state diagram of the pseudo-binary TiB₂–TiN system (see Table 3) is an eutectic type diagram, the mutual solubility of the components in this system being very low. A similar situation is found in the TiN–AlN and NbN–AlN systems. While the equilibrium solubility of Al in TiN at 1000 °C equals ~ 2 at.%, the cubic equiatomic phase (Ti,Al)N occurs in nanostructured films even at room temperature.³⁰ Thus, the pattern of state diagrams of nanocrystalline systems[†] and the homogeneity regions of individual compounds substantially change.

Study of the effect of annealing at 700 and 1000 °C ($t = 15$ min) on the structure of Ti(B,N) films did not reveal decomposition: the films remained phase-homogeneous and the grain size changed insignificantly (Table 5).¹⁰⁶ Some changes in the microhardness will be discussed below.

An extensive study of the effect of annealing in the temperature range from 850 to 1000 °C on the structure and composition of and the chemical bonding in plasmachemical SiCN films has been reported.¹⁰⁸ Using electron microscopy and X-ray diffraction analysis and resorting to the data of infrared, Raman and photoelectron spectra of the films, it was shown that high-temperature annealing leads to a decrease in the amorphous matrix and yields oblong oriented α -Si₃N₄ nanocrystals (in the amorphous matrix of the initial films, 2–3 nm crystallites were detected).

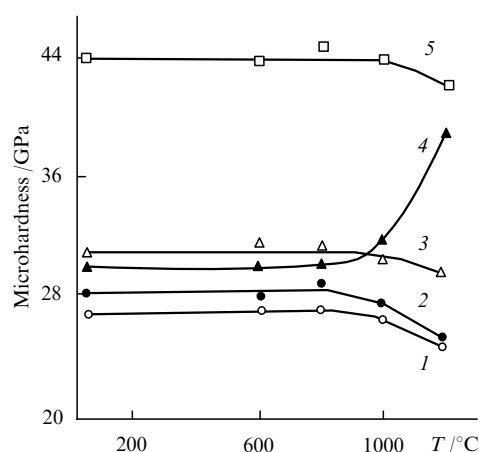
Interesting examples of spinodal decomposition of nanostructured solid solutions, TiN–ZrN and TiN–AlN, have been reported.^{30,50,109,110} The dependences presented in Fig. 15 allow one to follow the influence of the annealing temperature on the change in the microhardness of films of individual titanium and zirconium nitrides and multilayer (TiN–ZrN) and doped [(Ti,Zr)N] films.¹¹⁰ It can be seen that starting from $T > 1000^\circ\text{C}$, the microhardness of doped films tends to increase with an increase in the annealing temperature; this is due to evolution of the ultradisperse products of spinodal decomposi-

[†] Unlike the equilibrium state diagrams of usual polycrystalline objects, in the case of nanocrystalline systems, it is appropriate to speak of quasi-equilibrium diagrams to mean their lability and possible variation with time.

Table 5. Effect of annealing on the average size (L /nm) and the microhardness (H_M /GPa)^a of crystallites in boride–nitride films.¹⁰⁶

Target	Initial film		$T_0 = 700\text{ }^\circ\text{C}$		$T_0 = 1000\text{ }^\circ\text{C}$	
	L	H_M	L	H_M	L	H_M
TiB ₂	3–5	41–46	—	40–46	—	35–39
TiB ₂ + 25% TiN	2.3 ± 1.1	40–46	4.4 ± 1.4	40–45	—	32–38
TiB ₂ + 50% TiN	2.9 ± 1.1	46–52	3.7 ± 1.2	47–54	3.4 ± 1.9	38–45
TiB ₂ + 75% TiN	5.4 ± 4.0	53–59	8.1 ± 4.4	52–58	7.9 ± 3.8	32–42
TiN	9.9 ± 8.8	36–40	13.0 ± 6.6	38–42	10.2 ± 7.0	33–40

^a The H_M values refer to a procedure¹⁰⁷ largely eliminating the effects of the substrate and film thickness; *i.e.*, here, H_M is the microhardness of the proper films.

**Figure 15.** Effect of the annealing temperature on the microhardness of monolayer ZrN (1) and TiN (2), 10-layer ZrN/TiN (3), doped (Zr,Ti)N (4) and 20-layer ZrN/TiN (5) films.¹¹⁰

tion. These films provide an example of so-called ‘smart’ materials whose properties not only deteriorate during operation but can also be upgraded to a certain extent.

Annealing of the (Ti,Al)N–Si₃N₄ nanocomposition at different temperatures showed a microhardness maximum and a grain size minimum at 800 °C, which should also be attributed to spinodal decomposition of the (Ti,Al)N phase; a substantial decrease in the microhardness and an increase in the crystallite size is observed after annealing at 1200 °C ($t = 30$ min in an atmosphere of 90 vol.% N₂ + 10 vol.% H₂).¹¹¹

The nanocrystalline cubic phase (Ti,Al)N is highly stable against oxidation.^{103, 112} Therefore, it is not accidental that one of the (Ti,Al)N-based layers is highly resistant to change in industrial and pilot multilayer superhard nitride films.¹¹³

3. Relaxation and diffusion

Relaxation processes in nanocrystalline compounds were analysed in the review;¹¹⁴ the diffusion processes in nitride films have been characterised.³⁰ If an NM has been prepared by, for example, severe plastic deformation or vapour quenching and represents a disordered solid solution, a temperature rise restores the short-range order, establishes a long-range order and induces the growth of grains. These regularities were followed for the Ni₃Al intermetallic compound in calorimetric experiments.^{114, 115} However, the use of differential calorimeters does not always permit detection of processes related to the relaxation of internal microstresses during low-temperature annealing. The relaxation of residual stresses can be detected in X-ray diffraction studies based on line narrowing and splitting into doublets. Relaxation is believed to precede the grain growth.¹¹⁴ Turning back to the data of Table 5, we would like to note that some decrease in the microhardness during annealing of boride–nitride films can, apparently, be attributed

to relaxation of the residual compressive stresses, where the grain size changed insignificantly.

The residual stresses in nanostructured nitride and other films caused by differences in the linear thermal expansion coefficients and elastic properties in the film–substrate system or in multilayer films can be rather pronounced. For example, in nitride films, the residual compressive stresses can reach 10 GPa and they can contribute noticeably to the hindering of dislocation and fracture migration (and, correspondingly, to the increase in hardness).³⁰ Stress relaxation processes consisting in migration, redistribution and annihilation of various defects as well as grain boundary migration are known to be diffusional processes. The activation energy of stress relaxation (E /kJ atom^{−1}) and the temperature ranges of this process for the films of some refractory compounds are given below³⁰

Compound	TiN	TiN	Ti(C,N)	CrN
$T/^\circ\text{C}$	400–900	250–430	450–900	240–670
$E/\text{kJ atom}^{-1}$	~200	~120	200–400	200–300

The given E values are similar in magnitude to the activation energies of nitrogen self-diffusion in nitrides (which is, more likely, a boundary rather than a bulk process).¹¹⁶ Comparison of the residual stress relaxation in titanium nitride and carbide–nitride showed that an equal level of compressive stresses in carbide–nitride films is attained at temperatures ~200 °C higher than in TiN; therefore, the high-temperature hardness of Ti(C,N) is higher.³⁰

The relaxation processes and the evolution of nanostructures in metals, alloys and intermetallic compounds (Fe, Cu, Ni; Al, Fe, Cu alloys; Ni₃Al, see Fig. 12) subjected to severe plastic deformation have been discussed in detail in a monograph.¹⁸ However, the mechanism of stress relaxation in NM as a whole is not entirely clear.

The information concerning heterodiffusion processes is important for the analysis of the thermal stability of multilayer films. A study of the mutual diffusion in single-crystalline multilayer TiN/NbN films (the thicknesses of separate layers are 4.4 and 12.3 nm for a total thickness of ~1 μm; isothermal maintenance at 750–875 °C, non-isothermal heating to 1200 °C) revealed the predominant diffusion of titanium.¹¹⁷ The activation energies (Q /kJ per atom) for different temperature ranges have been determined.^{30, 117}

$T/^\circ\text{C}$	< 830	830–875	885–930
Q	115	250	430

The last Q value is similar to the activation energy for the self-diffusion of metal atoms in transition metal carbides and nitrides.¹¹⁶ According to estimates,¹¹⁷ the duration of homogenisation in multilayer TiN/NbN films and, correspondingly, the working life of this nanocomposite with ~2 nm thick layers is ~10 h at 750 °C or ~2 h at 850 °C. To study heterodiffusion in multilayer films, one should employ high-precision X-ray diffraction and electron-microscopy procedures and also use powerful sources such as synchrotron radiation. The versatile capabilities of

X-ray diffraction for the assessment of $\text{In}_x\text{Ga}_{1-x}$ films with one ~ 10 nm thick quantum well have been demonstrated.¹¹⁸

A study of the thermal stability of multilayer Mo/NbN films (the metal has a body-centred cubic lattice and the nitride has a face-centred cubic lattice) showed that the formation of the tetragonal (Mo,Nb)N phase starts after maintenance for 3 h at 1000 °C.¹¹⁹

The diffusion of oxygen in films determines the stability of films against oxidation. The abundance of interfaces in NM creates conditions for substantial oxygen streams. Characteristic features of oxidation of nanostructured films have been analysed.^{30, 103, 112, 113, 120} The resistance of nitride films against oxidation is markedly increased by chromium or yttrium additives which 'lock up' the crystallite boundaries.¹¹³ Amorphous films have demonstrated both a poorer oxidation resistance (800 nm TiN films)¹²⁰ and a higher scale resistance (2–3 μm AlN–TiB₂ and AlN–TiB₂–SiC films)¹¹² compared to the same characteristics of crystalline films or bulk specimens of the same composition.

IV. Other stability aspects of nanostructures

For some types of NM (for example, for nanoporous, nano-semiconducting and nanocarbon materials), studies of thermal stability have started only recently (see, for example, Refs 121–126). It should also be noted that nanoparticle-related problems have been barely considered above, because, in view of the multispect character of agglomeration and sintering processes, these topics require separate consideration. We would only like to note that the sintering of nanoparticles and the grain growth in NM have much in common. Figure 16 shows the temperature dependence of the compaction during sintering of ultradisperse powders of metals and metal-like substances and also ionic and covalent compounds.¹²⁷ Whereas active sintering (compaction) of metals and metal-like or ionic compounds starts at homologous temperatures $(0.3–0.5)T_m$, the powders of covalent compounds (B, Si, Si₃N₄) are actively sintered only at $T \geq (0.8–0.85)T_m$, i.e., at much higher temperatures. Aluminium nitride, as an ionic-and-covalent compound, occupies an intermediate position. This difference is due to specific features of the diffusion mobility in objects with different types of chemical bonds. In all probability, the temperatures of the onset of the

active grain growth in these materials should lie within the same ranges.

The aspects of NM thermal stability considered above are far from exhausting the general problem of nanostructure stability. For example, the NM stability is appreciably affected by various fields (force, radiation, etc.). In particular, the grain growth upon superplastic deformation of fine-grained ceramic materials has been considered theoretically taking into account the additional driving forces for migration.¹²⁸

The microstructure changes induced by NM implantation or irradiation have been the subject of only a few studies (see, for example, Refs 129–131). The appearance of nanoclusters in metal alloys (Fe–Ni, Cu–Ni, Fe–Cr, etc.) at high levels of radiation damage has been noted.¹³² The formation of nanocrystalline diamonds ($L = 2–70$ nm) was detected on graphite irradiation with Ar⁺ ions (the fluence was $\sim 10^{22}$ cm^{–2}).¹³³ Amorphisation of nanocrystalline zirconium oxide on exposure to radiation by high-energy Xe²⁺ and Ne⁺ ions has been reported;¹³¹ meanwhile, gold nanoparticles with dimensions of 3 nm remained crystalline after irradiation. It is noteworthy that NM based on ZrO₂ are under vigorous research now (see, for example, studies^{134, 135}). The behaviour of irradiated NM is an extensive field for further research.

It should be emphasised that the stability of NM largely depends on the process used for their manufacture. A number of techniques such as high-pressure processes, sintering with controlled heating rates, pulse sintering, pulse modes of electro-deposition, moderate substrate temperatures during film deposition, the formation of multiphase structures and boundary segregations and some other are widely used in the preparation of NM (see, for example, the studies^{24, 31, 52, 136–142}). However, problems of deliberate selection of conditions for the production of the initial NM with a narrow nanocrystallite size distribution, the optimal content of doping or impurity elements for decreasing the grain-boundary surface energy or for the formation of barrier layers, and many other problems are far from being solved. It is not accidental, therefore, that the Japanese national program 'Material Nanotechnology' pays considerable attention to the development of NM with optimal structures and to the prevention of anomalous grain growth phenomena.¹⁴³

V. Conclusion

When generally evaluating of the state-of-the-art research into the thermal stability of NM, we would like to stress the following points. On the one hand, there exist quite a few experimental and theoretical facts demonstrating the possibility of production of thermally stable NM; on the other hand, examples of anomalous grain growth in NM are documented.

Unfortunately, our knowledge is still inadequate to unambiguously explain many facts and to compare the efficiency of various methods for nanostructure maintenance, say nothing of the possibility of making predictions. Note that the latter depends not only on the theoretical works and availability of reliable experimental information but also on the general level of the nanostructure theory. For example, it is not entirely clear what are the grain dimensions (of phase components) down to which the classical thermodynamics remain valid. The point is that objects with crystallite dimensions of $\sim 1–2$ nm or even less are already involved in NM investigation and application (see Table 5 and the studies^{32, 103, 106, 144–146}). A ~ 1 nm grain of titanium nitride with a lattice spacing of ~ 0.424 nm contains ~ 8 ($\sim 2^3$) unit cells, i.e., in essence, it is a cluster-consolidated object (unlike cluster-aggregated materials^{16, 147}). In this connection, the points such as the effect of the grain boundary curvature on its energy parameters, the applicability of the concepts of statistical thermodynamics or thermodynamics of irreversible processes, the type of excessive thermodynamic functions, the energy characteristics of triple junctions, and so on have been scarcely studied so far. These aspects have to be thoroughly analysed to be used in estimations.

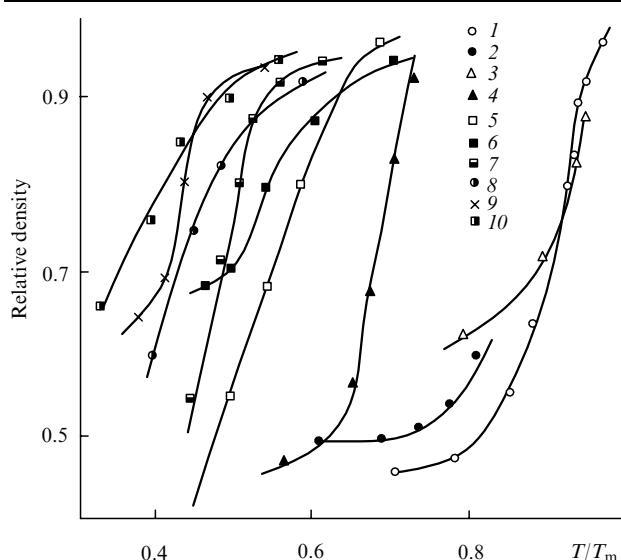


Figure 16. Temperature dependence of compaction during sintering of various ultradisperse powders.¹²⁵
(1) Si, (2) Si₃N₄, (3) B, (4) AlN, (5) WC, (6) ZrC, (7) MgO, (8) Mo, (9) CaF₂, (10) Ni.

Note that research into the determination of the energy characteristics of the surfaces of isolated clusters, cluster aggregates and colloids is also in progress.^{148–150}

In the long-term American forecasts (for 10–15 years) concerning the arrival of nanotechnological products on the world market, nanomaterials occupy a leading position — of the putative total volume of 1 trillion US dollars, a sum of 340 billion US dollars is predicted for NM.^{151, 152} It is clear that substantiation of the operation capacity of NM, including thermal stability characterisation, is among the most important problems facing the science of nanostructured materials.

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^a — *Phys. Met. Metallogr. (Engl. Transl.)*

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Institute of Physical and Organic Chemistry at the Rostov State University



This issue of the journal is composed of reviews prepared by scientists working at the Research Institute of Physical and Organic Chemistry at the Rostov State University (IPOC). The Institute was founded in 1971 as a subdivision of the North-Caucasian Scientific Centre of Higher School established a year before. The Institute includes six departments and four laboratories. Currently, the staff of the Institute comprises 200 associates, among them there are 14 Doctors of Science and 79 Ph.Ds. The Nuclear Magnetic Resonance Laboratory equipped with Varian spectrometers has the status of a Shared Access Centre of the Russian Foundation for Basic Research (RFBR). For RFBR grant holders from the south of Russia, similar functions are performed by the Laboratory for Quantum Chemistry, which implements the RFBR and Ministry for Industry, Science and Technology projects on computer network development and molecular simulation for higher education institutes in the south of Russia.

Since 1998, the Institute has been under the guidance of the Division of General and Technical Chemistry of the Russian Academy of Sciences (since 2001, the Division of Chemistry and Materials Sciences). This fact, together with the creation of joint laboratories with the Institute of the Problems of Chemical Physics and the Institute of Physical Chemistry of the RAS reflects the tendency towards the closer integration of Russian science and education, which has taken shape in the last decade, as a vital necessity dictated by the development of society. Related to this, an obvious advantage of research institutes affiliated to a university is the absence of departmental or other problems hampering the selection and recruitment of the most gifted students to work on scientific projects. The IPOC actively uses this opportunity in cooperation with the Department of Chemistry of the Rostov State University. The post-graduate course and the facilities for working towards doctorate degree, and the Academic Council for defending Ph.D. and Doctoral theses functioning at the Institute, provide the conditions necessary for raising the scientific level of young scientists.

The main fields of research developed at the Institute are related to fine organic synthesis, photochemistry, the synthesis

and study of the properties of metal coordination compounds, structural theory, and the mechanisms of organic reactions.

Of the interesting results of investigations performed at the Institute in recent years, noteworthy is the theoretical development of the principle of structural design of compounds with dynamic molecular behaviour able to undergo reversible low-barrier intramolecular rearrangements. This principle has underlain the targeted synthesis of bi-stable compounds existing as two or several stable forms whose interconversions can be induced by electromagnetic or electric fields. Studies into photocontrolled bi-stable structures have resulted in the development of new types of photochromic and fluorescent systems functioning as abiotic converters of light energy, highly sensitive photochemical chemosensors, effective molecular switches and 3D data recording media (molecular memory).

A traditional field of investigation at the Institute is the synthesis of polycyclic nitrogen- and oxygen-containing heterocycles and monosaccharides. The scientists working at the Institute have received more than 100 patents, including foreign ones, for physiologically active compounds exhibiting more than 50 types of biological activity including antidiabetic, antiaggregant, antiarrhythmic, antiulcer, local anaesthetic, antioxidant and others. Some of these products have already been authorised for clinical trials and the antiarrhythmic drug Ritmidazol has passed these trials and is allowed to be used in clinical practice by the Russian Federation Pharmacological Committee.

The organic ligands synthesised at the Institute serve for the preparation of coordination compounds of transition and non-transition elements with variable polyhedral types of chelate units. Efficient polymerisation catalysts, compounds with valuable magnetic characteristics, UV light converting luminophores, laser dyes, additives to lubricating oils, and so on, have been found among the new metal complexes.

The applied studies carried out at the Institute concentrate on electrochemistry (study of metal corrosion mechanisms, development of effective corrosion inhibitors for drilling tools operating in highly acidic and hydrogen sulfide environments), geochemistry (regional analytic surveys, landscape pollution mapping, analysis of man-caused pollution), development of new compo-

sites, coatings, lubricants and antifriction materials for aerospace and the automotive industry (some materials elaborated at the Institute were used in the spaceshuttle Buran). The process of manufacture of the Drotaverin drug (No-spa analogue) from Russian raw materials developed at the IPOC is currently under industrial development at the Volgograd chemical plant.

During the last 5 years, the scientists working at the Institute have published sixteen scientific monographs (six of them were published by companies in the USA, Germany and the Netherlands) with more than 500 scientific papers published in Russian and other international journals. More than 80 patents were granted, two inventions being patented abroad (in 23 countries). There are three State Prize laureates and a number of A M Butlerov and Alexander von Humboldt Prize winners, and winners of other prizes.

As in other scientific institutions of Russia, the Institute has faced severe financial problems and a shortage of personnel during the last decade. Suffice it to say that today's budgetary financing of the Institute does not exceed 5% of the pre-reform finances (on a comparable price schedule). The scientific potential and the 'critical mass' of the Institute and the intake of young specialists needed for future prospects are maintained almost exclusively by RFBR grants (the Institute has annually 10 to 12 initiative grants, and also leading scientific school grants and grants of the shared access laboratory 'Molecular spectroscopy' and of the library and database electronic access network), grants and programmes of the Ministry of Education and the Ministry for Industry, Science and Technology of the Russian Federation. Of special significance are international programmes and grants from the European Union (INTAS), Civilian Research and Development Foundation (CRDF, USA), Alexander von Humboldt and Volkswagen Stiftung Foundations (Germany), International Science and Technical Centre (ISTC), Council of National Research and Science (CNRS, France), SPECS and BioSPECS companies (Netherlands), the Servier pharmaceutical company (France), *etc.* Other forms of international collaboration and exchange are also used. Research dealing with photochromic and fluorescent chemosensors carried out at the Institute is a part of a Project executed by the Basic Research and Higher Education Centre at the Rostov, Kuban' and Taganrog Radio Engineering Universities financed by the CRDF, the Ministry of Education of the Russian Federation and the administrations of the Rostov Region and Krasnodar Territory. Within the framework of this project, more than 30 students and post-graduates were recruited on a competitive basis to work at the Institute where they received an additional scholarship.

The reviews presented in this issue illustrate the main fields of investigations carried out at the Institute and also some results of the collaboration with Universities in the USA and France. The paper by A D Dubonosov, V A Bren and V A Chernoi vanov entitled 'Norbornadiene – quadricyclane as an abiotic system for the storage of solar energy' and the paper by V Lokshin, A Samat (Marseilles University) and A V Metelitsa dealing with the synthesis and photochromic properties of spirooxazines represent the rapidly progressing research into photochemically active systems — molecular switches and optical memory elements, abiotic converters of light energy and fluorescent chemosensors.

The review by Yu A Zhdanov and Yu E Alekseev entitled 'Basic achievements in the coordination chemistry of modified monosaccharides' characterises the new trends in the development of carbohydrate chemistry, in particular, the possibility of preparing effective enantioselective catalysts by chirality transfer from the carbohydrate ligand to the metal centre.

The review by A D Garnovskii and I S Vasil'chenko 'Rational design of metal coordination compounds with azomethine ligands' gives a concentrated survey of the many-year research into targeted synthesis of mono- and polynuclear chelates and molecular complexes with coordination units of the type MN_xZ_y (where $Z = NR, O, S, Se, Te$), typical of the most important metal enzymes and metal proteins.

An original field of investigation carried out at the Institute is the chemistry of organotellurium compounds. Organotellurium compounds are not only precursors of some efficient semiconductor materials but, owing to specific features of the valence and hypervalent bonds formed by tellurium, they are also useful synthons for the synthesis of new heterocycles; this allows development of a peculiar synthetic strategy. I D Sadekov's review ' β -Telluroacroleins and β -tellurovinyl ketones: synthesis, reactions and structure' is devoted to one of the classes of organotellurium compounds studied at the IPOC.

Finally, the paper by V I Minkin, R M Minyaev, R Hoffmann 'Non-classical structures of organic compounds: unusual stereochemistry and hypercoordination' summarises the main results of investigations in this intriguing field of theoretical chemistry, including the results obtained in cooperation with the group of theorists headed by Nobel Prize winner, a foreign member of the RAS, Roald Hoffmann (Cornell University, USA).

Of course, the size of the issue does not permit all the fields of research carried out at the Institute of Physical and Organic Chemistry to be covered. Additional information concerning the Institute and its personnel can be found at the Institute websites (<http://www.ipoc.rsu.ru> and <http://rec.ipoc.rsu.ru>).

The increase in students' interest in scientific research and in the intake of post-graduates and young scientists, which has become evident in recent years, allows one to hope that the studies published in this issue will be continued in future years.

Academician V I Minkin,
Director of the Institute
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Non-classical structures of organic compounds: unusual stereochemistry and hypercoordination

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Abstract. Non-classical structures of organic compounds are defined as molecules containing non-tetrahedral tetracoordinate and/or hypercoordinate carbon atoms. The evolution of the views on this subject is considered and the accumulated theoretical and experimental data on the structures and dynamic transformations of non-classical organic compounds are systematised. It is shown that computational analysis using the methods and the software potential of modern quantum chemistry has now acquired high predictive capacity and is the most important source of data on the structures of non-classical compounds. The bibliography includes 227 references.

I. Introduction

Molecular structure is a key concept of theoretical organic chemistry. The description of molecular structures of organic compounds is underlain by the fundamental concept of two-centre two-electron covalent bonds, the tetravalence of carbon, and the tetrahedral geometry of the four single bonds it forms. Using only these concepts, which can be easily extended to other Main Group elements of the Periodic Table, it is possible to describe and predict all the key types of organic structures and kinds of isomerism. By means of a molecular meccano, these views can assume a material form as simple stereochemical models; these models appear to be an invention of Jacobus Henricus van't Hoff.[†] The fundamental nature of the principles that underlie these models can be compared only with the simplicity of their practical implementation, which can be understood by looking at the cardboard models

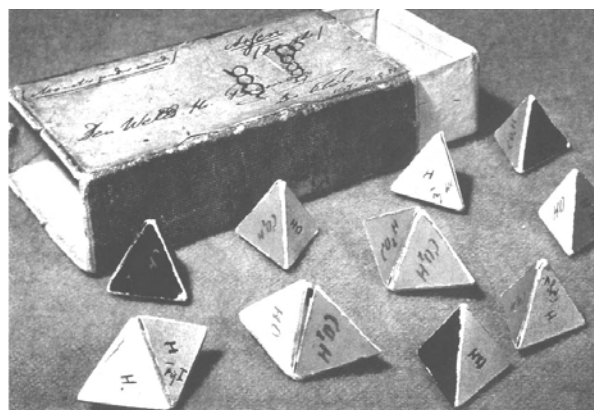


Figure 1. Three-dimensional stereochemical models hand-made personally by van't Hoff (courtesy Leyden Museum of Natural History).

made personally by van't Hoff (Fig. 1). By the same procedure, one can easily assemble molecular models of millions of organic and organoelement compounds. Actually, the prediction of the double-helix DNA structure (which is, perhaps, the most important discovery of the last century) required only one further structural concept — the notion of the hydrogen bond.

The development and extensive use of new methods for the investigation of molecular structure and dynamics as well as the development of organometallic chemistry, which linked organic chemistry to images and theoretical views of coordination chemistry, have extended the scope of the classical structural theory. Thus, it has become impossible to describe the whole diversity of the new types of structures and their dynamic transformations using only the ideas and the language of the classical structural theory. This triggered the development of two interrelated concepts, namely, the concepts of stereochemically non-rigid (fluxional) compounds and multicentre bonds. The development of the

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[†] The Russian version of van't Hoff's article 'Sur les formules de structure dans l'espace'¹ and his original drawings illustrating the construction of spatial structures of molecules can be found in the monograph by Bykov.²

multicentre bond concept, in turn, has entailed the notions of hypervalence and hypercoordination. Thus, the description of molecular structures in terms of the notion of multicentre bonds can be likened to a complication in the standard molecular meccano by adding a set of new units, *i.e.*, multicentre bonds ($mc-ne$, where $n = 1, 2$ and $m > n$), for example, three-centre two-electron bonds ($3c-2e$). Examples of consistent application of this approach to the analysis of chemical structures of compounds containing hypercoordinate carbon atoms and derivatives of polyhedral boranes can be found in monograph.³

The orbital approach to the analysis of molecular structures and their transformations, developed in the second half of the XX century and based on semiquantitative orbital interaction theory, is more general and has a much more extensive predictive capacity.^{4–6} This theory focuses on the closure of the electron shells of valence molecular orbitals and on the presence of a rather large energy gap between the frontier MO as the key factors that influence the thermodynamic stability of a molecular structure. Kinetic stability of a molecular structure with respect to rearrangements or fragmentation may be due to the possibility that these processes are thermally forbidden by the orbital symmetry rules. An important advantage of the orbital approach as a qualitative theory of modern theoretical chemistry is that its views and notions can be directly transferred to and used in organometallic chemistry, in the coordination chemistry of transition metals and even in solid-state chemistry.^{7,8} Detailed analysis of the data accumulated by the early 1990s on the structures and properties of non-classical organic compounds carried out using the orbital interaction theory has been reported in our monographs^{9,10} and reviews.^{11,12}

The reliability of any qualitative views needs to be validated by strict theoretical calculations. By the early 1990s, the capacity for performing such calculations for compounds with more than 6–7 non-hydrogen atoms was quite limited; therefore, calculations for molecular systems were mainly carried out in the valence approximation by semiempirical quantum chemistry methods. The semiempirical methods have played and still play an important role in the theoretical simulation of structural chemistry problems. However, these methods are hardly applicable to non-classical structures, as they are parametric techniques in which parameters are selected by adjusting the calculated data to well-known experimental results obtained for classical molecular structures (references).

The situation has markedly improved during the last decade. Enormous progress in the manufacture of a new generation of high-performance computers and in the development of concomitant software made possible (and almost routine now) calculations of rather complicated molecules by means of high-level *ab initio* quantum chemistry techniques.¹³ The accuracy of calculations of this type is quite comparable with that attained in the experiment. This opens up new routes both for additional analysis of the previously developed qualitative structural theory of non-classical organic compounds made at a higher quantitative level and for the computational design of new molecular systems and new structural patterns with unusual geometry and unusual coordination types.

The purpose of this review is to consider the main results of the above-mentioned evolution of the views on non-classical organic structures. Whereas in the early stages of development, considerations of non-classical structures were focused on discussion of the structures of carbonium cations with a hypercoordinate carbon atom,^{3,14} in recent years, they have been markedly extended due to the appearance of new data on unusual stereochemistry of organic compounds. Currently, non-classical organic structures constitute a rather diverse field of theoretical and structural chemistry, which cannot be covered within the framework of a single review. Therefore, we restricted ourselves mainly to the analysis of recent data concerning non-classical types of carbon coordination.

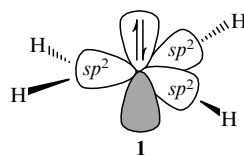
Defining of the problem is as important for each investigation as the results obtained during its solution. Therefore, to preserve the general outlook, we have composed the first sections of this review in such a way as to allow the evolution of each problem to be followed starting from its background up to the most recent results. This strategy is employed to consider the structures of compounds containing a non-tetrahedral tetracoordinate carbon atom[‡] (so-called anti-van't Hoff–LeBel chemistry) and structures of compounds with penta- and hexacoordinate carbon atoms.

The final sections of the review are devoted to the theoretical design of compounds in which hypercoordinate (with coordination numbers from five to eight) carbon atoms, and atoms and ions isoelectronic with them, are encapsulated into planar organic and organoelement cages.

II. Tetracoordinate carbon atom with a planar configuration of bonds in the molecules and ions of organic and organoelement compounds: stereoelectronic strategies of stabilisation

The idea of the existence of a tetracoordinate carbon atom with a planar bond configuration[§] in organic molecules was rejected long ago by van't Hoff and LeBel² because it fails to explain the numbers of isomers of methane derivatives. Subsequently, this idea did not attract the attention of researchers for almost a century until Hoffmann, Alder, and Wilcox,^{15,16} relying on the orbital interaction method, defined the problem of stabilisation of such a centre and proposed ways in which its structure could exist. Seemingly paradoxical at first glance, this problem immediately became (and still remains) one of the most intriguing challenges to the imagination and the capabilities of theoreticians and experimentalists. The initial and later stages of development of this problem have been the subject of detailed reviews.^{9,17–23} Our goal is to consider the most recent results and to distinguish the key strategies directed at solving the problem of stabilising a planar tetracoordinate carbon atom. In this context, the data of earlier studies are resorted to for discussion.

The reasons for the instability of the planar bond configuration at a tetracoordinate carbon atom become clear on examining the Walsh diagram for the methane molecule (Fig. 2). It can be seen that one of the triply degenerate bonding t_{1u} MO of the tetrahedral (T_d) structure is transformed in the planar D_{4h} form (**1**) into a nonbonding a_{2u} MO, which is the p_z AO of the carbon atom and is occupied by two electrons.



Thus, only six electrons are used in the formation of four C–H bonds in the planar structure. According to the most precise calculations, the planar D_{4h} form of the methane molecule is unstable with respect to dissociation giving a hydrogen atom and a methyl radical. This structure is 138.4 [QCISD(T)(fc)/6-311+G(3df,2p)//CISD(fc)/6-311G**]²⁴ or 136.2 kcal mol^{–1} [CCD(full)/6-311++G**]²⁵ energetically less favourable than the tetrahedral T_d form.[¶] Moreover, the D_{4h} configuration does

[‡] Here and below, we mean the topological tetrahedral type rather than the exact tetrahedral geometry with angles of 109°28'.

[§] Below, carbon atoms with this bond configuration are referred to as planar tetracoordinate carbon atoms.

[¶] Expansion of the abbreviations and description of calculation techniques and the orbital basis sets can be found in the book by J B Foresman, A Frish *Exploring Chemistry with Electronic Structure Methods* (Pittsburg: Gaussian Inc., 1996).

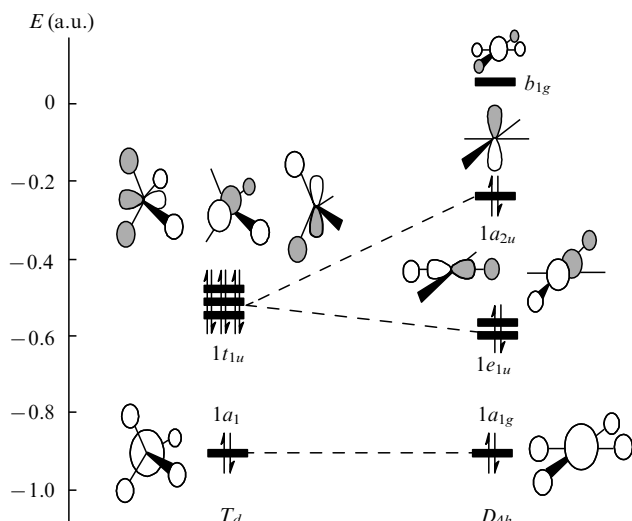
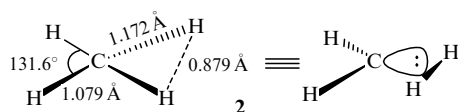


Figure 2. Correlation diagram of the molecular orbitals for tetrahedral and square-planar configurations of the methane molecule.

not even correspond to any local minimum in the potential energy surface (PES) of methane. As predicted by both earlier (MINDO/3) and later (RHF/4-31G) calculations,^{9,26} the vibrational spectrum of the planar structure contains four imaginary frequencies, which imply the occurrence of four types of deformations resulting in barrier-free rearrangements of the molecule.

A different planar form of methane with C_{2v} symmetry, structure **2**, is preferred from the energy standpoint.



This form is not matched by any local minimum in the PES either, but it presents interest as illustrating the adaptation of a planar structure to the electron deficiency experienced by its C–H bonds. This structure and the energetically more favourable structure **3g** (C_s symmetry), which is shown in Fig. 3, can be considered as complexes formed by singlet methylene ($^1A_1$) and a hydrogen molecule. Both structures (**2** and **3g**) are stable with respect to dissociation into CH_2 and H_2 . Figure 3 shows the geometric structures of methane corresponding to all the stationary points in the PES found in calculations.²⁵

The electronic and steric structures of the model methane molecule with D_{4h} symmetry provide a key to the quest for stabilisation routes for compounds with a planar tetracoordinate carbon atom. Now we consider these routes.

1. π -Acceptor and σ -donor substituents

The replacement of hydrogen atoms in planar methane by π -acceptor groups results in delocalisation of the lone electron pair in the $1a_{2u}$ orbital (see Fig. 2), while σ -donor substituents partially make up for the electron deficiency of the σ -bonds in the D_{4h} and C_s structures of methane. The concept of electronic stabilisation first put forward by Hoffmann *et al.*^{15,16} and soon supported by extensive *ab initio* calculations²⁷ is the key and the most successful strategy used in computational and experimental quests for compounds with a planar tetracoordinate carbon atom. A recent review²¹ contains a rather comprehensive collection of data on the structures of a broad range of so-called polar organometallic compounds — derivatives of methane, ethene, and cyclopropane in which the hydrogen atoms have been replaced by lithium or sodium atoms or BeH , MgH , BH_2 or AlH_2 groups. This review considers both the results of early theoretical studies and the recent results obtained by Schleyer's group²⁸ using the density functional theory with an extended orbital basis set (B3LYP/6-

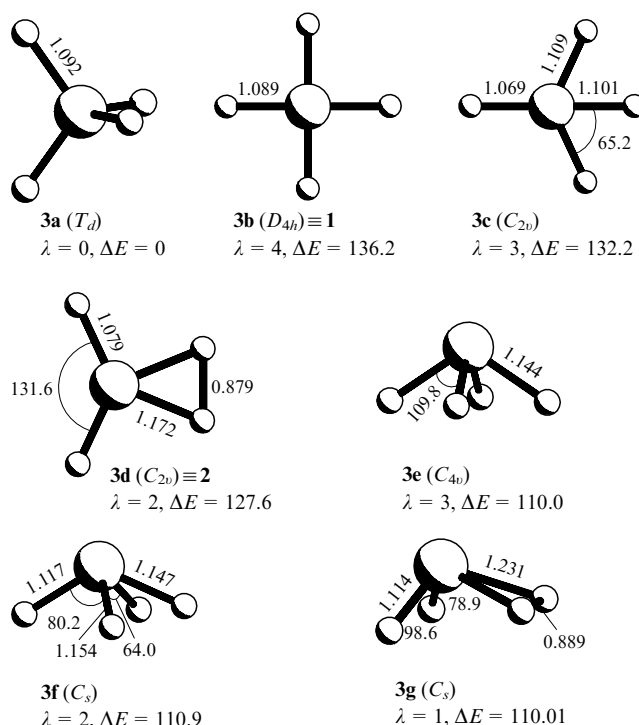
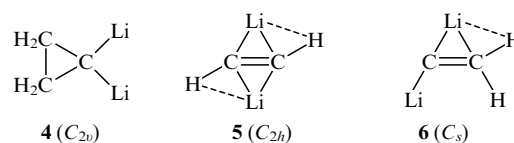


Figure 3. Geometric parameters of the structures corresponding to stationary points in the PES of the methane molecule found²⁵ by CCD(full)/6-311++G** calculations.

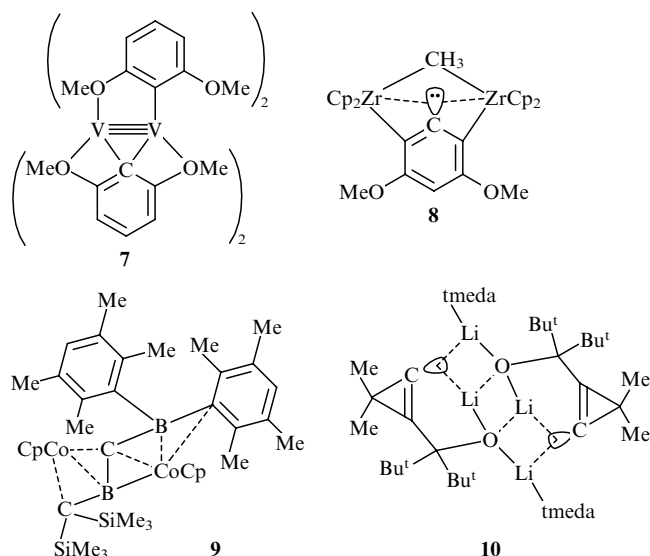
Here and below, λ is the number of negative eigenvalues of the Hessian matrix in the given stationary points: for a minimum, $\lambda = 0$; for a transition state (first-order saddle point), $\lambda = 1$; for a second-order saddle point (the top of a two-dimensional hill), $\lambda = 2$. The relative energies (ΔE /kcal mol⁻¹) of configurations are corrected for the zero-point energy (ZPE) of harmonic vibrations. Here and below, the bond lengths are given in Ångströms and the bond angles are in degrees.

311++G**). The results fully confirm the expected effect, namely, a substantial decrease in the energy gap between the planar and tetrahedral structures (here and below, the tetrahedral topology is meant). For compounds such as 1,1-dilithiocyclopropane or 1,2- and 1,1-dilithioethenes, structures with planar tetracoordinate carbon centres (structures **4**–**6**, respectively) are energetically the most favourable.



Divanadium complex **7** was, apparently, the first compound with a planar tetracoordinate carbon atom to be studied experimentally. Its structure was established by X-ray diffraction analysis.²⁹ In this compound and in the structurally related dizirconocene complex **8**, the planar configuration exists due to the multicentre bond formed by the carbon sp^2 orbital of the phenyl anion, similar to binding in the C_{2v} form of methane (structure **2**). Complex **9** belongs to the extensive class of bimetallic complexes in which planar tetracoordinate carbon atoms are linked to transition (or nontransition) metal atoms.³⁰ A virtually planar geometry of the carbon centre was found in compound **10**, which is related to substituted 2-lithiocyclopropene,³¹ and in a number of carbides, for example, in $Ca_4Ni_3C_5$, which was studied in detail both experimentally³² and theoretically.³³ Numerous examples of bimetallic complexes with structures similar to **7**–**10** and a description of the methods for their synthesis can be found in reviews.^{22,23} All these data can serve as a good illustration for

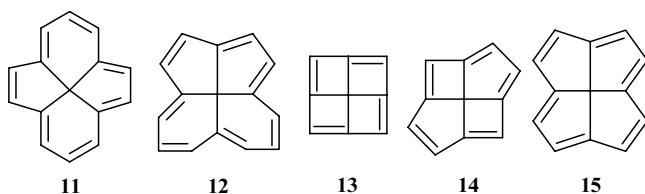
the effectiveness of R Hoffmann's concept of electronic stabilisation of a planar tetracoordinate carbon centre.



Cp is cyclopentadienyl, tmeda is tetramethylethylenediamine.

2. Carbon atom in the centre of the annulene ring

Yet another idea of stabilising a planar configuration of carbon, also proposed by R Hoffmann and coworkers,¹⁶ implies incorporation of this carbon atom into an annulene ring having an aromatic ($4n + 2$) electron shell. This gives rise to structures such as, for example, compounds **11** and **12**. Indeed, extended Hückel calculations showed that these structures actually have a closed electron shell characterised by a rather wide energy gap between the highest occupied and lowest unoccupied molecular orbitals. Meanwhile, structures **13**–**15** with antiaromatic annulene rings proved to be unstable.



The MINDO/3³⁴ and MNDO³⁵ semiempirical calculations with geometry optimisation confirmed the instability of planar structures **13**–**15**. However, according to these calculation techniques, the planar configuration is not realised for compounds **11** or **12** either. Figure 4 shows the stable conformations of fenestranes **11**, **12** and **15** which we determined by B3LYP/6-311 + G** calculations. It can be seen that the central carbon atom in these structures retains the tetrahedral configuration of bonds, although the angular distortions may reach 30°. It is of interest that in compounds **11** and **12**, the charges on the central carbon atom are +3.6 and +3.7, respectively,[†] i.e., all the valence electrons of carbon are displaced to the periphery of the molecule. The aromaticity of the 14-membered rings ($\sim 18 \pi$ electrons) is retained and the effective radius of the central atom decreases, which results in a lower steric strain. However, in compound **15**, the charge on the central carbon atom is 2e lower (+1.9) and, as a consequence, the conjugated 12-membered ring contains 14 π electrons, which complies with the aromaticity condition.

[†] From here on, Mulliken charges are considered.

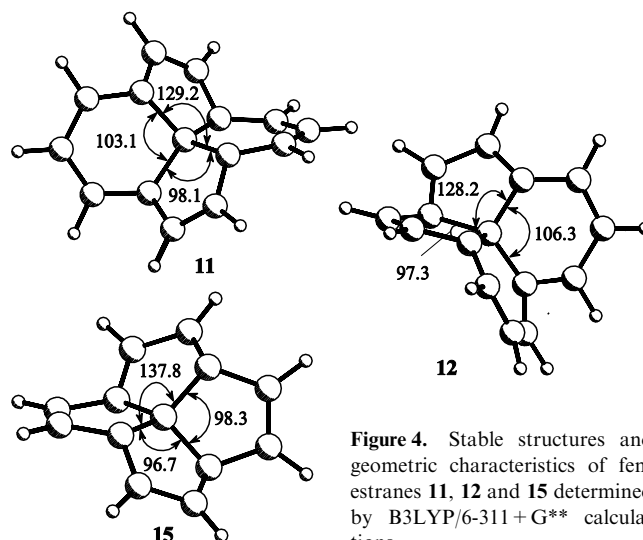


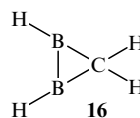
Figure 4. Stable structures and geometric characteristics of fenestranes **11**, **12** and **15** determined by B3LYP/6-311 + G** calculations.

3. Carbon atom in a small ring

One conclusion drawn by Schleyer and coworkers²⁷ on the basis of extensive calculations states that stabilisation of a planar tetracoordinate carbon atom could be attained by incorporating it into a small ring. This was explained by the fact that the angular strain in three- and four-membered rings (the HCH angle in planar structure **1** is 90°) would be lower than in the case of the tetrahedral configuration (the HCH angle is 109.5°). This conclusion is also supported by the fact²⁶ that the HCH angle in molecule **2** (C_{2v} symmetry) is close to the bond angles in small rings. The role of this factor shows itself, for example, in comparison of the relative stabilities of the acyclic dilithiomethane and 1,1-dilithiocyclopropane. In the latter case, structure **4** with a planar carbon atom is more stable, whereas for the former case, the tetrahedral configuration is 2.5 kcal mol⁻¹ energy preferred (B3LYP/6-311 + G** calculation).²¹

4. Planar tetracoordinate carbon atoms in organoboron cages. The stabilising role of ligand–ligand interactions

This approach to stabilisation of structures with a planar tetracoordinate carbon atom is focused on the combined realisation of the electronic and steric effects considered above. Even early *ab initio* calculations by the Hartree–Fock procedure³⁵ showed that incorporation of a tetracoordinate carbon atom into a three-membered 1,2-diboracyclopropane ring creates favourable conditions for ring flattening: the boron atoms have vacant p_z orbitals involved in the delocalisation of the lone electron pair of carbon and, hence, they exhibit σ -donor properties. However, allowance for electron correlation in terms of the MP2/6-31G* (see Refs 36, 37) or B3LYP/6-311 + G* (see Ref. 21) approximations showed that neither structure **16**



nor planar 2,3-diborapentane **17c**, incorporating a diboracyclopropane ring, is a true minimum on the PES. According to the most precise MP2(full)/6-311 + G** calculations,³⁸ compound **17c** is a transition state of an almost barrier-free (the activation energy $\Delta E = 0.23$ kcal mol⁻¹) enantiotopomerisation of the tetrahedral conformation.

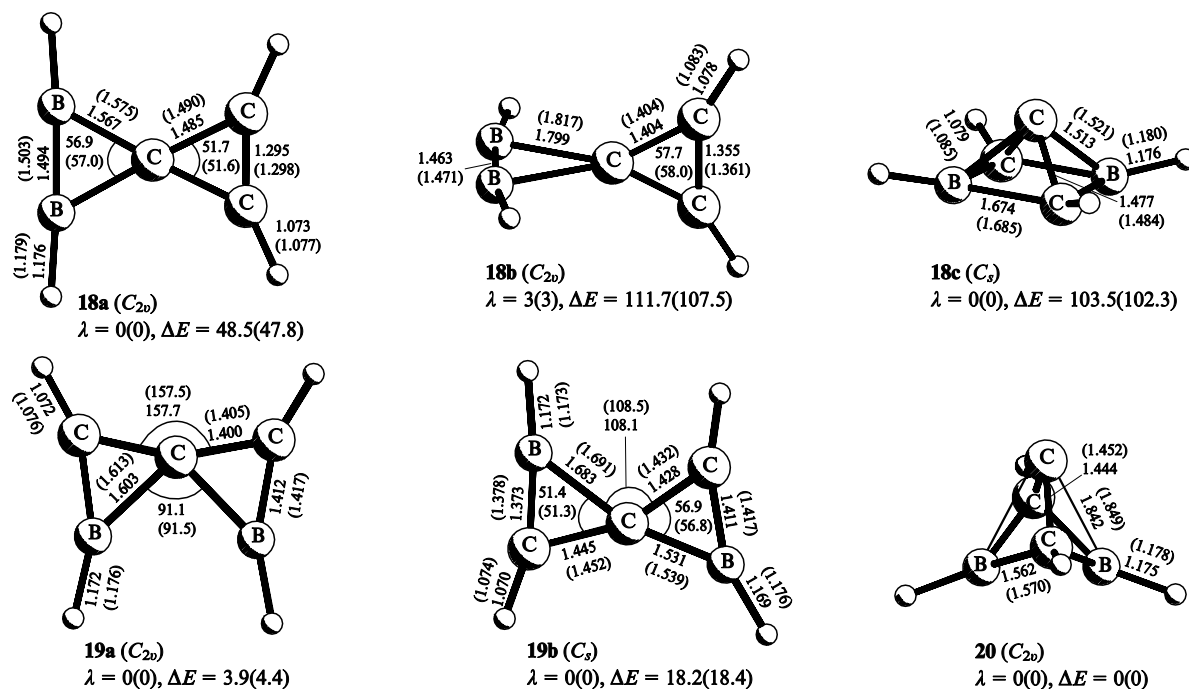
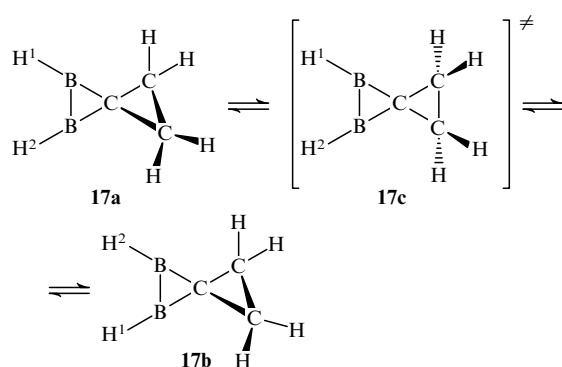


Figure 5. Geometric characteristics, relative energies (ΔE , kcal mol⁻¹), and λ values for boron-containing heterocyclic compounds **18a-c**, **19a,b** and **20** determined by MP2(full)/6-31G** and MP2(full)/6-311++G** calculations (the values in parentheses).³⁸



On passing to 2,3-diboraspicyclopentene, the energy levels of the tetrahedral (**18b**) and planar (**18a**) structures (Fig. 5) are reversed. In the planar structure **18a**, each three-membered ring contains two π electrons, *i.e.*, possesses a certain degree of aromaticity; this provides additional stabilisation to this structure. It can be seen from Fig. 6 that two bonding π MOs of structure **18a** fully correspond to the bonding π MO of the cyclopropenium ion. As a consequence, structure **18a** is indeed a true minimum on the PES. According to MP2(full)/6-311++G**+ZPE calculations, the structure with the planar carbon atom is 58.2 kcal mol⁻¹ energetically more favourable than structure **18b** with the tetrahedral spiro carbon atom. The latter corresponds to the top of a hill in the PES ($\lambda = 3$).

Figure 5 presents the data on the geometry of structures **18a** and **18b** and the type of PES stationary points corresponding to these structures. The same Figure also shows data for the isomeric stable species **19a** and **19b**, containing a planar tetracoordinate carbon atom. The structure **19a** is only 3.9 kcal mol⁻¹ energetically less favourable than the singlet carbene structure **20**, corresponding to the global minimum in the PES of $C_3B_2H_4$.

The stabilisation of the planar carbon centre in compounds **18a** and **19a,b** is due to a combination of all factors including the σ -donor and π -acceptor effects of the neighbouring boron atoms, the incorporation of this carbon in the small ring, and the presence

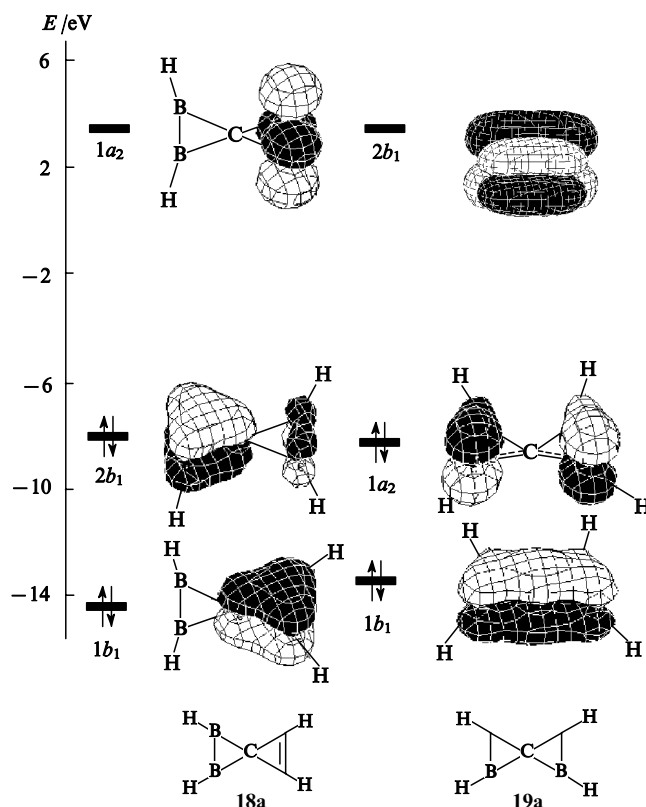
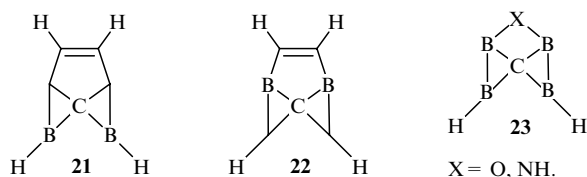


Figure 6. Shapes of the π -molecular orbitals of planar structures **18a** and **19a**.³⁸

of the stable π -conjugated system. The last-mentioned factor is nothing but creation of the conditions for stabilising ligand–ligand interactions, which are weaker or totally missing in the structures with tetrahedral carbon atoms. The enhancement of

this interaction following an extension of the π -system of the ligand environment provides additional stabilisation to structures with a planar carbon atom, for example, in compounds **21**–**23**.³⁸



5. The Jahn–Teller instability of tetrahedral structures

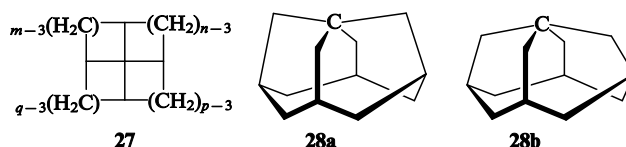
The ligand–ligand bonding interactions play an especially important role in the pentaatomic structures CX_2Y_2 , CX_3Y^{n-} and CX_4^{n-} ($X = Al, Ga; Y = Si, Ge; n = 0, 1$) which incorporate a planar tetracoordinate carbon atom.^{39–42} For example, the planar Al_4 cage in CAI_4^- behaves as an aromatic 2π -electron system.⁴³ According to calculations,⁴³ the stability of the planar structures for these compounds is directly related to the formation of bonding four-centre σ - and π -type orbitals in the ligand. In addition, the higher stability of the planar structures with respect to the tetrahedral isomers can be attributed to the fact that the 17- or 18-electron valence shells in the tetrahedral compounds CX_4 ($1a_1^2 1t_2^6 2a_1^2 2t_2^6 1e^1$ and $1a_1^2 1t_2^6 2a_1^2 2t_2^6 1e^2$) correspond to degenerate electronic states and, hence, they are subject to Jahn–Teller deformations.⁴⁰ Meanwhile, 16-electron compounds with the closed $1a_1^2 1t_2^6 2a_1^2 2t_2^6$ electron shell, for example, CAI_4 , retain the tetrahedral structure. It can be seen from the data shown in Fig. 7 that the structures of the CSi_2Ga_2 (**24c**) and CGe_2Al_2 (**25c**) 18-electron compounds with tetrahedral carbon atoms are energetically less favourable than the planar *cis*- (**24a** and **25a**) and *trans*-isomers (**24b** and **25b**). They do not correspond to local minima on the PES, being transition states. It is of interest that in the case of CSi_2Al_2 (**26a**), the four-membered ring formed by the

ligands is not sufficiently large for the carbon atom to occupy its centre. As a consequence, the carbon atom is expelled from the ring plane to form a somewhat more stable pyramidal form **26c**. However, the energy gap and the vibration frequency with a negative force constant are so small that the fluctuating structure CSi_2Al_2 should be considered as having C_{2v} effective symmetry.

The photoelectron spectra of the CAI_4^- , CAI_3Si^- and CAI_3Ge^- anions generated by laser vaporisation of the corresponding carbide clusters and detected using time-of-flight photoelectron spectroscopy^{40–42} are consistent with a planar structure of these anions. Theoretical and experimental facts supporting the planar structure for the 17-electron $SiAl_4^-$ and $GeAl_4^-$ anions were obtained in a similar way. Planar and nearly planar C_s forms were found for the 16-electron species, $SiAl_4$ and $GeAl_4$.⁴⁴ The simple planar clusters such as **24**–**26** represent, in principle, new types of structural patterns that can exist in solid-state compounds with properties useful for high-technology materials.^{43–45}

6. Flattening of the tetrahedral configuration of the carbon atom in sterically strained saturated systems

The strategy for steric stabilisation of the planar angular deformation of bonds at a tetrahedral carbon atom by placing the atom at the centre of a saturated polycyclic system is similar to that considered above in Section 1.2. Numerous theoretical and experimental studies have been devoted to the development of this approach (see the reviews^{17–20, 46} and references therein). Particular attention was drawn to $[m.n.p.q]$ fenestranes **27** and, subsequently, to bowlanes **28**. The most important result of these studies, as in the case of compounds of the type **11** and **12**, was the conclusion that complete flattening of the tetrahedral structure cannot be attained.



Both semiempirical (MINDO/3^{12, 47} and MNDO⁴⁸) and *ab initio*^{49, 50} calculations showed that the [4.4.4.4]fenestrane molecule (**29**), which is the best candidate to form a planar structure, exists preferentially as a flattened tetrahedral D_{2d} form (**29a** and **29b**). Contrary to suggestions,⁵¹ the isomeric pyramidal C_{4v} conformation proved to be energetically less favourable [by 28.5

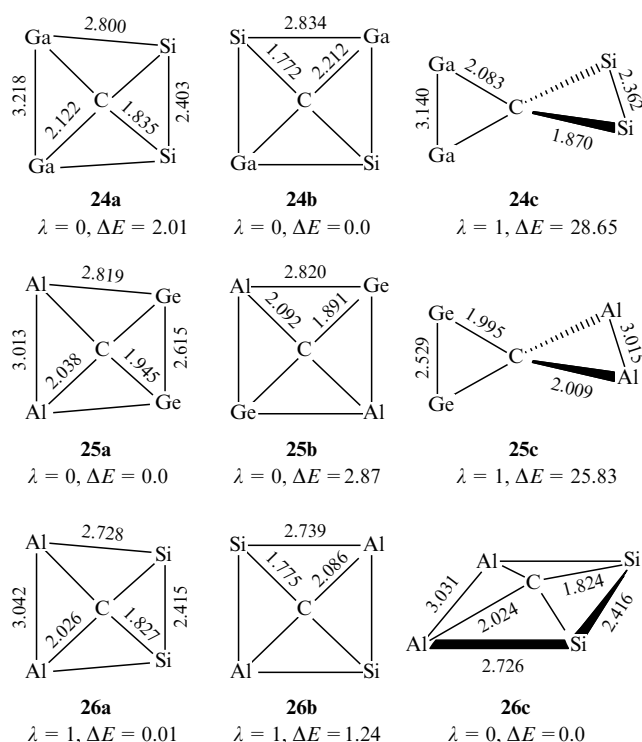
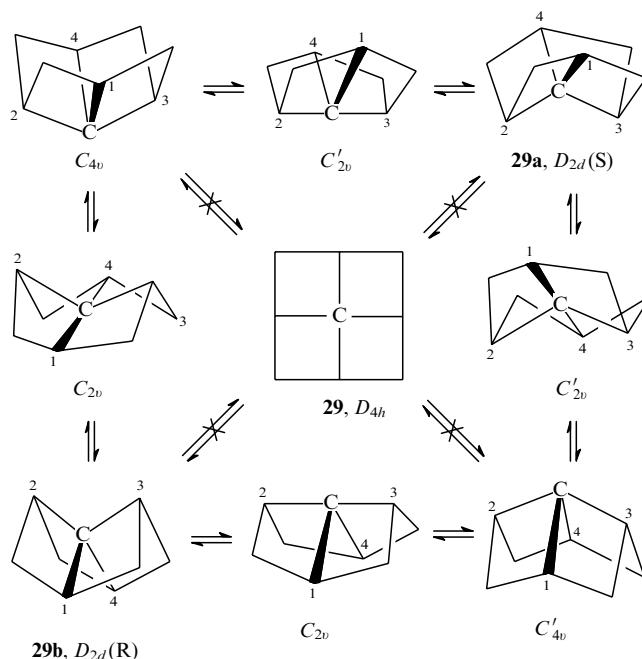


Figure 7. Geometric parameters, relative energies ($\Delta E/\text{kcal mol}^{-1}$) and λ values for the CGa_2Si_2 (**24a**–**c**), CAI_2Ge_2 (**25a**–**c**) and CSi_2Al_2 (**26a**–**c**) clusters calculated by the MP2(fc)/6-31G** (for CGa_2Si_2 and CAI_2Ge_2) and MP2(full)/6-311 + G** (for CSi_2Al_2) techniques.⁴⁰

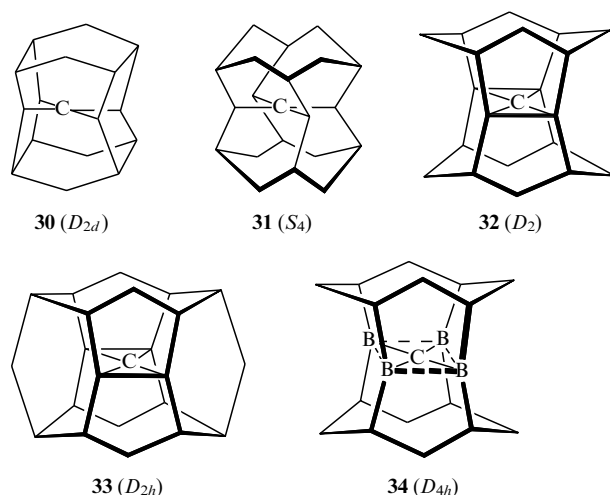


or 48.3 kcal mol⁻¹ according to MINDO/3⁴⁷ and MP2(fc)/4-31G⁵⁰ calculations, respectively]. Interconversion of the *D*_{2d} and *C*_{4v} forms proceeds *via* a transition state with *C*_{2v} symmetry, which is 17 kcal mol⁻¹ higher in energy than the *C*_{4v} form. The planar *D*_{4h} form **29** is unstable; it corresponds to the top of a hill on the PES. The pattern of conformational transitions given below reflects the general topology of the PES of [4.4.4]fenestrane.⁴⁷

Analogous structural transformations take place in the case of bowlane **28**. According to RHF/6-31G* calculations,⁵² the energy minimum corresponds to the flattened tetrahedral structure **28a**, while the structure **28b** with a pyramidalised quaternary carbon atom is a transition state in the interconversion of the mirror topomers **28a**.

7. Planar tetracoordinate carbon atom inside a rigid three-dimensional cage of bonds

A successful (in theory) route of development of the steric (mechanic) strategy for planarisation of bonds around a tetracoordinate carbon atom has been provided by computational design of alkaplans and spiroalkaplans. These polycyclic structures can be constructed from planar neopentane and spiro-pentane units by incorporating peripheral carbon atoms into rigidly connected cycloalkane fragments.^{53–56} Complete flattening of bonds around the central carbon atom is not attained in alkaplans; according to RHF/6-31G* calculations, the C–C–C angles in the hexaplane **30** and octaplane **31** molecules are 168.6° and 168.8°,^{53,54} In the case of spirooctaplane **32**, the deviation from the ideally planar configuration is only 3.1°. The complete planarisation of bonds around the central carbon is found in dimethanospiro[2.2]octaplane **33**; note that this result has been obtained by a rather high-level calculation (MP2/6-311+G**).⁵⁵ The higher occupied MO of each of the compounds **30–33** is a *p*_z orbital localised on the planar carbon atom. This accounts for the exceptionally low ionisation potentials of these hydrocarbons (4.5–5.0 eV), which are comparable with the ionisation potentials of alkali metals.



An interesting route of development of the alkaplans design can be found in a study by Wang and Schleyer.⁵⁷ In this case, flattening of a tetracoordinate carbon atom was attained using not only steric (mechanical) factors but also electronic factors which are favourable for this type of deformation. The calculations (B3LYP/6-311+G**) carried out by the researchers cited showed that boraplane **34**, formed from octaplane **31** *via* replacement of four carbon atoms adjacent to the central atom by boron atoms, has *D*_{4h} symmetry and, hence, contains a planar carbon atom. A peculiar feature of structure **34** is the perpendicular orientation of two B–C bonds with respect to the bonds of the central carbon atom. Unlike octaplane **31**, in the case of boraplane **34**, the highest occupied MO is not localised at the central atom but is distributed over the perimeter of the borocarbon skeleton. This involvement

of the lone electron pair in multicentre bonding is responsible for the additional stabilisation of the planar form, realised in neither octaplane **31** nor the C(BH₂)₄ fragment simulating the structure of the boraplane mirror plane.

III. The mechanism of intramolecular inversion of the tetrahedral configuration of bonds at the carbon atom

The results of theoretical and experimental studies of molecules and ions in the ground electronic state considered in the previous Section attest to the possibility of stabilisation of a planar tetracoordinate carbon atom. This brings up the question — whether it is possible to stabilise the structures of transition states of these compounds in such a way as to decrease substantially the energy barrier to the inversion of tetrahedral forms and to identify the classes of organic and organoelement compounds stereochemically non-rigid with respect to this inversion.[‡]

Even early semiempirical and *ab initio* (RHF/DZ) calculations^{58,59} of the PES for enantiotomerisation of the methane molecule carried out assuming that the four C–H bonds remain equivalent along the whole reaction path showed that the square-planar structure **1** does not correspond to a first-order saddle point and does not represent a transition state of stereoisomerisation. When this constraint was eliminated,^{9,60} MINDO/3 calculations showed that inversion of the tetrahedral configuration of the methane molecule proceeds as an asymmetrical digonal twist deformation, the transition state being a *C*_s structure the geometry of which is quite similar to the geometry of the transition *C*_s structure **3g** and to other structures of this type determined using rigorous *ab initio* calculation techniques.^{24,61,62} The data presented in Table 1 show that the relative energy of the *C*_s transition state is approximately 25–30 kcal mol⁻¹ lower than the energy of the planar methane structure with *D*_{4h} symmetry. However, this structure is still unstable with respect to the CH₄ → CH₃⁺ + H⁺ decomposition, which requires 104 kcal mol⁻¹. This means that the non-dissociation route of methane inversion is impracticable under usual conditions.

Table 1. Inversion barriers of the methane molecule obtained in the most precise *ab initio* calculations.

Method	Δ <i>E</i> ^a /kcal mol ⁻¹	Ref.
MCSCF/TZV + + G(<i>d, p</i>)	125.6	61
SOCI/TZV + + G(<i>d, p</i>)	117.9	61
MP2(full)/6-311 + G**	109.2	24
CISD(fc)/6-311G**	117.9	24
QCISD(T)(fc)/6-311 + G(3 <i>df, 2p</i>)// CISD(fc)/6-311G**	110.2	24
QCISD(T)(fc)/6-311 + G(3 <i>df, 2p</i>)// CISD(fc)/6-311G** + ZPE	105.1	24
B3LYP/6-311G** + ZPE	109.4	62
CCD/6-311 + + G**	115.4	25
CCD/6-311 + + G** + ZPE	110.1	25

^a Energy difference between structures **3g** (transition state with *C*_s symmetry) and **3a** (ground state with *T*_d symmetry).

The inversion of the tetrahedral structure is one of the most important structural types of polytopal rearrangements. The reaction trajectories corresponding to digonal twist

‡ Stereochemically non-rigid molecules have low barriers to an intramolecular rearrangement (too low to be detected on the NMR time scale); therefore, they undergo fast (on the NMR time scale) reversible rearrangements.

($T_d - D_2 - \bar{T}_d$) or tetrahedral compression ($T_d - D_{2d} - \bar{T}_d$) deformations are symmetry allowed.^{15, 63, 64} The latter mechanism is also referred to as edge inversion^{65, 66} (as opposed to vertex inversion, characteristic of the stereoisomerisation of tricoordinated pyramidal structures). Detailed investigations^{61, 62} of the reaction pathway of methane stereoisomerisation using the method of intrinsic reaction coordinate (*i.e.*, the trajectory obtained by moving down from the point on the PES corresponding to the transition state along the transition vector⁶⁷) showed that these trajectories are actually more intricate (Fig. 8). As follows from Fig. 8, the change in the geometry can be described by the digonal twist pattern only at early stages of inversion, while after the initial rotation of the plane of one CH_2 fragment relative to the other, the central atom undergoes pyramidalisation, which is not taken into account in the above schemes.

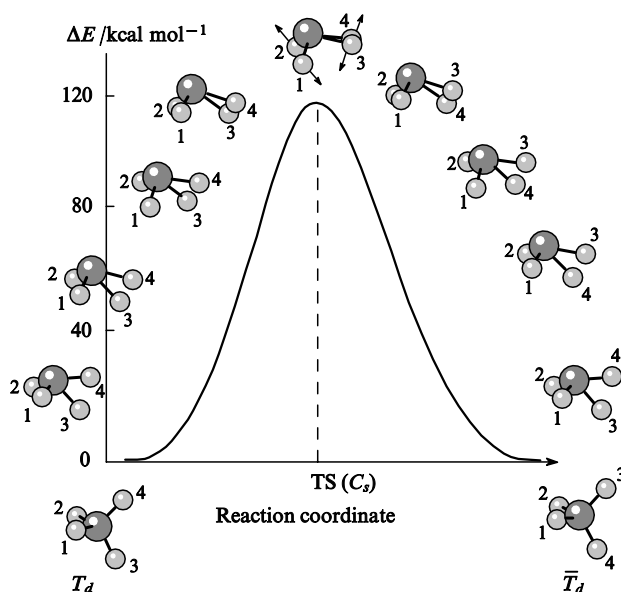
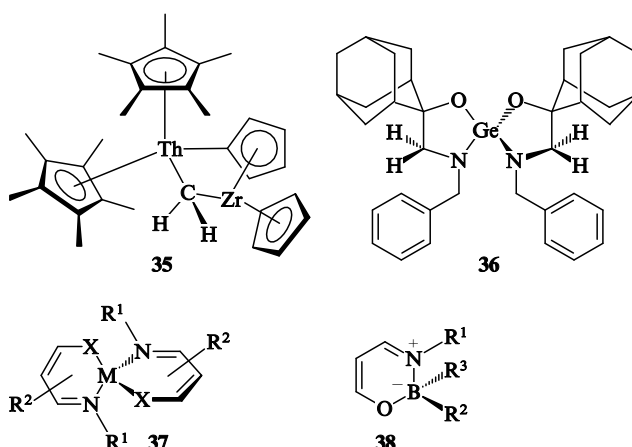


Figure 8. Geometry evolution of the methane molecule along the energy profile of the tetrahedral configuration $T_d - C_s - \bar{T}_d$ according to *ab initio* calculations.^{25, 62}

It would be of interest to find out how the decrease in symmetry caused by partial replacement of the hydrogen atoms in the methane molecule by other atoms or groups would influence the type of reaction trajectory in the inversion process. Such calculations based on the intrinsic reaction coordinate technique have so far been performed only for the difluoromethane molecule (the Hartree–Fock method in a small STO-3G basis set).⁶⁸ Two transition states (planar *cis*- and *trans*-structures) were identified; they correspond to the reaction pathways typical of the digonal twist and tetrahedral compression mechanisms, respectively.

The question of what structural factors could stabilise the C_s form of the transition state of the inversion of type **3g** tetrahedral configuration has not been discussed in the literature. In principle, it is clear that a solution of this problem is the same as the solution of the problem of stabilisation of a planar tetracoordinate carbon atom. Thus in complex **35**, due to the presence of two electro-positive metal atoms at the carbon center, the barrier to inversion decreases to a level that can be determined by dynamic ^1H NMR from coalescence of the signals for the methylene group protons. According to EHMO calculations, stereoisomerisation of complex **35** proceeds *via* a non-dissociative mechanism and the transition state contains a planar tetracoordinate carbon atom.⁶⁹

The energy gap between the tetrahedral and planar structures formed by Main Group elements is known to narrow with a decrease in the electronegativity of the central atom.^{9, 70} On passing from carbon atom to isoelectronic Be^{2-} , B^- , Al^- , Si ,



$\text{M} = \text{Be, Zn, Cd, Hg; X} = \text{O, S, Se;}$ $\text{R}^1, \text{R}^2, \text{R}^3 = \text{Alk, Ar, Hal, NO}_2$.
 $\text{R}^1, \text{R}^2 = \text{Alk, Ar, Hal, NO}_2$.

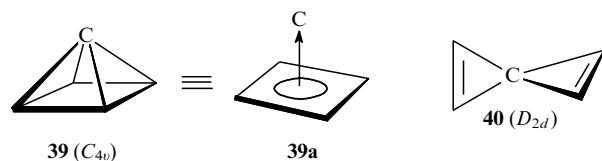
and Ge atoms and to d^{10} atoms (Zn, Cd, Hg), the ordering in energy of the frontier orbitals is reversed; as a consequence, stabilisation of the planar configuration can be attained by introducing electronegative substituents containing lone electron pairs. There are quite a few examples of stereochemically non-rigid compounds of this type, in particular, one can mention bis(ethanolamino)germanium derivative **36** (see Ref. 71) and the extensive group of bis-chelate complexes **37** (see Refs 72, 73). It should be noted, however, that in the general case, the non-dissociative intramolecular inversion of configuration is not the only mechanism responsible for the exchange processes observed by NMR.^{72–74} Among compounds **35–37**, quite reliable proof for the non-dissociative mechanism of inversion has been obtained only for complexes **37** with d^{10} metals,^{72, 75} whereas for complexes **35** and **36**, a mechanism involving cleavage–recombination of one bond at the central atom also cannot be ruled out. This mechanism is realised for beryllium complexes **37** and 1,3,2-oxazaboroles **38**.^{72, 76, 77}

IV. Structures with a pyramidal configuration of bonds at a tetracoordinate carbon atom

Analysis of the stereochemical configurations and chirality of compounds containing tetracoordinate atoms, in particular, tetracoordinate carbon atoms, is based on consideration of topological characteristics of three possible simplexes (configurations whose symmetry ensures equivalence of all four bonds).⁷⁸ Apart from the tetrahedral T_d and planar D_{4h} structures, this condition is satisfied only by the square-pyramidal C_{4v} form. Early EHMO and *ab initio* (RHF/DZ)^{58, 59} calculations predicted that the C_{4v} structure **3e** of methane (see Fig 3) is energetically more favourable than the D_{4h} form; it is this structure that is formed as the transition state in the inversion of the tetrahedral configuration. This sets the task of stabilising a pyramidal tetracoordinate carbon atom in the molecules of organic compounds. High-level *ab initio* calculations carried out in recent years^{24, 25} fully confirmed the first conclusion: the total energy of the C_{4v} configuration of the methane molecule (calculated with allowance for the zero-point energy) is lower than the total energy of the C_s structure **3g**. However, it was found that the stationary point corresponding to the methane molecule with C_{4v} symmetry on the PES of methane is a third-order saddle-point, and, hence, this structure is not a transition state.

The search for routes for stabilisation of compounds containing tetracoordinate carbon atoms with a pyramidal configuration of bonds (below, pyramidal carbon) is mainly carried out in two ways: (1) electronic stabilisation and (2) steric stabilisation. The most important results obtained along the former route include the theoretical prediction of stability of the parent compound of

this class, namely, tetracyclo[2.1.0.0.1³0^{2,5}]pentane (**39**), which was called pyramidane, interpretation of the nature of the stability of structure **39** and a description of the possible methods for pyramidane synthesis.^{59, 79, 80}



The fact that structure **39** is a rather deep minimum on the PES of C_5H_4 was first established in a theoretical (EHMO, MINDO/3, HF/4-31G) study^{12, 59} of isomerisation routes of spiropentadiene **40**, the simplest spiroalkene, which was successfully synthesised only relatively recently.^{81, 82}

It can be seen from Fig. 9 that deformation of structure **40** with variation of the angle coordinates α and β gives rise to four topomers (degenerate isomers) of pyramidane **39**, having lower energies. However, structures **39** and **40** are separated from each other by a high energy barrier, which prevents the exothermic rearrangement **40** $\rightarrow$ **39**. This is the reason for the kinetic stability of spiropentadiene and the possibility of its synthesis. The pyramidane structure does not correspond to the global energy minimum in the PES of C_5H_4 ; however, as in the case of spiropentadiene, it is characterised by high kinetic stability with respect to the possible decomposition and rearrangement reactions.

Pyramidane **39** is computed to be the simplest organic system with a pyramidal carbon atom. As [3.3.3]fenestrane, this compound is the first member of the $[m.n.p.q]$ fenestrane **27** family. Therefore, it comes as no surprise that study of the structure and

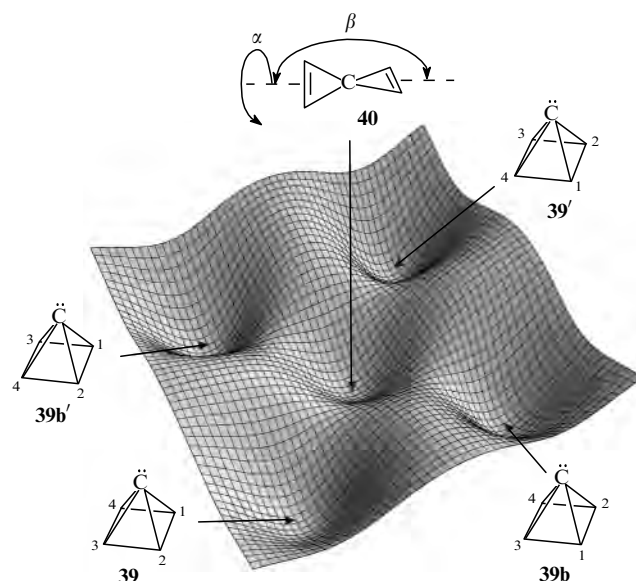


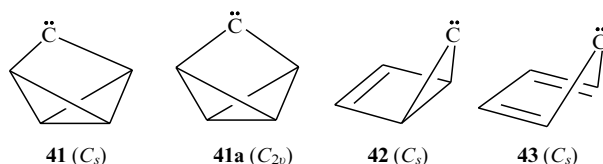
Figure 9. Topography of the PES of C_5H_4 for structures **39** and **40** during deformation of the latter along the angular coordinates α and β .⁵⁹

properties of this compound was the object of a large number of studies,^{83–88} in which *ab initio* calculations were carried out at different approximation levels. The results of calculations of the total and relative energies of the pyramidane **39** molecule and its most stable isomers **40–43** and some other parameters of these molecules are summarised in Table 2.

Table 2. Total ($-E_{\text{tot}}$ /a.u.) and relative (ΔE /kcal mol⁻¹) energies of the pyramidane molecule **39** and its isomers **40–43** in the ground singlet electronic state, charges on the quaternary carbon atoms and dipole moments calculated by *ab initio* quantum-chemistry methods.

Calculation method	$-E_{\text{tot}}$	ΔE	q_C	μ /D	Ref.	Calculation method	$-E_{\text{tot}}$	ΔE	q_C	μ /D	Ref.
Pyramidane 39 (C_{4v})						Isomer 41a^a (C_{2v})					
RHF/3G	189.08749	0	-0.102	1.43	84	RHF/3G	189.06525	13.7	-0.24	3.2	84
RHF/6-31G*	191.45834	0	-0.43	1.79	86	RHF/6-31G*	191.41790	24.4	—	—	86
MP2(fc)/6-31G*	192.09980	0	—	—	86	MP2(fc)/6-31G*	192.03046	42.8	—	—	86
OCISD(T)//MP2/6-31G*	192.15317	0	—	—	86	OCISD(T)//MP2/6-31G*	192.0954	35.4	—	—	86
B3LYP/6-311 + G**	(192.78107)	0	-0.46	1.83	88	B3LYP/6-311 + G**	(192.72932)	32.5	-0.34	3.65	88
MP2(full)/6-311 + G**	192.30990	0	-0.42	1.77	88	MP2(full)/6-311 + G**	192.22987	50.2	-0.29	3.67	88
CCSD/6-311 + G**	192.31312	0	-0.46	1.84	88	CCSD/6-311 + G**	192.26066	32.9	-0.22	3.41	88
Isomer 40 (D_{2d})						Isomer 42 (C_s)					
RHF/3G	189.07558	27.3	-0.123	0	84	RHF/3G	—	—	—	—	84
RHF/6-31G*	191.44637	6.2	+0.25	0	86	RHF/6-31G*	191.44109	10.3	-0.84	—	86
MP2(fc)/6-31G*	192.07803	12.1	—	0	86	MP2(fc)/6-31G*	192.06529	21.3	—	—	86
OCISD(T)//MP2/6-31G*	192.13976	6.8	—	0	86	OCISD(T)//MP2/6-31G*	191.13154	13.2	—	—	86
B3LYP/6-311 + G**	(192.71311)	5.0	+0.40	0	88	B3LYP/6-311 + G**	(192.76380)	10.8	-0.40	3.97	88
MP2(full)/6-311 + G**	192.26986	25.1	+0.59	0	88	MP2(full)/6-311 + G**	192.26111	30.6 ^b	-0.36	3.86	88
CCSD/6-311 + G**	192.29504	11.3	+0.48	0	88	CCSD/6-311 + G**	192.28738	16.1 ^b	-0.55	3.90	88
Isomer 41 (C_s)						Isomer 43 (C_s)					
RHF/3G	—	—	—	—	84	RHF/3G	189.11556	-17.8	—	1.1	84
RHF/6-31G*	191.43272	15.8	-0.77	—	86	RHF/6-31G*	191.48997	-19.9	-0.34	—	86
MP2(fc)/6-31G*	192.06434	22.3	—	—	86	MP2(fc)/6-31G*	192.10866	-6.2 ^c	—	—	86
OCISD(T)//MP2/6-31G*	192.12006	20.8	—	—	86	OCISD(T)//MP2/6-31G*	192.17408	-13.7	—	—	86
B3LYP/6-311 + G**	(192.74965)	19.7	-0.46	4.26	88	B3LYP/6-311 + G**	(192.81089)	-18.7	+0.15	1.02	88
MP2(full)/6-311 + G**	192.26209	30.0	-0.24	4.53	88	MP2(full)/6-311 + G**	192.30280	4.4	+0.28	0.68	88
CCSD/6-311 + G**	192.28218	19.4	-0.36	4.31	88	CCSD/6-311 + G**	192.32741	-9.0	-0.155	1.46	88

^a The C_{2v} structure **41a** is a transition state for the conformational isomerisation of **41** proceeding according to the pattern of wagging vibrations of the carbene centre with respect to the plane of the other four carbon atoms.^{85, 87, 88} ^b At this level of approximation, the C_s structure **42** has one imaginary frequency in the vibrational spectrum. ^c At this approximation level, the C_s structure **43** is a flattened region in the C_5H_4 PES (a first-order saddle point). The adjacent minimum corresponds to a C_2 cumulene form whose total energy is 0.6 kcal mol⁻¹ lower than the energy of the C_s structure.



It follows from the above data that the structure of pyramidine **39** is only 9 kcal mol⁻¹ energetically less favourable than the structure of its carbene isomer **43** which is most stable in the singlet electronic state. The singlet–triplet splitting calculated for structure **39** is rather large (46.8 kcal mol⁻¹) and the strain energy per C–C bond (19 kcal mol⁻¹) is lower than the strain energy in the tetrahedrane molecule (~25 kcal mol⁻¹).^{9, 84} However, it can be expected that pyramidine **39** has a relatively high kinetic stability. The lowest vibration frequencies calculated for the C_{4v} structure of pyramidine^{85, 88} are rather high: 453.6 and 478.9 cm⁻¹ (CCD/6-311 + G**). The PES of C_5H_4 contains no reaction valley to connect the two minima corresponding to isomers **39** and **43**.^{12, 85} The pyramidine structure is energetically more favourable than the structures of other classical carbenes, **41** and **42**. As shown by semiempirical^{79, 83} and *ab initio*^{85, 87, 88} calculations, both carbenes can serve as precursors of pyramidine and appropriate precursors can be found for each of these carbenes.^{89, 90} It has been reported⁸⁷ that the potential barrier to thermal isomerisation of bicyclo[2.1.0]pent-2-en-5-ylidene (**42**) into pyramidine **39** is equal to 16.3 kcal mol⁻¹, while a similar transformation of tricyclo[2.1.0.0^{2,5}]pent-3-ylidene (**41**) requires overcoming a potential barrier of only 3.5 kcal mol⁻¹. This implies that the generation of these precursors would be accompanied by immediate isomerisation in pyramidine. Simultaneously, structure **39** is separated from more stable isomers, for example 3-ethynylcyclopropene, by relatively high barriers corresponding to a half-life of more than 4–5 h at room temperature. Thus, synthesis of pyramidine should be possible.

The nature of the stability of the pyramidine molecule and features of its geometric structure (Fig. 10) are adequately interpreted using the scheme of orbital interactions (Fig. 11) between the fragments forming this molecule — the basal cyclobutadiene fragment and the apical carbon atom (structure **39a**). Stabilisation is mainly due to the formation of the bonding $1e$ MO of the pyramidine molecule upon overlap of the $p_{x,y}$ AO of the apical carbon atom with the degenerate e_g MO of the cyclobutadiene fragment. The sp_z AO pair of the carbon atom and the cyclobutadiene a_{2u} MO form a bonding ($1a_1$), a nonbonding ($2a_1$), and a high-lying antibonding MO of molecule **39**; only the first two of these orbitals are occupied with electrons.

This type of electronic structure is typical of all the pyramidal molecules formed by a π -conjugated cyclic fragment and an apical atom or group. Pyramidal structures of this type have only four bonding (or three bonding and one nonbonding) MOs, which can be populated by π -electrons of the basal fragment and by all valence electrons of the apical atom (or group). The eight-electron

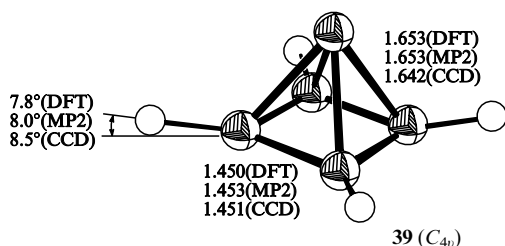


Figure 10. Geometric characteristics of the pyramidine molecule (**39**) calculated by the B3LYP/6-311 + G** (DFT), MP2(full)/6-311 + G** (MP2) and CCD(full)/6-311 + G** (CCD) techniques.⁸⁸

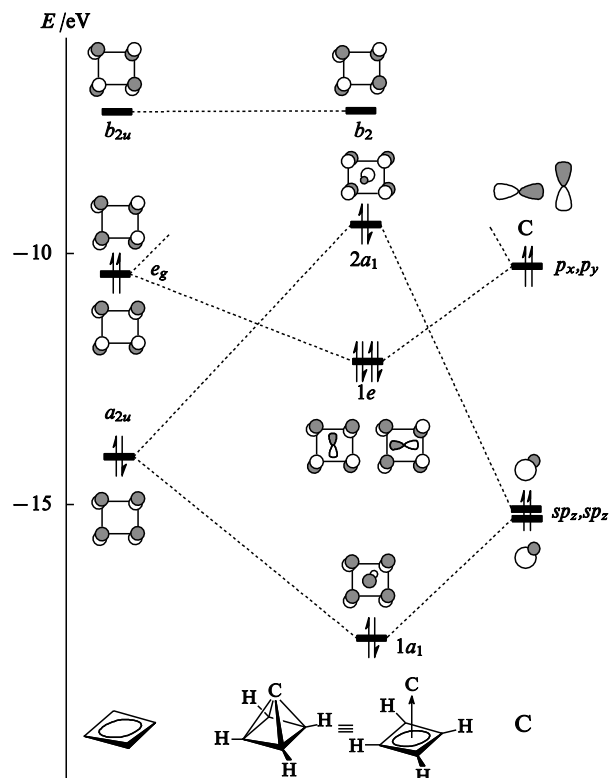
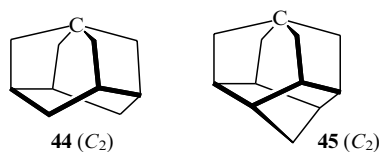


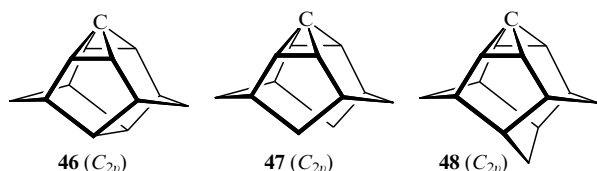
Figure 11. Diagram of the orbital interactions of the fragments of pyramidine molecule **39** ↔ **39a** according to Refs 9 and 12.

The π -MO energy levels of the cyclobutadiene molecule with D_{4h} symmetry were calculated using the EHMO method, the energy levels of the hybrid orbitals of carbon correspond to those given in Ref. 91.

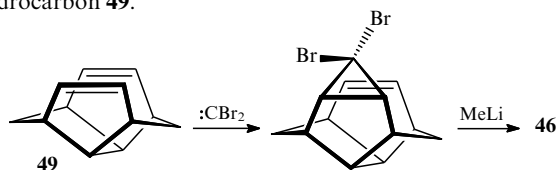
rule determining the stability of pyramidal structures follows from the foregoing.^{9, 11, 12} This rule, attributed to three-dimensional aromaticity conditions,^{92, 93} holds for both heteroatomic systems and transition metal π -complexes (provided that isolobality relations are taken into account).⁷ Numerous examples of pyramidal structures can be found in reviews^{9, 12, 94–97} and recent works.^{25, 98}

The stability of non-classical pyramidal structure **39** is completely dictated by electronic factors. The efficiency of steric (mechanical) stabilisation of organic compounds with a tetra-coordinate pyramidal carbon atom was demonstrated by Rasmussen and Radom.⁸⁶ As in alkaplans and spiroalkaplans (see Section II.7), in compounds with a pyramidal carbon atom, the rigid cage of bonds is based on neopentane and spironeopentane structures with an additional cycloalkane fragment attached. The B3LYP/6-31G* and MP2(fc)/6-31G* calculations showed that the stable hemialkplane (**44**, **45**) and hemispiroalkplane (**46–48**) hydrocarbon structures obtained in this way contain a pyramidal quaternary carbon atom. The degree of pyramidalisation of bonds at the carbon atom in hemialkplanes is low but in spirohemialkplanes, this value approaches that in pyramidine **39** and the calculated lengths of the C–C bonds involving the apical carbon atom (1.632–1.650 Å) are similar to the corresponding bond lengths in pyramidine.



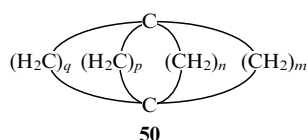


The strain energies of structures **44**–**48** are comparable with the strain energies of well-studied strained structures such as cubane and prismane. Thus, there are reasons for assuming that these compounds could be synthesised. Relying on an efficient method for the preparation of bridged spirooctaplanes,^{99–101} Rasmussen and Radom⁸⁶ proposed the following method for the synthesis of hemispirooctaplane **46** from the available hydrocarbon **49**.



It follows from the data of Table 2 that the apical carbon atom in structure **39** bears a considerable negative charge, while the highest occupied MO is localised almost entirely on this atom and can actually be regarded to be a lone electron pair orbital (see Fig. 10). Similar results have also been obtained for hydrocarbons **44**–**48**. This fact is responsible for fairly low (4.5–5.0 eV) ionisation energies calculated for pyramidal, hemialkyl, and hemispiroalkyl, commensurate in magnitude with the ionisation potentials of light alkali metals, as well as the exceptionally high basicity of these compounds. The proton affinities of compounds with a pyramidal tetracoordinate carbon atom calculated using various methods (they are given in Table 3) are record-breaking values for organic compounds including superbases such as proton sponges.

Formerly, it has been considered that $[m.n.p.q]$ paddlanes **50**, like $[m.n.p.q]$ fenestranes **27**, can also contain pyramidal carbon atoms in the molecule.^{51, 104}

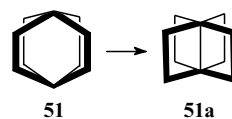


However, all paddlanes known to date contain at least one large ring ($m > 8$), which leads to flattening of the tetrahedral configuration of the quaternary carbon atoms. The structures of lower [1.1.1.1]- and [2.2.2.2]paddlanes (structure **51**) do not

Table 3. Proton affinity PA (kcal mol^{−1}) in the gas phase (298 K) for structures with a tetracoordinate pyramidal carbon atom.

Compound	Calculation method	PA	Ref.
39	CCD/6-311 + G**	236.8	88
	HF/3-21G	253.3	82
	MP2/6-311 + G**//MP2/6-31G*	230.6	86
	MP2/6-311 + G**//MP2/6-31G*	269.3	86
28b	MP2/6-311 + G**//MP2/6-31G*	280.1	86
46	MP2/6-311 + G**//MP2/6-31G*	280.8	86
47	MP2/6-311 + G**//MP2/6-31G*	281.8	86
48	MP2/6-311 + G**//MP2/6-31G*	285.1	86
Tetramethyl-substituted hemispirooctaplane 47	MP2/6-311 + G**//MP2/6-31G*	245.5	102
1,8-Bis(dimethyl-amino)naphthalene (proton sponge)	Experimental data	245.7	103

correspond to minima in the PES;^{48, 52, 105} according to the results of MINDO/3 and MNDO semiempirical calculations,⁴⁸ structure **51** relaxes towards unusual structure **51a** in which the distance between two planar carbon atoms is only 1.56 Å.



Essentially pyramidalised tetracoordinate carbon atoms are found in yet another group of sterically strained compounds, tricyclo[$n.1.0.0^{1,3}$]alkanes.^{99–101, 106–109} The first member of this series of bridged spirooctaplanes, compound **52**, has a sufficient lifetime along the pyramidal-to-spiropentane rearrangement pathway to be detected at -55°C .^{107, 110} Tricyclo[2.1.0.0^{1,3}]alkane (**53**) is still unknown but the next members of this series — compounds **54**, **55** and some of their derivatives — have been prepared and isolated.^{99–101}

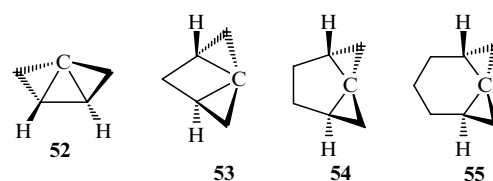
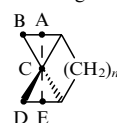


Table 4 summarises the data characterising the spatial structures and strain energies of molecules **52**–**55**. As the ring size increases, *i.e.*, on passing from compound **52** to compound **55**, the $\text{CH}_2\text{—C—CH}_2$ angle rapidly decreases, together with the strain energy of the molecule. For compound **55**, the strain energy almost does not differ from that of spiropentane (63 kcal mol^{−1}).

Table 4. Angular parameters characterising the configuration of the quaternary carbon atom in molecules **52**–**55** and strain energies of these structures found by MP2/6-31G** *ab initio* calculations.¹⁰¹

Compound	n	Folding angle ^a /deg	Twisting angle ^b /deg	Strain energy /kcal mol ^{−1}
52	0	71.5	21.3	137.2
53	1	47.8	6.1	115.5
54	2	26.1	6.3	79.2
55	3	15.0	1.5	66.0

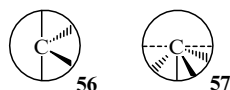
^a The folding angle is $180^\circ - \angle ACE$; ^b the twisting angle is $90^\circ - \gamma$ (γ is the dihedral angle between the ABC and CDE planes).



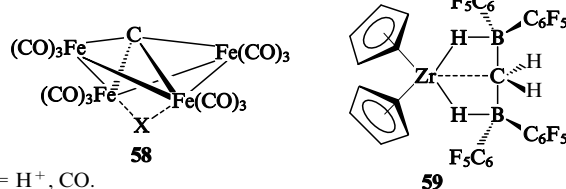
V. Tetracoordinate carbon atom with a bisphenoidal configuration of bonds and inverted tetracoordinate carbon atom

The size of the $\text{CH}_2\text{—C—CH}_2$ angle in tricyclo[2.1.0.0^{1,3}]alkane **53** approaches 180° , and the bond configuration at a quaternary carbon atom is fairly close to that found in bisphenoid **56** ('butterfly' conformation). It has been proposed to call tetracoordinate carbon centres of this type 'half planar'.⁶⁴ In terms of the topological definition,⁹ according to which structures with tetracoordinate carbon atoms are divided into classical and non-classical (anti-van't Hoff–LeBel) ones, depending on the arrangement of the four bonds around carbon — either in both or in only one hemisphere, respectively, — structures of type **56** should be considered non-classical. For compounds containing tetracoordi-

nate carbon atoms, the only other non-classical topological form is represented by structure **57** with an inverted configuration of bonds at the carbon atom.



The half planar tetracoordinate carbon atom occurs in the structures of carbide clusters **58**^{111–113} and in zirconium complex **59**.¹¹⁴



X = H⁺, CO.

The electronic factors promoting stabilisation of the half planar carbon atom in these structures are similar to those effective in structures with planar or pyramidal centres (Fig. 12). In this case, as in the case of planar (D_{4h}) or pyramidal (C_{4v}) structures, the highest occupied MO of the methane molecule having C_{2v} symmetry is formed by the $2a_1$ AO of the lone electron pair of carbon (this AO is delocalised to a very low extent over equatorial C–H bonds). The electrons of this orbital are not involved in bonding, which results in weakening of the σ bonds formed by a half planar carbon atom. Therefore, σ -donor (for example, BHAr[–] groups in compound **59**) and π -acceptor groups are expected to stabilise the tetracoordinate half planar carbon atom. These views have been confirmed by calculations⁶⁴ for model compounds **60**. The results of these calculations are given in Table 5.

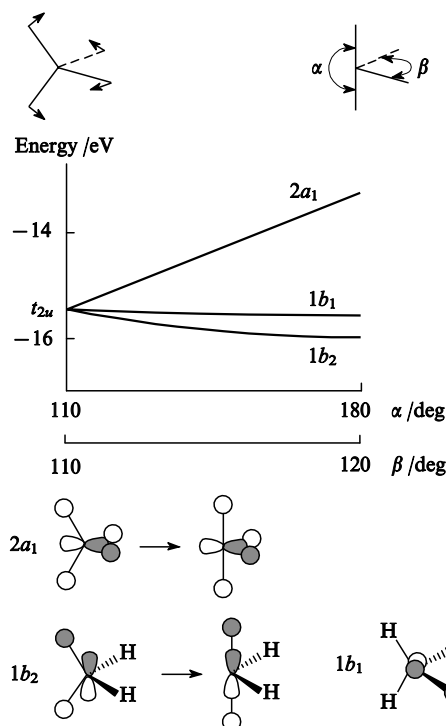
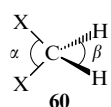


Figure 12. Walsh diagram illustrating the transformation of the t_{2u} orbitals of tetrahedral methane (see Fig. 2) during its deformation into the structure with a half planar carbon atom.⁶⁴

Table 5. Deformation energies (eV) of tetrahedral structures (the α and β angles correspond to structures with the minimum energy) and charges on the carbon atom in compounds **60** determined by EHMO calculations.⁶⁴

X	α^a /deg	β^a /deg	ΔE^b /eV	$\Delta E'^c$ /eV	q_C
H	109.5	109.5	3.06	0.98	–0.44
Me	117	105	3.76	1.15	–0.39
OH	112	117	6.46	2.65	+0.82
CN	114	107	2.70	0.93	–0.01
BH ₃ [–]	120	102	2.06	0.54	–0.96

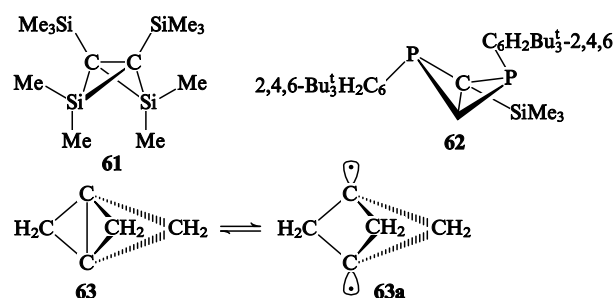
^a The α and β values are given for the tetrahedral configuration corresponding to the global minimum in the PES of disubstituted methane **60**.

^b The deformation energy of the tetrahedral structure into a structure with a half planar carbon atom ($\alpha = 180^\circ$, $\beta = 140^\circ$). ^c The deformation energy of the tetrahedral structure into a structure with a carbon atom geometry identical to that in complex **59** ($\alpha = 180^\circ$, $\beta = 140^\circ$).

In derivative **60** with σ -donor substituents (X = BH₃[–]) in the axial positions, the energy gap between the tetrahedral and bisphenoidal conformations decreases by 1.0 eV, mainly, due to substantial charge transfer to the central carbon atom (*cf.* the charges q_C on half planar carbon atoms).

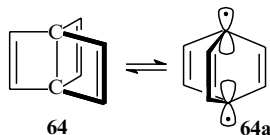
It should be noted that the conformation **56** is destabilised by the strong effect of the π -donor and σ -acceptor hydroxy group, pulling the electron density off the half planar carbon. As a result, the carbon atom acquires a positive charge. Stabilisation of configuration **56** in complex **59** and the rare earth metal complexes (Me₃SiCH₂)Y[(μ -CH₂)₂SiMe₂][(μ -OBu^t)Li(THF)₂]₂ (see Ref. 115) and (Me₃SiCH₂)Sm[(μ -OPh)(μ -CH₂SiMe₃)Li(THF)][(μ -OPh)₂.Li(THF)] (see Ref. 116) is also promoted by the additional coordination of a half planar carbon atom to a metallic centre formed due to electron donation from the carbon $2a_1$ AO to the metal AO.

An inverted (umbrella) configuration of bonds at the carbon atom (structure **57**) can be found in the molecules of some bicyclobutane derivatives, for example, in structures **61**¹¹⁷ and **62**,¹¹⁸ and undoubtedly, in the molecule of highly strained [1.1.1]propellane (**63**), which was synthesised by Wiberg and Walker¹¹⁹ in 1982.



The structures, methods of synthesis and the chemistry of [1.1.1]propellane and its derivatives and higher homologues have been considered in numerous reviews^{120–122} and theoretical studies.^{85, 123–126} As noted by Wiberg,¹²² [1.1.1]propellane appears to be the first multiatomic molecule whose stability, structure, vibrational and photoelectron spectra, and the enthalpy of formation were predicted before its synthesis and all the theoretical predictions were successfully confirmed by subsequent experimental research. Theoretical investigations of compound **63** were mainly focused on elucidating the nature of the central C–C bond and the possibility of its dissociation to give the isomeric biradical **63a**. The results of *ab initio* calculations^{122, 125, 126} convincingly confirm the conclusion, drawn on the basis of orbital interaction analysis,¹²³ stating that the non-dissociated form **63** is preferred. According to HF/6-31G* calculations, the energy benefit is equal to 65 kcal mol^{–1}. The energy gap between structures **63** and **63a**, interrelated by ‘bond-stretch isomer-

ism',^{127, 128} is rather narrow (the difference between the heats of formation of these compounds is only ~ 5 kcal mol⁻¹). The situation is reversed on passing to [2.2.2]propellatriene (**64**). Although the structure **64** with an inverted carbon atom is an energy minimum, the singlet biradical **64a** is energetically more favourable (by 5.1 kcal mol⁻¹), as shown by CASSCF/6-31G* calculations.¹²⁹



The inverted configuration of carbon atoms has been predicted by MP2/6-31G** and B3LYP/6-31G** calculations (see Ref. 130) for a series of polycyclic structures with a bicyclooctane skeleton.

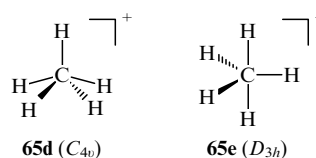
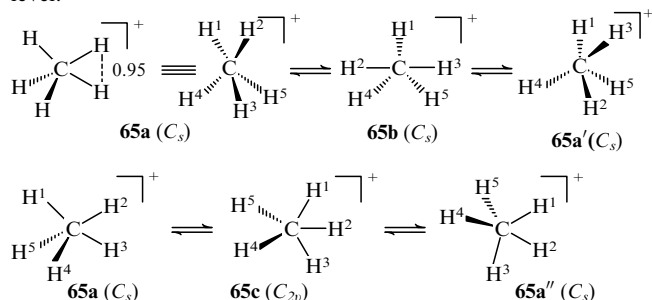
VI. Carbonium ions with penta-, hexa- and heptacoordinate carbon atoms

The preceding Sections of the review were devoted to unusual (*i.e.*, other than tetrahedral) types of carbon coordination. In this and subsequent Sections, we consider compounds of hypercoordinate carbon in which a carbon atom is linked by covalent bonds to five and more atoms. Since a carbon atom has only four valence electrons, it can form only four two-electron (classical) bonds; hence hypercoordination of carbon implies delocalisation of σ -electrons.¹³¹ This effect does not fit into the scope of classical octet theory.^{3, 132} It is noteworthy that the notion of non-classical structure was first introduced to describe the structures of hyper-coordinate carbon.^{131, 133}

1. Methonium ion

The methonium ion is the parent compound for pentacoordinate carbon derivatives. Protonated methane (**65**) was first detected in the gas phase by mass spectroscopy by Talrose and Lubimova^{134, 135} and in superacid liquid media by Olah and co-workers.^{136–138} The methonium ion is important for astrophysics, as its microwave spectrum serves as an indicator of methane content in molecular galactic clouds. The methonium ion is the prototype of intermediate structures formed upon ion–molecular interactions¹³⁹ and, what is more important, in the reactions of saturated hydrocarbons with electrophiles;^{3, 140–143} therefore, it comes as no surprise that the study of its structure and properties has received particular attention from theoreticians. The results of calculations (up to the MP4SDQ/6-311G**//MP2/6-31G* level) carried out before 1984 are summarised in a monograph.¹⁴⁴

The possible structures of the CH₅⁺ cation are described by conformations **65a–e**. The global minimum in the PES of CH₅⁺ corresponds to structure **65a** with C_s symmetry, which can be regarded as a complex of the CH₃⁺ (C_{3v}) cation with an H₂ molecule. The stability of this complex is ensured by the formation of the 3c–2e bond (according to theoretical and experimental data, the energy of dissociation into fragments is 42–44 kcal mol⁻¹). This conclusion was confirmed by recent calculations at the most advanced (of those attainable to date) theoretical level.^{145–149}



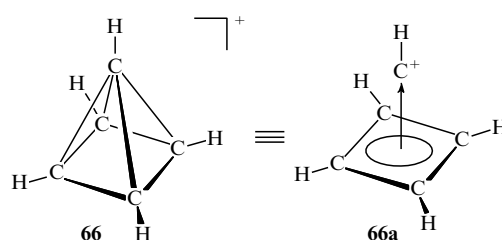
Structure **65b** (C_s) corresponds to a first-order saddle point in the PES and serves as the transition state for rotation of the H₂ fragment; the potential barrier to this process found using various calculation methods is exceptionally low (less than 0.1 kcal mol⁻¹). Structure **65c** (C_{2v}) is also a transition state but of another process, namely, the exchange by hydrogen atoms between the CH₃ and H₂ fragments. A number of experimental studies have been devoted to isotope exchange reactions of this type proceeding at high rates.^{3, 137, 140} The energy of structure **65c** is only 0.9 kcal mol⁻¹ higher than the energy level of structure **65a**; with allowance for the zero-point vibrations, structures **65a–c** are nearly equivalent in energy. This means that proton 'exchange' in the methonium ion is almost barrier-free even at 0 K. Thus it has been hypothesised that the CH₅⁺ cation does not have any definite structure at all. It was proposed that the methonium cation should be considered as an intramolecular liquid and its structure described by statistical functions rather than atomic coordinates (see the publication¹⁵⁰ concerning the structure of the methonium cation entitled 'Cheshire cat smiles'). Powerful experimental proof pointing to an extremely high degree of stereochemical non-rigidity (fluxionality) of methonium cation was obtained when a high-resolution IR spectrum of this cation was finally recorded (after many years of unfruitful efforts) in a matrix of a small number ($n = 1–6$) of hydrogen molecules whose presence is needed for retarding the exchange processes. This spectrum proved to be much more complicated than would be expected for a structure having any definite type of symmetry. Indeed, in the 2770–3150 cm⁻¹ range alone, ~ 900 spectral lines were found.

The question of whether the methonium cation with its unusual fluxional behaviour can be described by a particular molecular structure is still debatable.^{148, 150–152} However, such a question does not arise for its derivatives. There exist a fairly broad spectrum of compounds in which structures like **65a,c**,^{3, 138, 139, 149} or **65b** are realised. The latter is found, in particular, in the structures of σ -complexes formed by metal ions (from Sc⁺ to Cu⁺) with the methane molecule. The structure and stereodynamics of these complexes have been studied theoretically (using density functional theory techniques) in relation to simulation of the problem of decreasing the barrier to the stereomutation of the methane molecule.⁶² It was shown that, when this transformation is catalysed by metal ions, the potential barrier to enantiotopomerisation decreases to 43–50 kcal mol⁻¹. In addition to the stationary points corresponding to structures **65a–c**, the PES of CH₅⁺ was found to contain higher-order stationary points corresponding to highly symmetrical forms **65d,e**.

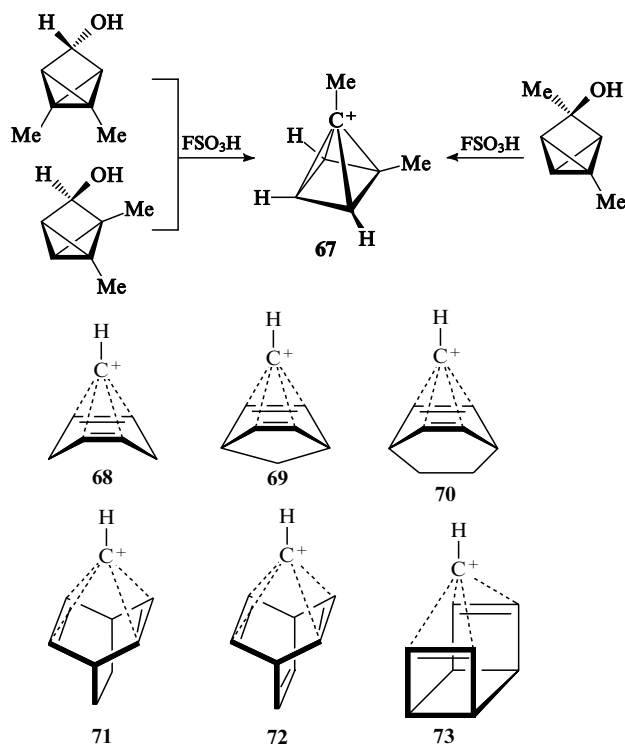
Stabilisation of such bond configurations at a pentacoordinate carbon atom can be achieved only in more complicated structures.

2. The pyramidal cation (CH)₅⁺

The (CH)₅⁺ cation (**66**) is a classical example of a structure with a square-pyramidal configuration of bonds about a pentacoordinate carbon atom.^{153–155}



Almost simultaneously, Masamune *et al.*¹⁵⁷ synthesised the first derivative of the pyramidal $(\text{CH}_5)^+$ cation, compound **67**, its bishomo-derivatives and other analogues (**68–73**).^{158–160}



The pyramidal cation **66** has an unusual electronic structure: its electron density is concentrated on the apical carbon atom. Thus according to CCD/6-311+G** calculations, the negative charge on this carbon equals -0.18 and the whole positive charge

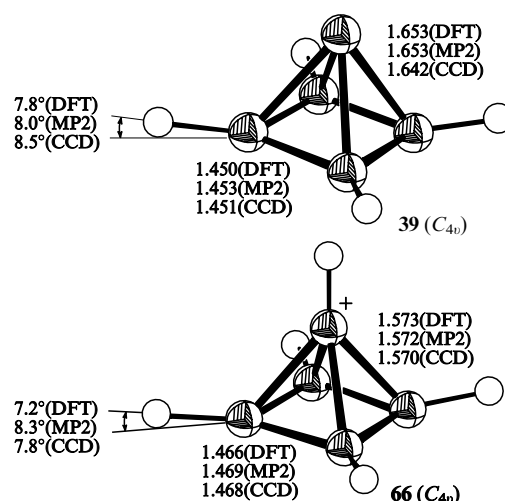
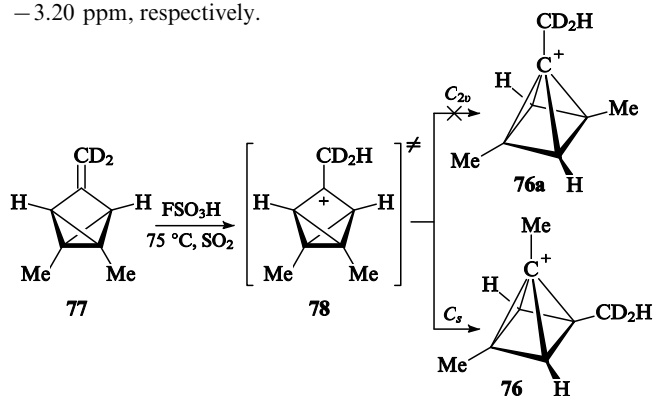


Figure 13. Geometric characteristics of the pyramidane molecule **39** and the $(\text{CH})_5^+$ (**66**) cation determined by the B3LYP/6-311 + G** (DFT), MP2(full)/6-311 + G** (MP2) and CCD(full)/6-311 + G** (CCD) calculations.⁸⁸

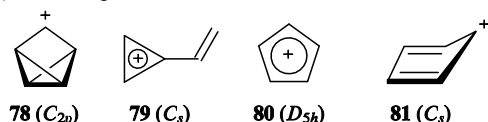
The synthesis of the 1,3,5-trimethyl derivative **76** from 1,5-dimethyl-3-methylenetricyclo[2.1.0.0^{2,5}]pentane (**77**) serves as a good illustration for the mechanism of transformation of the tricyclo[2.1.0.0^{2,5}]pentane skeleton in the pyramidal structure precursors **78**.¹⁶¹ It was found that the CD₂H group formed upon protonation of the deuterated compound **77** occupies only the basal position in cation **76**, *i.e.*, during the transformation of compound **77** into cation **76**, the deuterium label is not transferred from the basal carbon to the apical one. Thus, the formation of cation **76** does not proceed along the C_{2v}-symmetry pathway but follows the C_s pathway, allowed by the principle of orbital symmetry conservation.⁴ The chemical shifts ($\delta^{13}\text{C}$) of the apical quaternary carbon atom and the methyl-group carbon atom attached to it in compound **76** are about -20.89 and -3.20 ppm, respectively.



The eight-electron rule, like more general electron count rules for polyhedral structures,^{92, 162, 163} explains adequately the kinetic stability of the $(\text{CH})_5^+$ cation and its derivatives. The only difference in the orbital interaction diagram of cation **66** from the orbital interaction diagram of the pyramidane molecule presented in Fig. 11 is the fact that the nonbonding $2a_1$ MO localised on the

apical carbon atom in pyramidane **39** is transformed into the orbital of the C–H σ -bond in cation **66**.⁹

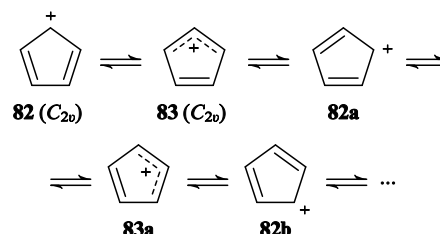
The square-pyramidal structure **66** is not the most stable form of $(\text{CH})_5^+$. According to the data of *ab initio* calculations^{164–166} (Table 6), the global minimum in the PES of $(\text{CH})_5^+$ is the vinylcyclopropenyl cation (**79**), which is only 2–3 kcal mol^{–1} more favourable than the D_{5h} structure of the cyclopentadienyl cation (**80**) in the triplet electronic state.



However, the rearrangements **66** → **79** and **66** → **80** do not take place, the former — due to the absence of a reaction valley connecting the cations **66** and **79** in the PES of the singlet electronic state of $(\text{CH})_5^+$ and the latter rearrangement is spin forbidden. Therefore, it is important to know to what extent the pyramidal structure **66** is energetically less favorable than the other possible structures of the $(\text{CH})_5^+$ cation which are stationary points in the PES of the singlet electronic state.

Early MINDO/3 semiempirical calculations^{167–169} provided the conclusion that the nonplanar C_s structure of the cyclopentadienyl cation **81** is preferred from the energy standpoint. However, more recent *ab initio* calculations^{88, 164, 165} showed that the C_s structure (**81**) does not correspond to a minimum on the PES and relaxes to the planar C_{2v} form (**82**), which is only 3–4 kcal mol^{–1} energetically more favourable than the pyramidal structure **66** and is separated from it by a rather high potential barrier. In the case of the cyclopentadienyl cation, one more C_{2v}

form (**83**) is possible; it is almost equivalent in energy to the C_{2v} structure **82**. According to the most advanced calculations,^{88, 165} structure **82** is a local minimum on the PES, while structure **83** is a first-order saddle point. Structure **83** corresponds to the transition state between the degenerate isomers (topomers) of structure **82**. The potential barrier to interconversion of the topomers of the singlet cyclopentadienyl cation **82** is only 0.1–0.2 kcal mol^{–1}, i.e., the reaction proceeds almost without a barrier (*cf.* the topomerisation of CH_5^+).^{88, 165} The most important results of calculations^{88, 92, 164–166} are summarised in Table 6.



The C_{4v} configuration of bonds at the pentacoordinate carbon atom can be realised in electrically neutral structures formed upon replacement of the CH^+ group by the isolobal BH group. This can give rise to a series of stable square-pyramidal *nido*-carboranes whose electronic structure would satisfy the eight-electron rule. Carboranes **84b,c**, which are isomers of borole **84a**, shown in Fig. 14 are examples of such structures. As shown by calculations,⁹⁸ structure **84c** containing a pentacoordinate pyramidal

Table 6. Total and relative energies of the pyramidal $(\text{CH})_5^+$ cation **66** and isomeric structures **78**, **82** and **83** in the ground singlet electronic state calculated by *ab initio* quantum chemistry methods.

Calculation method	$-E_{\text{tot}}$ /a.u.	ΔE /kcal mol ^{–1}	λ	Ref.
Isomer 66 (C_{4v})				
HF/6-31G*	191.86520	0 (42.7) ^a	0	165
MP2/6-31G**//6-31G*	192.5263	0 (12.9) ^a	0	164
MP4SDTQ/6-31G**//MP2/6-31G*	192.58611	—	0	165
B3LYP/6-311+G**	(193.1679)	—	0	88
MP2(full)/6-311+G**	192.68932	—	0	88
CCSD/6-311+G**	192.70330 ^b	—	0	88
Isomer 78 (C_{2v})				
B3LYP/6-311+G**	(193.0098)	—	1 ^c	88
MP2(full)/6-311+G**	192.64397	—	1 ^c	88
CCSD/6-311+G**	192.66056	—	1 ^c	88
Isomer 82 (C_{2v})				
HF/6-31G*	191.90215	–23.2	0	165
MP2/6-31G**//6-31G*	191.9105	–3.7	1 ^c	164
MP4SDTQ/6-31G**//MP2/6-31G*	192.52005	–3.5	0	165
Isomer 83 (C_{2v})				
HF/6-31G*	191.90235	–23.3	0	165
MP4SDTQ/6-31G**//MP2/6-31G*	192.51986	–3.4	1 ^c	165

^a The values in parentheses are the energies of the relatively most stable cyclic D_{5h} structure **80** of the cyclopentadienyl cation in the triplet state.

^b Calculation by the G2 method [approximately equivalent to QCISD(T)/6-311+G(3df,2dp) in the approximation level with allowance for the zero-point vibration energies] gives the values $-E_{\text{tot}} = 192.68503$ a.u. and $\Delta E = 13.1$ kcal mol^{–1} for structure **66** (relative to the energy of **80**) (see Ref. 166). ^c First-order saddle point (transition state).

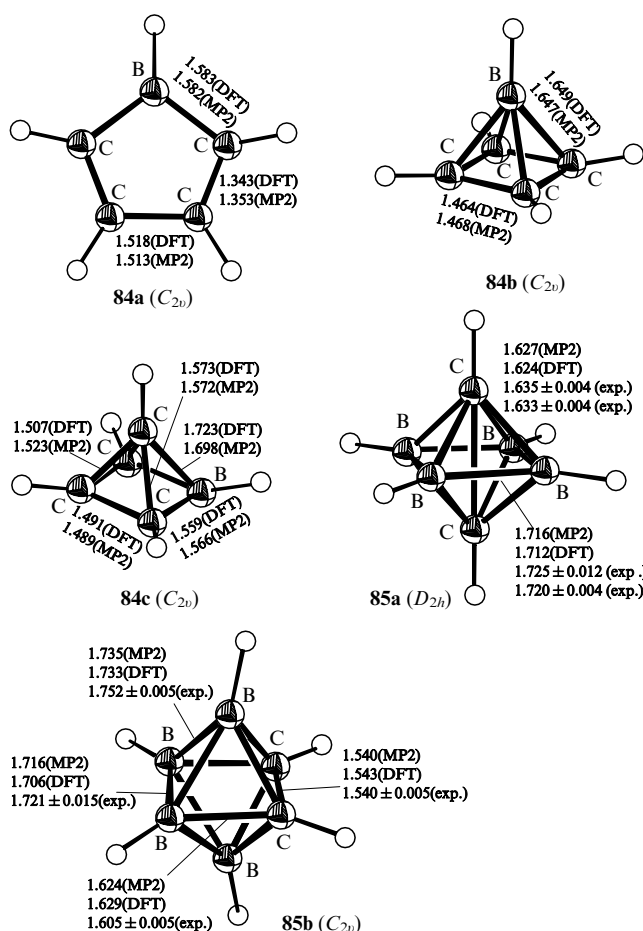


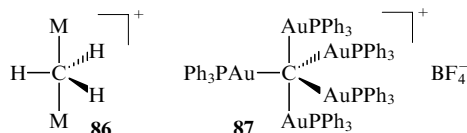
Figure 14. Geometric characteristics and relative energies of the structures of borole (**84a**), its non-classical pyramidal isomers **84b** and **84c**, and 1,6- (**85a**) and 1,2-*closo*-carboranes $\text{C}_2\text{B}_4\text{H}_6$ (**85b**) calculated using the MP2(full)/6-311+G** and B3LYP/6-311+G** methods.^{98, 172} (Experimental data for *closo*-carboranes $\text{C}_2\text{B}_4\text{H}_6$ were taken from Ref. 172.)

carbon atom, being thermodynamically less stable than structures **84a,b**, is likely, nevertheless, to have rather high kinetic stability. A similar configuration is found for the carbon atoms in square-bipyramidal *closo*-carboranes whose structures have been studied in detail both experimentally³ and theoretically.^{170–172}

The stability of the bipyramidal systems produced by adding apical groups to a π -conjugated ring is controlled by the ten-electron rule.⁹ Irrespective of the size of the central ring, these structures have only five bonding MO, and the total number of electrons (the number of ring π -electrons + the number of valence electrons in the apical group) in a stable bipyramidal molecule or ion should not exceed 10. The simplest hydrocarbon system which meets this condition is the octahedral $C_6H_6^{4+}$ ion. However, this compound is unstable for electrostatic reasons. The replacement of four CH^+ groups by BH groups results in two stable electrically neutral bipyramidal 1,6- (**85a**) and 1,2-carboranes (**85b**), which contain pyramidal pentacoordinate carbon centres (see Fig. 14).

3. Trigonal-bipyramidal configuration of bonds at a pentacoordinate carbon atom

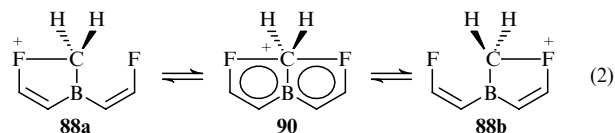
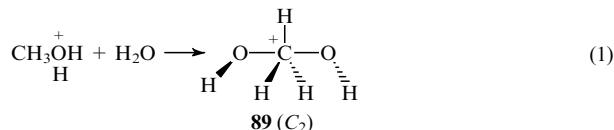
A trigonal-bipyramidal configuration of bonds is not realised in the methonium ion CH_3^+ , but can be stabilised by replacing the hydrogen atoms by electropositive atoms or groups. According to HF/4-31G calculations,¹⁷³ the D_{3h} conformation is preferred for disubstituted cations **86**. As shown by X-ray diffraction analysis, this configuration occurs in penta-aurated methonium ion **87**^{174,175} (the ligand AuL is isolobal to single-electron H and CH_3 groups).



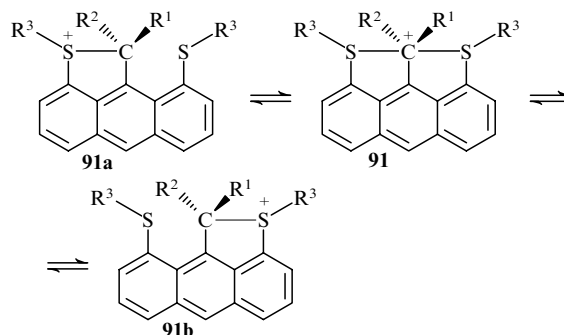
M = Li, BeH.

The electronic structure of compounds with the D_{3h} configuration of bonds at the central atom, which is a Main Group element, can be represented by a combination of three equatorial $2c-2e$ bonds formed by the sp^2 orbitals of the central atom and one hypervalent $3c-2e$ bond of the central atom with two apical ligands. The greater the difference between the electronegativities of the atoms forming this bond, the lower its electron deficiency and the greater the contribution of the electrostatic component which stabilises the structure (for discussion of factors determining the structure of hypervalent compounds, see Refs 5, 176–182). Higher stability of such polarised structures is attained when ligands with like charges are separated in space, *i.e.*, placed in the apical positions of the D_{3h} structure.

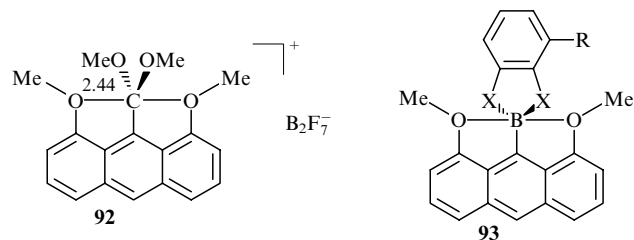
By following this scheme, one can also propose another way of stabilising the trigonal-bipyramidal configuration of bonds at pentacoordinate carbon atoms in carbonium ions. In this case, a considerable difference between the electronegativities of the central atom and the apical ligands is attained by using atoms or groups with high electronegativity as the ligands. This type of stabilisation of trigonal-bipyramidal structures of transition states is peculiar to S_N2 reactions at tetrahedral carbon atoms involving compounds with highly nucleofugal (including positively charged) groups. Examples are¹⁸³ two model reactions, namely, degenerate gas-phase hydrolysis of protonated methanol [reaction (1)] and intramolecular rearrangement of hypothetical cation **88** [reaction (2)].



The results of MP2(full)/6-31G** and MP2(full)/6-311++G** calculations showed that putative intermediates **89** and **90** containing pentacoordinate carbon atoms with the trigonal-bipyramidal configuration of bonds, which are formed presumably in these reactions, are considerably stabilised: the differences between the energies of the intermediates and the initial structures amount to 12.8 and 3.8 kcal mol⁻¹. However, neither these nor other similar structures correspond to minima in the PES and, hence, they are not intermediates but are transition states. A similar result has been obtained in an attempt to 'freeze' (this term was proposed by Martin¹⁸⁴) the pentacoordinate structure of transition state **91** formed during the rearrangement of 1,8-bis(arylthio)anthracene-9-carbonium ion.¹⁸⁵ In this cation, the heteropentallene fragment is incorporated in a rigid cage, which fixes both the attacking and leaving groups in the orientation required by the S_N2 reaction conditions.^{10,186–188} The structure **91** corresponds to a transition state (rather than an intermediate) of a reaction with a low potential barrier whose height is 10–20 kcal mol⁻¹ (depending on the solvent and the substituents).



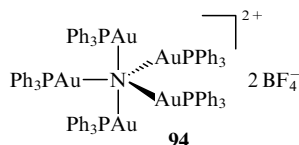
Stabilisation of a structure with a trigonal-bipyramidal configuration of bonds at the pentacoordinate carbon atom was achieved by Akiba *et al.*¹⁸⁹ They modified the dynamic system **91** by replacing the sulfur atoms by more electronegative oxygen atoms and thus ensured better conditions for collinearity of the axial bonds. They isolated and characterised the salt **92**, the cation of which contains a pentacoordinate carbon atom with a trigonal-bipyramidal configuration of bonds. The complete structural analogy between compound **92** and compounds with a pentacoordinate boron atom was confirmed by X-ray diffraction analysis of neutral pentacoordinate compounds of boron **93** (10-B-5) prepared recently by the same researchers.¹⁹⁰



X = O, S; R = H, OMe.

Thus, by varying the structure, one can embody all the theoretically possible types of coordination of a pentacoordinate carbon atom. Incidentally we would like to mention interesting results of theoretical^{155,191,192} and experimental^{175,192,193} studies of the structures of dications containing pentacoordinate nitrogen atoms, which are isoelectronic to carbonium cations. In these studies, relying on high-level (QCISD/6-311G** and CCSD(T)/

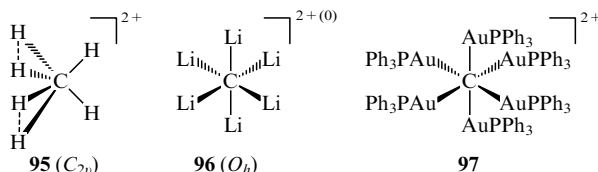
aug-cc-pVTZ) calculations, a structure with C_{4v} symmetry was attributed to the NH_5^{2+} dication (according to X-ray diffraction analysis,¹⁹³ its penta-aurated analogue **94** has a perfect D_{3h} configuration).



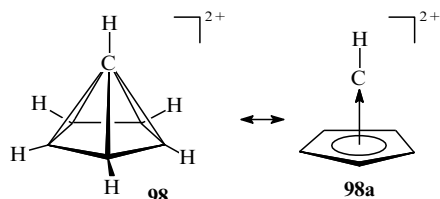
4. Hexa- and heptacoordinate carbonium ions

In the most symmetrical octahedral O_h configuration, structures of type AH_6 , where A is a Group IV element, have four bonding molecular orbitals, which can be occupied by eight electrons ($1a_{1g}^2 1t_{1u}^6 e_g 2a_{1g}$).^{5,6,9} One might expect that this type of octahedral structure would exist for the diprotonated methane CH_6^{2+} . Nonempirical calculations^{194–197} confirm the expected stability of the CH_6^{2+} dication. Besides, they indicate that the C_{2v} form in which the eight valence electrons are distributed over two $2c-2e$ and two $3c-2e$ C–H bonds, rather than the O_h form, is preferred for dication **95** for energy reasons.

As for the methonium ion **65**, dication **95** is a stereochemically non-rigid structure. According to MP3/6-31G**//6-31G** calculations,¹⁹⁵ redistribution of hydrogen atoms between the C–H bonds in the structure **95** in the gas phase requires overcoming a small potential barrier (only 4.3 kcal mol^{−1}). The octahedral bond configuration, which is unfavourable for the diprotonated methane, can be stabilised for its derivatives. Examples of this type are the CLi_6^{2+} (**96**)^{198,199} and $\text{C}(\text{AuPPh}_3)_6^{2+}$ (**97**) dications.¹⁷⁴ The latter has been isolated preparatively as the tetrafluoroborate salt.¹⁷⁴

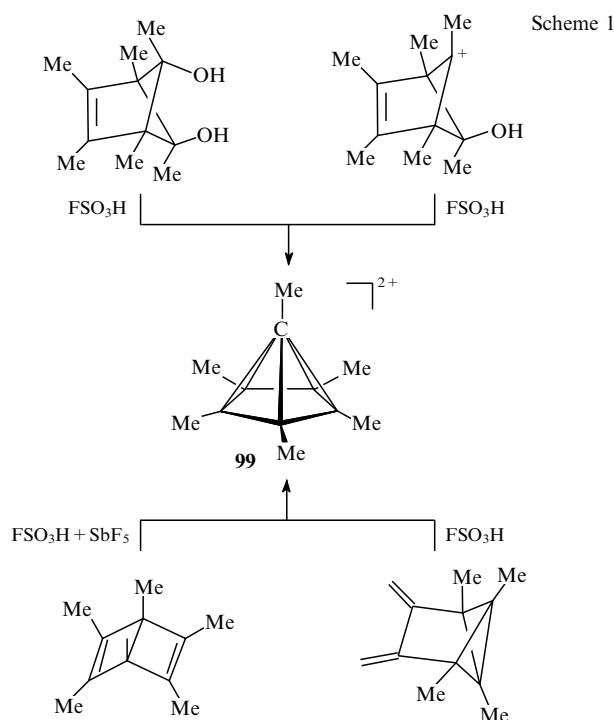


The pyramidal dication **98** is the prototype of polyhedral organic structures containing a hexacoordinate carbon atom.

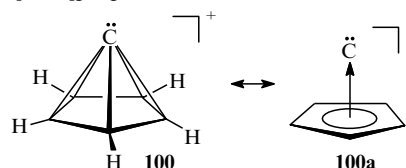


The hexamethyl derivative **99** of this dication has been prepared by Hogeveen and Kwant^{200,201} in superacid media using various precursors (Scheme 1).

The ^1H and ^{13}C NMR signals of the apical centres in **99** occur at a high field ($\delta^{13}\text{C} = 2.0$ ppm).^{200,201} As in the case of the $(\text{CH})_5^+$ (**66**) cation, the pyramidal structure of $(\text{CH})_6^{2+}$ (**98**) does not correspond to the deepest minimum in the PES. The transition of this structure to the energetically favourable isomer (according to HF/3-21G calculations), the fulvene dication, is associated with overcoming a high potential barrier.²⁰² The kinetic stability of the dication **98** is interpreted by the eight-electron rule.⁹ This rule also predicts the existence of another pentagonal-pyramidal non-classical structure **100**, which is the conjugate base of the dication **98** (in the same way as pyramidane **39** is the conjugate base for the pyramidal cation **66**). Nonempirical calculations⁸⁸ carried out at different approximation levels indicate that structure **100** actually corresponds to a minimum on the C_6H_5^+ PES. As can be seen from the data presented in Fig. 15, the bonds connecting the apical and the basal carbon atoms in the dication **98** are substantially



elongated with respect to similar bonds in the square-pyramidal ion **66**. In the cationic carbene **100**, the lengths of these bonds approach the greatest values known for C–C bonds.^{203,204} The longest single C–C bond known to date (1.80 Å) has been found in a [1.1.1]propellane derivative.⁴⁶



A hexacoordinate carbon atom can exist not only in ions but also in electrically neutral species. The octahedral CLi_6 (**96**) molecule can serve as an example.^{144,198,205} This molecule contains two valence electrons more than could be accommodated in the four bonding MO of the octahedral structure. These electrons

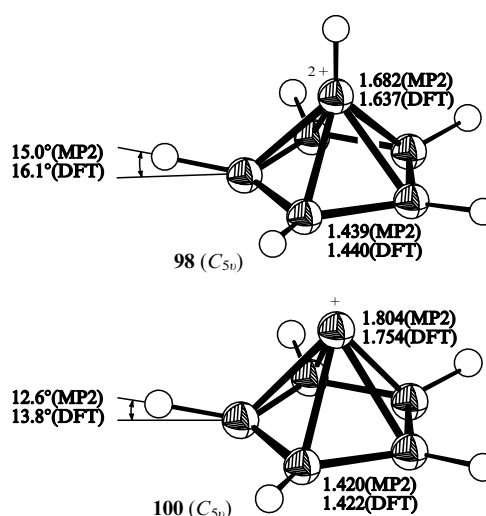
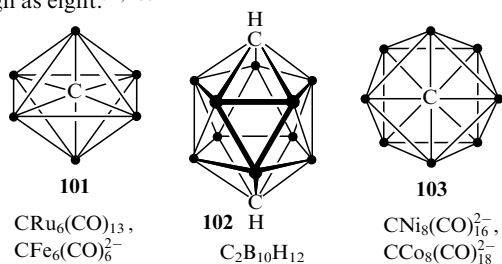
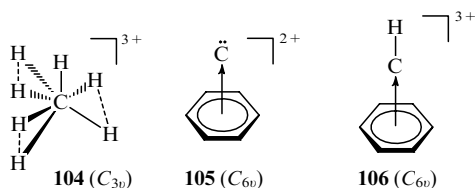


Figure 15. Geometric characteristics of the C_6H_5^+ cation (**100**) and $\text{C}_6\text{H}_6^{2+}$ (**98**) dication calculated by the B3LYP/6-311+G** and MP2(full)/6-311+G** methods.⁸⁸

are localised in the C–Li bonds. An additional bonding a_{1g} MO having a spherical symmetry is formed by delocalisation of orbitals of the lithium atoms surrounding the central carbon atom. In relation to the C–Li bonds, this MO is antibonding; nevertheless, it makes a substantial contribution to the molecular stabilisation due to ligand–ligand interactions [cf. stabilisation of the tetracoordinate planar carbon atom in structures **24**–**26** (see Fig. 7)]. Multicentre bonds also determine the stability of a series of carbide clusters **101** and carboranes **102** in which the formal coordination number of carbon is six. In nickel and cobalt clusters **103** with an antiprism structure, the coordination number is as high as eight.^{94, 206}



The simplest stable structure containing a heptacoordinate carbon atom is triprotonated methane **104**. In this compound, eight valence electrons are distributed over three $3c-2e$ C–H₂ bonds and one $2c-2e$ C–H bond.¹⁹⁷ The results of MP2/6-31G** and QCISD(T)/6-311G** calculations indicate that the whole positive charge in structure **104** is concentrated on the hydrogen atoms (each carries a charge of $\sim +0.6$), whereas the carbon atom is negatively charged ($q_C = -1.27$). Thus, the stability of this three-charged ion is mainly due to electrostatic forces.



Electrostatic interactions are also important for stabilisation of pyramidal cations with a six-membered basal ring. According to MP2/6-311 + G** and B3LYP/6-311 + G** calculations,⁸⁸ the di- and trication structures **105** and **106** in which the apical carbon atoms are coordinated to six and seven centres, respectively, exist, as predicted by the octet rule, as fairly deep minima in the PES.

The geometry calculated for structures **105** and **106** is shown in Fig. 16. In both cases, the C_{ap}–C_{bas} distances exceed the critical values for the single C–C bond lengths and the electron populations of the C_{ap}–C_{bas} bonds are rather low.

The presence of one $2c-2e$ C–H bond in the structure of triprotonated methane **104** provides an opportunity to replace this bond by a three-centre $3c-2e$ C–H₂ bond and thus to approach the CH₈⁴⁺ tetracation. However with a charge of +4, the Coulomb repulsion of the hydrogen atoms, which carry the entire positive charge, becomes the predominant destabilising factor. The results of MP2/6-31G** calculations showed that the CH₈⁴⁺ ion is unstable. The corresponding PES contains no minima for any of the possible CH₈⁴⁺ structures.^{143, 197} Meanwhile, the isolobal trinuclear boronium ion BH₈³⁺ is kinetically stable, although the calculation indicates that various pathways of its dissociation are highly exothermic. The structure of BH₈³⁺ (**107**) found by MP2/6-31G** and QCISD(T)/6-311G** calculations has four tetrahedrally oriented $3c-2e$ B–H₂ bonds.²⁰⁷

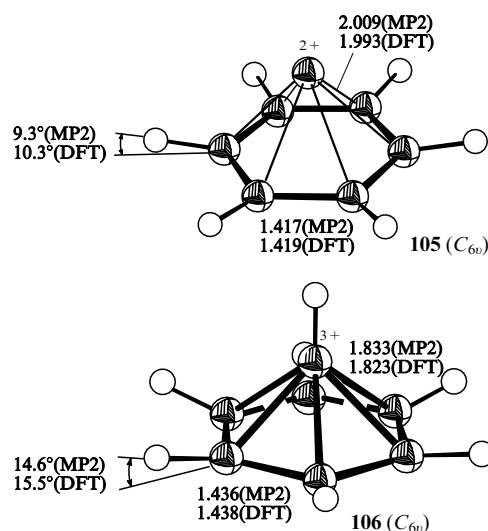
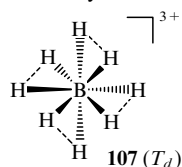
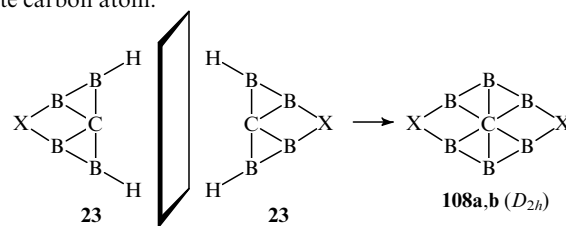


Figure 16. Geometric characteristics of the C₇H₆²⁺ dication (**105**) and C₇H₇³⁺ trication (**106**) calculated by the B3LYP/6-311 + G** and MP2(full)/6-311 + G** methods.⁸⁸

VII. Planar hexacoordinate carbon atom inside a cyclic borocarbon cage

A new line in the study of compounds with hypercoordinate carbon atoms is the quest for structures with a planar hexacoordinate carbon atom. The problem of stabilisation of these structures has been attacked simultaneously by two research groups, which have arrived at similar solutions.

One approach^{25, 208, 209} is based on expansion of the rigid cage of bonds formed by a planar tetracoordinate carbon atom in cyclic structures like **21**–**23**. This expansion results in a higher coordination number of the carbon atom. For example, 'doubling' of molecule **23** (by reflecting it in a mirror accommodating the central carbon atom and two boron atoms in the plane of the mirror) furnishes structure **108** containing a planar hexacoordinate carbon atom.

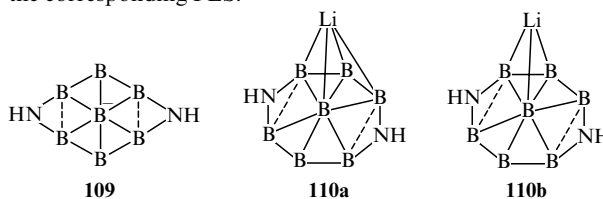


X = O (a), NH (b).

According to MP2(full)/6-311 + G** calculations, the resulting structure **108** has D_{2h} symmetry and corresponds to a minimum on the PES.

The calculated geometry of molecule **108a,b** is shown in Fig. 17. The C–B bond lengths are only ~ 0.1 Å longer than the length of the typical single C–B bond.²¹⁰ The replacement of the central carbon atom in structure **108** by the B[–] isolobal centre, as expected, does not weaken the stability of the structure.

The anion **109** and molecules **110a,b** (Fig. 18) are minima on the corresponding PES.²⁰⁹



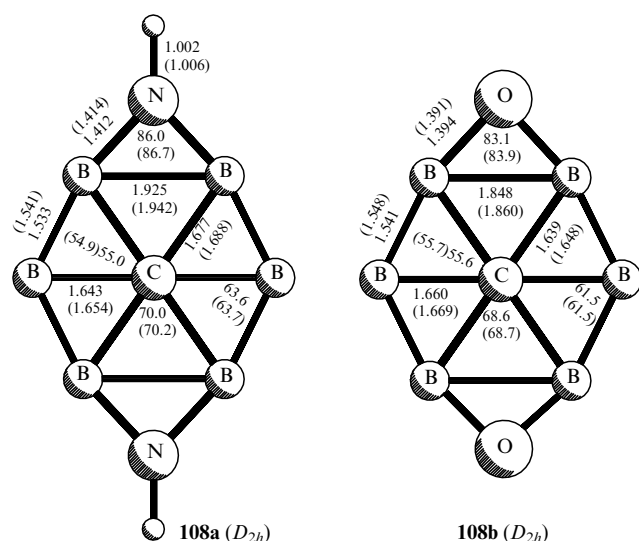
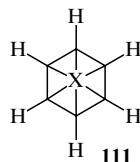


Figure 17. Geometric characteristics of molecules **108a,b** (X = NH, O) containing hexacoordinate carbon atoms calculated by the MP2(full)/6-31G** and MP2(full)/6-311++G** methods (values in parentheses).²⁵

The lengths of the B–B bonds formed by the central boron atom (~ 1.7 Å) are within the limits of values typical of these bonds.²¹¹ Analysis of the electronic structure of compounds **108–110** shows that they are 6π -electron aromatic systems. The two electrons lent by the central carbon atom or by the B^- anion are delocalised in the π -system of the ligands. As a consequence, the carbon atom in the structure **108** bears a positive charge (+0.8 to +0.9), which decreases its effective radius and reduces the steric strain in the planar system. The aromatic nature of molecule **110** is emphasised by the presence of shortened peripheral B–B bonds, which are 0.06–0.08 Å shorter than the double B=B bond (~ 1.63 Å).²¹²

The second approach to solving the problem of stabilisation of a hexacoordinate carbon centre²¹³ is also underlain by the idea of surrounding this centre by a rigid cage composed of boron atoms. At the first stage of the investigation,²¹³ carried out by B3LYP/6-311++G** calculations using the density functional theory, a model planar structure **111** was considered with various atoms or ions X being placed at the midpoint of the benzene ring.

For none of the structures designed in this way (even for the structure with X = He or C^{4+}), were the researchers able to locate an energy minimum on the PES. Since the geometry of structure **111** (X = C^{4+}) was quite realistic (the $C_{\text{centre}}-C$ bond lengths were normal, 1.516 Å) and the instability of the structure was mainly due to excess charge, subsequent modification of the structure **111** with X = C^{4+} was carried out in the usual way.



The total charge of the molecule was neutralised by successive replacement of the carbon centres in the ring by boron atoms. Along this route, a number of stable structures **112–116**, containing a planar hexacoordinate carbon atom, have been identified. Two factors contribute to the stability of these structures: first, expansion of the inner cavity containing the carbon centre caused by the fact that C–B bonds are longer than C–C bonds; and second, aromaticity of these structures. It was noted²¹³ that, although structures **112–116** are not the most stable isomers,

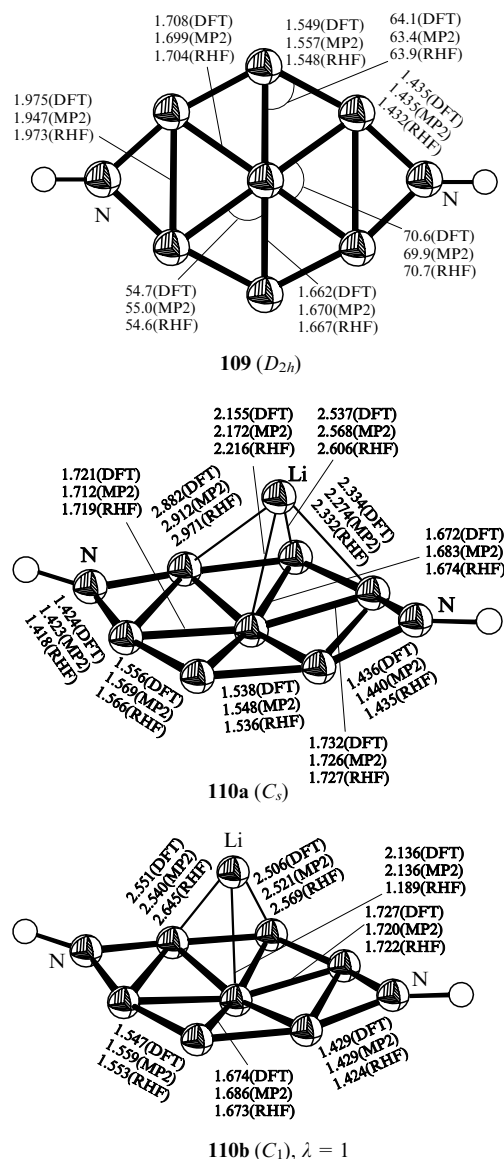
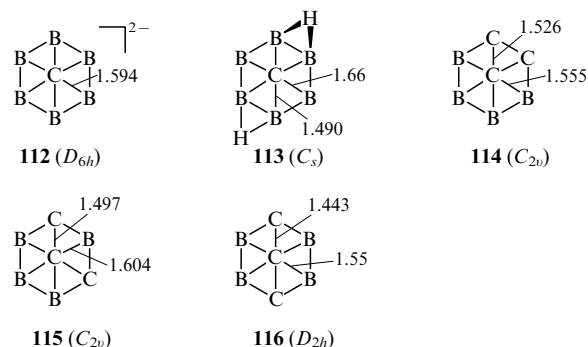


Figure 18. Geometric characteristics of anion **109** and molecules **110a,b** containing hexacoordinate boron atoms calculated by the RHF/6-31G** (RHF), MP2(full)/6-31G** (MP2) and B3LYP/6-311++G** (DFT) methods.^{208,209}

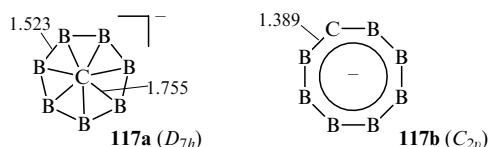
The molecular configuration of **110b** is the transition state structure for rotation of the lithium atom above the ring (topomerisation) with a potential barrier of 0.20 (RHF), 0.63 (MP2) or 0.03 kcal mol^{−1} (DFT).

they are separated from the latter by rather high potential barriers and, therefore, the synthesis of these species may be practical.



VIII. Molecules and ions containing planar penta-, hepta- and octacoordinate carbon atoms or atoms of other non-transition elements

The possibility of the existence of stable compounds incorporating a planar heptacoordinate carbon atom is pointed out by the results of B3LYP/6-311+G** calculations for the cyclic CB₇ anion.²¹⁴ In this approximation, the *D*_{7h}-symmetric structure **117a** is a local minimum in the PES, which is separated from another local minimum corresponding to a more stable (by 9 kcal mol⁻¹) isomer **117b** by a fairly high potential barrier. The ion pairs formed by anions **117a** and **117b** with the Li⁺ counterions have the same energy. Like the cyclic structures with a hexacoordinate carbon atom considered above, the seven-membered analogue **117a** is also aromatic. Figure 19 shows the shapes of the four π MO of anion **117a**, three occupied orbitals and the lowest unoccupied one. The B–B (1.523 Å) and C–B (1.389 Å) bond lengths in the seven- and eight-membered rings in anions **117a** and **117b** are close to the C–B bond length in the H₂C=BH molecule (1.376 Å) and B–B bond length in the HB=BH molecule (1.523 Å), calculated by the same technique;²¹³ this indicates that these are conjugated double bonds.



The ring in compound **117a** is larger than the B₆ and C₂B₄ rings in compounds **108**–**116**; this entails an increase in the C_{centre}–B bond lengths in anion **117a** by approximately 0.2 Å. Due to this elongation, the bond becomes markedly weaker than the usual bonds in carboranes.²¹⁵ Therefore, even minor symmetry distortions can lead to substantial changes in the type of structure. The symmetry of the structure of ion pair **118** is reduced

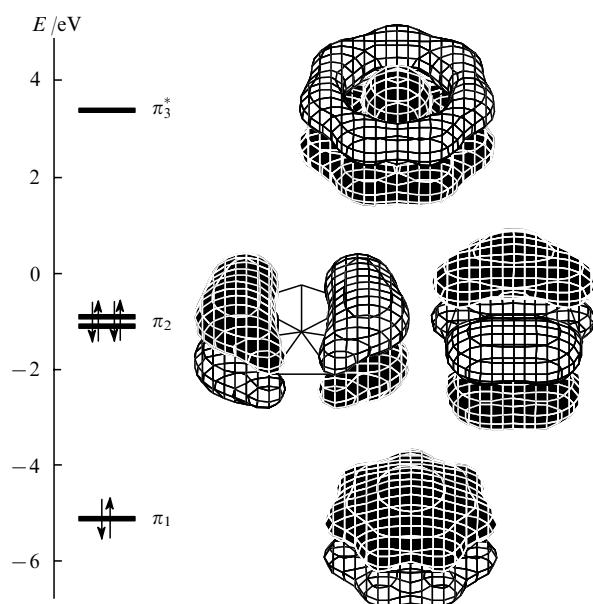
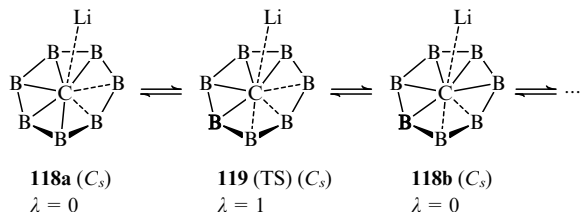


Figure 19. Shapes and energy levels of the π -orbitals of anion **117a** calculated by the B3LYP/6-311G** method (see Ref. 214).

to *C*_s. These structures should be fluxional, following a bond switching isomerisation pattern (see Refs 216, 217), the calculated potential barrier being not higher than 0.1 kcal mol⁻¹.

A similar structure and the same type of structural rigidity are typical of neutral C₂B₆ (**120**) and NB₇ (**121a,b**) rings. The cyclic structure **120** is formed from cyclic structure **117a** through replacement of the B⁻ anion by an isoelectronic carbon atom, while **121** is produced when the central carbon is replaced by nitrogen. Calculations of the geometry of these molecules (Fig. 20) demonstrate that the central carbon atom in structure **120** forms only five (of the seven possible) rather short (within the range of usual lengths of C–B bonds) C–B bonds, and the nitrogen atoms in structures **121a** and **121b** form four and five short N–B bonds. However, the calculated potential barriers to migration of the central atoms inside the seven-membered rings do not exceed 0.8 kcal mol⁻¹, which permits these atoms to be regarded as effectively heptacoordinate planar atoms.²¹⁴

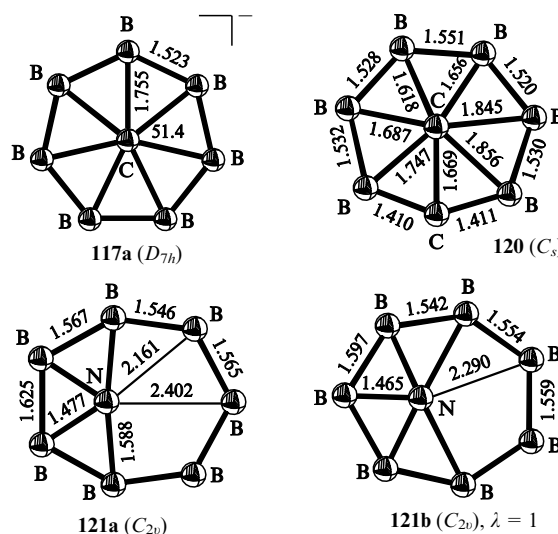
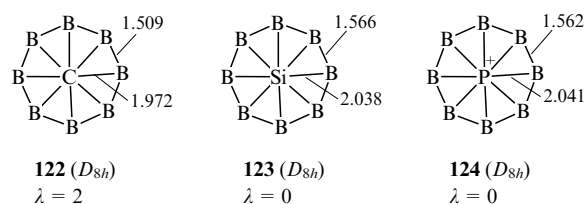


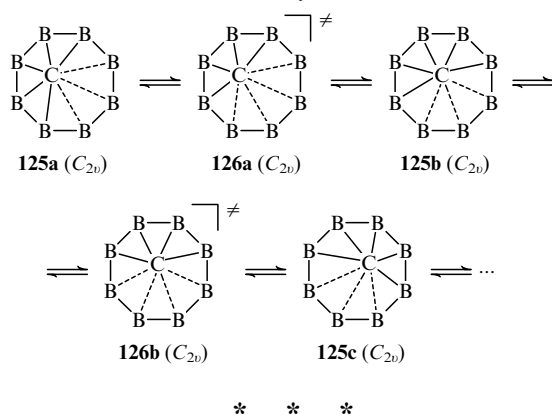
Figure 20. Geometric characteristics of anion **117a** and molecules **120** and **121a,b** calculated by the B3LYP/6-311+G(2df) methods.²¹⁴

The symmetrical *D*_{8h} structure **122** resulting from insertion of a carbon atom inside an eight-membered ring composed of boron atoms is unstable, according to the results of B3LYP/6-311G** calculations.²¹⁸ On the PES of the CB₈ molecule, this structure is matched by a flattened top of a hill (two imaginary vibration frequencies). Although the B–B bonds in the rings are double, the size of the eight-membered ring is so large that the B–C distances in structure **122** exceed the longest known value for B–C bond length. If the carbon atom in structure **122** is replaced by an isoelectronic atom or cation (Si or P⁺) with a greater atomic radius, structures **123** and **124** obtained in this way will be stable (matched by potential energy minima). The calculated B–Si (2.038 Å) and B–P (2.041 Å) bond lengths exceed only slightly the corresponding sums of the covalent radii (1.98 and 1.91 Å). Structures **123** and **124**, like structures **112**–**117**, contain aromatic sextets of π -electrons.



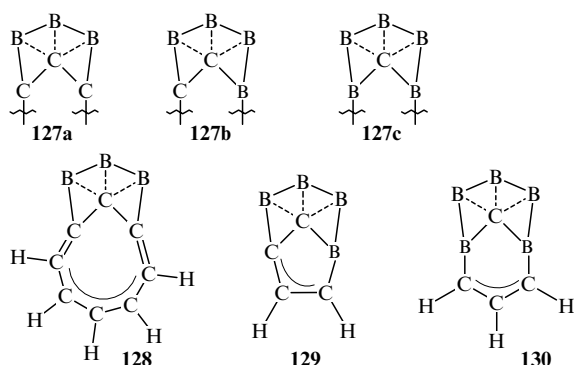
For the cyclic CB₈ molecule, the stable form is structure **125** (*C*_{2v} symmetry) in which the C–B bond lengths are 1.627 and

1.753 Å, and the other C...B distances (non-bonding contacts) occur within the limits of 2.5–2.9 Å. This structure, like analogous seven-membered structures **118**, **120** and **121**, tend to undergo low-barrier rearrangements [the potential barrier calculated in the CCD(fc)/6-311G**//B3LYP/6-311G** approximation is 2.05 kcal mol⁻¹] resulting in fast exchange of ligand positions in the environment of the central atom. Thus, the carbon atom in structure **125** is effectively octacoordinated.

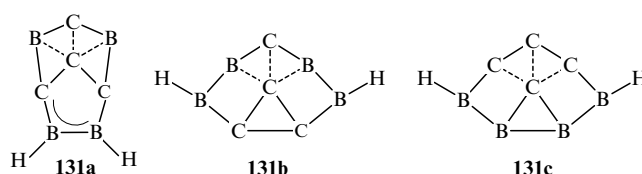


As this review was being prepared for publication, new important studies devoted to derivatives of planar tetracoordinate and hypercoordinate carbon were published.

Wang and Schleyer²¹⁹ further developed the strategy described in their preliminary communication⁵⁷ involving delocalisation of the non-bonding higher occupied MO of alkylanes over the molecular cage by replacing the carbon centers in various positions of the cage by boron atoms and carried out B3LYP/6-31G* calculations for a series of new boroalkanes with a planar tetracoordinate carbon atom. The same researchers also proposed a general approach to the design of stable organoboron structures incorporating planar pentacoordinate carbon centres.²²⁰ It was found that the replacement of two-electron π -donor groups (O, NH, HC=CH) in structures **21**–**23** containing a planar tetracoordinate carbon atom by single-electron π -donor B or C atoms provides the possibility of increasing the coordination number of the planar carbon center. The insertion of non-classical substituents **127a**–**c** thus obtained into the skeletons of various aromatic hydrocarbons in place of the three-carbon (CH)₃ chains gives rise to structures with pentacoordinate planar carbon atoms (for example, structures **128**–**130**), whose stability was confirmed by B3LYP/6-311 + G** calculations.

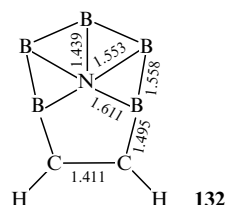


This result is also confirmed by our MP2/6-311 + G** *ab initio* calculations for a number of other structures (for example, isomers **131**) with a pentacoordinate carbon atom.²²¹ We showed that by observing the above conditions of aromatic stabilisation of non-classical structures (see Sections II.3 and VII), stable structures with a pentacoordinate carbon atom can also be produced by other permutations of atoms in units **127** and in structures of type **128**–**130**.

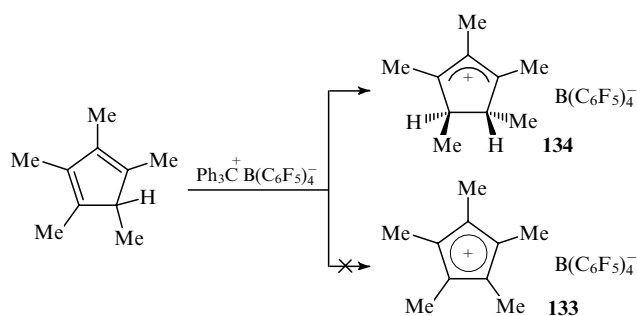


Compound	$\Delta E/\text{kcal mol}^{-1}$	
	B3LYP/6-311 + G**	MP2/6-311 + G**
131a	0	0
131b	11.6	7.1
131c	32.4	21.9

The requirement of aromatic stabilisation and the selection of appropriate fragments of type **21**–**23**, **127a**–**c** and others allow one to predict rather reliably the existence of stable molecules and ions with hypercoordinate planar centres of any other element. The B3LYP/6-311 + G** calculations for stable structure **132** with a planar pentacoordinate nitrogen atom serves as an example.²²¹



In relation to the discussion of the pyramidal (CH)₅⁺ cation and its isomers (see Section VI.2), of interest is the debate initiated by the recent publication²²² reporting the synthesis of the unexpectedly stable pentamethyl derivative of the singlet cyclopentadienyl cation (CMe)₅⁺ (**133**). According to X-ray diffraction analysis data, the cation structure corresponds to structural type **83**. However, the subsequent high-level quantum-chemical calculations²²³ suggested that in reality, the researchers were dealing with the dihydro derivative **134** rather than with the cation **133**; this was recognised as proven after additional analysis.^{224, 225}



The outcome of this debate is an illustrative example of the increasing role of precise quantum-mechanical calculations in the study of structures with non-standard geometric and electronic characteristics.

IX. Conclusion

The results of the theoretical and experimental studies considered demonstrate the diversity of structural types of molecules containing atoms with a non-standard spatial orientation of bonds and coordination numbers other than those dictated by the valence rules. Not that these compounds are necessarily thermodynamically or kinetically stable — they often are metastable local minima. But one can think of generating them, and studying them. The advances in theoretical simulation methods and the stupendous progress in the development of the computing power of modern quantum chemistry enabled quite substantiated state-

ment of the problem of looking for new structures which might have been rejected only a few years ago by researchers with a classical way of thinking on the basis that 'that can't be so because it can never be so' (see, for example, the caustic remark²²⁶ concerning the studies searching for compounds with a planar tetracoordinate carbon atom). Meanwhile, these studies initiated by theoretical analysis have received some experimental validation. Many compounds of this type have already been synthesised.

Currently, theoretical investigations of new non-classical organic compounds are directed at elucidating the factors influencing stability and investigating the unusual dynamics and properties of such molecules and ions. Elucidation of unusual structural patterns presents substantial interest in the design of new high-tech materials with specific properties, while technological developments, especially ultralow-temperature laser vaporisation,²²⁷ allow one to expect that more theoretical predictions will be confirmed by experimental proof. The situation in this field seems to resemble the history of the development of fullerene chemistry.

As has already been noted, high-level *ab initio* calculations with obligatory allowance for the electron correlation energy are the most accurate and reliable methods for theoretical identification and evaluation of the possible existence of non-classical structures. The question thus arises of how one might choose particular structures on which calculations are to be performed. It is clear that exhaustive screening of atomic compositions cannot be a suitable strategy. There is good reason to believe that analysis of orbital interactions of molecular fragments based on the perturbation theory still remains conceptually the most comprehensive and the most fruitful way of designing stable non-classical structures. This conclusion is based on the fact that orbital interactions make, as a rule, the major contribution to stabilisation or, conversely, destabilisation of molecular structures.

Yet another, more utilitarian line is to simulate a non-classical organic structure that would resemble one or another inorganic or organometallic complex or cluster. The stability of molecules and ions of such compounds is ensured by the formation of multi-centre bonds, of a type which is dictated by the structure of the complex or cluster and can be reproduced in the organic analogue on the basis of the isolobal analogy.

It is evident that the principles of stabilisation of non-classical organic structures, *i.e.*, carbon compounds, can be directly extrapolated to the compounds of other non-transition elements. Some examples of unusual geometric configurations and types of coordination of boron, nitrogen, silicon, and phosphorus atoms have been included in this review.

The notion of 'non-classical compounds' appeared 50 years ago when the first examples of these structures became known, the term itself being introduced mainly to designate exceptions to customary rules. Nowadays, the exceptions appear to become indistinguishable from the rules. George Olah, who has been awarded the Nobel Prize for his contribution to the development of this field of chemistry, believes¹⁴³ that classification of structures into classical and non-classical ones will gradually vanish from chemists' language and chemists' practice, as the understanding of the general principles of the chemical bond becomes more profound.

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Spirooxazines: synthesis, structure, spectral and photochromic properties

V Lokshin, A Samat, A V Metelitsa

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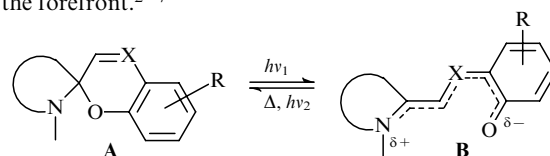
Abstract. The review surveys synthetic approaches to spiro[1,4]oxazines belonging to one of the most promising classes of organic photochromes. The relationships between the structures of spirooxazines and their spectral properties as well as characteristics of thermal and photoinduced processes are considered. The bibliography includes 201 references.

I. Introduction

Reversible molecular rearrangements are of great interest because they play an important role in studies of many chemical and biological processes, which find use in modern technologies. Of special interest are light-induced rearrangements, the so-called photochromic rearrangements. These are reversible transformations of a chemical species between two states with different absorption spectra induced (at least in one direction) by electromagnetic radiation.¹ In recent years, photochromic organic compounds have been extensively studied because of their application in optical systems for recording and retrieval of information, molecular switches, dynamical chemosensors and biosensors, systems for accumulation of solar energy, transport systems, catalysis, optoelectronics and optobioelectronics.^{1–7} Since organic photochromic compounds find application in diverse fields, requirements on their characteristics are rather wide. In this connection, the directed synthesis of these compounds assumes great importance. Directed syntheses are planned taking into account the results of investigations on general relationships

between the molecular structure and spectral-kinetic properties of photochromic compounds.

Photochromism was first described at the end of the 19th century. However, extensive studies of organic photochromes were started only in the second half of the 20th century. Spirocyclic compounds composed of two heterocyclic fragments, which are linked through the sp^3 -carbon atom, immediately have come to the forefront.^{2–7}

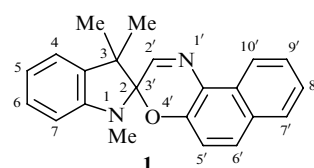


X = CH (spiropyran, SPP), N (spirooxazine, SPO).

The spirocyclic form **A** of these compounds has absorption in the UV region. Excitation of this form with light of the corresponding wavelength causes the cleavage of the C_{sp^3} –O bond followed by isomerisation to give the flattened conjugated form **B**, which has absorption in the visible region.

Of the two above-mentioned classes of spiro compounds, spiropyrans were the first to be synthesised. In the 1960–70s, spiropyrans were the best studied organic photochromes.² On the background of these extensive studies, the synthesis of the first spirooxazines in 1961⁸ as well as two subsequent publications dealing with these compounds^{9,10} went unnoticed.

The starting point for the studies of the chemistry of SPO were investigations by Chu.^{11–13} In the beginning of the 1980s, he was the first to discover the extraordinary high photostability[†] of spiro{indoline-2,3'-naphtho[2,1-*b*][1,4]oxazine} (**1**) and its derivatives under continuous irradiation.



[†] Hereinafter, the photostability is taken to mean the resistance to photo-degradation.

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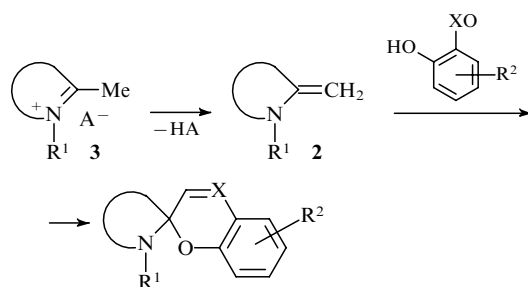
Due to this discovery, SPO have attracted the attention of researchers as photochromes showing promise for the practical use in materials with varying optical density. Since the mid-1980s, the number of publications (especially patents) devoted to SPO sharply increased, which gave impetus to their systematisation and analysis.

Spirooxazines were the subject of three reviews,^{4,6,14} two of which were chapters of monographs. Unfortunately, problems of the synthesis and structural modifications of SPO remained virtually beyond the scope of the reviews^{4,6} and received proper attention only from Japan researchers.¹⁴ However, the latter review was published more than a decade ago. In recent years, abundant new data on the synthesis of SPO have become available. Taking into account an importance of synthetic aspects, which, to a great extent, determine new areas of practical application of SPO, we believe that there is a need to consider these problems in more detail, with emphasis on the results obtained in the last 10–12 years. In citing patent data, we take into account only studies (with rare exception), which gave clear characteristics of the compounds (melting points and/or informative NMR spectra). The effects of the structural factors on the spectral properties and characteristics of thermal and photo-induced processes of spirooxazines in solutions are considered. For a correct comparison, prominence is given to the results obtained in approximately identical conditions.

II. Synthesis of spirooxazines from aromatic *o*-hydroxynitroso compounds

1. Conditions and reaction mechanism

One of the most commonly used procedures for the synthesis of SPO from aromatic *o*-hydroxynitroso compounds and alkylidene derivatives of nitrogen-containing heterocycles **2** (hereinafter, the 'nitroso' method) was borrowed directly from the chemistry of SPP with the only difference that the reactions with alkylidene derivatives **2** were carried out with aromatic *o*-hydroxynitroso compounds instead of aldehydes, such as salicylaldehyde.



X = CH (SPP), N (SPO).

Alkylidene derivatives **2** are generally prepared *in situ* by the reactions of bases (most often, triethylamine) with the corresponding quaternary salts **3**. Ethanol^{9,10} or methanol¹³ are traditionally used as solvents, although trichloroethylene,^{15–17} toluene,^{18,19} dioxane,²⁰ acetone,²¹ chloroform,²² amyl alcohol²³ and a heptane–ethanol mixture^{24,25} have also found use in recent years.

Unfortunately, as have been mentioned in the review by Chu,⁴ this method affords SPO in low yields (on the average, 30%–50%). The main reasons for low yields are as follows:

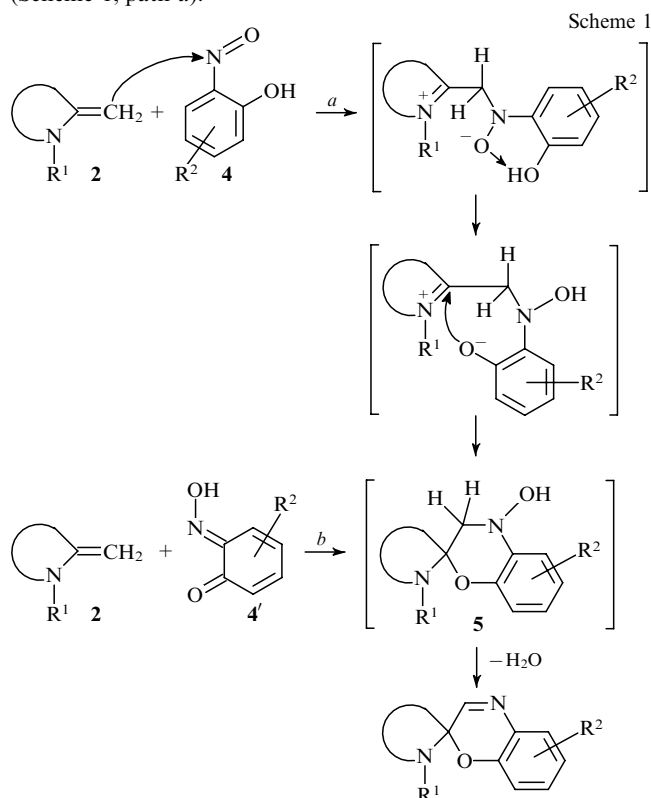
- low reactivity of the nitroso group due to the low electrophilicity of the nitrogen atom;
- instability of some SPO and nitroso compounds in the reaction conditions;
- difficulties associated with the chromatographic isolation of SPO (close values of R_f of SPO, starting compounds and by-products).

A number of recent studies were aimed at optimising the yields of SPO in these reactions. Thus, it has been found²⁶ that the presence of a drying agent and elevated pressure have a positive

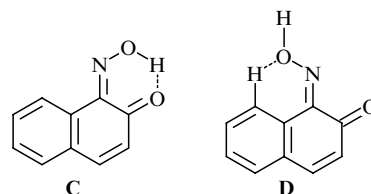
effect on the yield of SPO **1** (determined by liquid chromatography). An excess of nitrosonaphthol and the use of toluene as the solvent have the same effect (however, this hinders the isolation of the final product).

Recently, it has been demonstrated[‡] that the reactions performed in the absence of a solvent under microwave activation led not only to a noticeable increase in the yield of SPO but also to an essential decrease in the reaction time (up to ~15 min) and reduction in the amount of impurities. This procedure for the synthesis of spirooxazines deserves further investigation.

The mechanism of the reactions of aromatic *o*-hydroxynitroso compounds **4** with alkylidene derivatives of nitrogen-containing heterocycles **2** remains virtually unknown. It was assumed that this mechanism is analogous to that of the synthesis of SPP²⁷ and involves the attack of the negatively charged carbon atom of enamine on the nitrogen atom of the nitroso group as the first step (Scheme 1, path *a*).



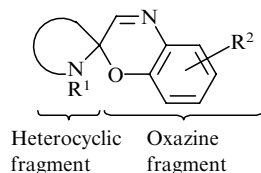
However, another point of view was expressed in the study.²⁸ The authors of the cited study believed that the key step involves the electrocyclic reaction of enamine **2** with the quinone oxime tautomer of *o*-hydroxynitroso compound **4'** giving rise to intermediate **5** (Scheme 1, path *b*). This mechanism is indirectly supported by the fact that the quinone oxime forms are much more stable in solutions than the nitrosophenol forms. For example, the NMR spectroscopic study of 1-nitroso-2-naphthol in such solvents as CDCl₃, C₆D₆, DMSO-*d*₆ and dioxane-*d*₈ revealed the presence of two isomers of the quinone oxime type (**C**



[‡] A Samat, V Lokshin, R Guglielmetti, J Hamelin, F Texier-Boullet, A V Koshkin, O A Fedorova, S P Gromov *Synth. Commun.* (in preparation).

and **D**), the ratio between these isomers being dependent on the nature of the solvent.²⁹

2. Modification of the heterocyclic fragment of spirooxazines
Hereinafter, two fragments involved in the SPO molecule will be referred to as the heterocyclic and oxazine fragments.

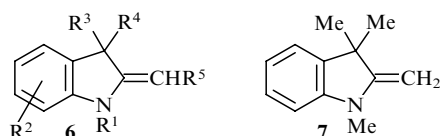


Although these names are not strict (oxazine fragment is also heterocyclic), they are, in our opinion, better than such terms as 'left' and 'right' heterocycles, which are sometimes used.

a. Substitution in the indoline ring

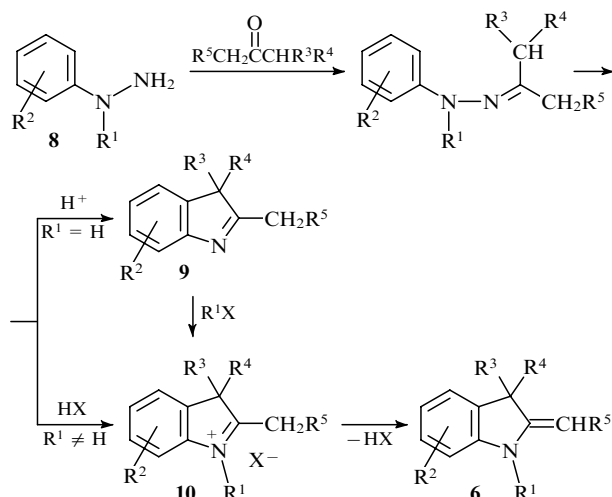
The majority of the known spirooxazines involve the indoline ring as the heterocyclic fragment. This preference of researchers is attributable to both the historical tradition associated with the chemistry of SPP and the fact that the replacement of this fragment in SPO by other fragments presents a very difficult problem (see below).

In the synthesis of indoline-containing SPP and SPO, 2-alkylidene derivatives of indoline **6** are used as the starting compounds, of which 2-methylidene-1,3,3-trimethylindoline (**7**) (Fischer's base) is the most well-known representative.



Procedures for the synthesis of these compounds have been developed in considerable detail and have been comprehensively surveyed in reviews.^{2,5,30} Hence, we will not discuss these procedures in the present review. Let us only note that most of 2-alkylideneindolines were prepared according to the Fischer synthesis (Scheme 2).

Scheme 2



If the starting phenylhydrazine **8** contains hydrogen as the substituent R^1 , the reaction affords indolenine **9**. Subsequent alkylation of compound **9** yields quaternary salt **10**, which is converted into 2-alkylideneindoline **6**. In the case that the substituent R^1 cannot be introduced by alkylation, it is inserted into the starting phenylhydrazine **8**.

The Fischer synthesis of indoline-containing synthons is a rather simple process, which accounts for the fact that the

substitution in the indoline fragment is most commonly used for the modification of SPO. A substituent is most often inserted at position 1 (at the nitrogen atom) as well as at position 5. Examples of selected 1- and 5-substituted spironaphthooxazines **11–32** are given in Tables 1 and 2.

Table 1. 1-Substituted spironaphthooxazines of the indoline series.

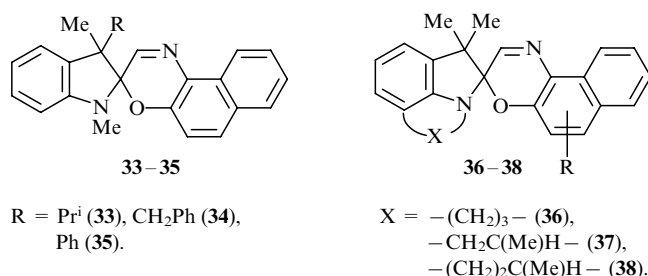
SPO	R	Ref.	SPO	R	Ref.
11	$-(CH_2)_{17}Me$	31 ^a	18	$-(CH_2)_2CO_2H$	9, 36
12	$-CH_2Bu^t$	32	19	$-(CH_2)_5CH(CO_2Et)_2$	31
13		33	20		37
14	$-CH_2CH(Me)Ph$	32	21		38
15	$-(CH_2)_2OMe$	34	22	$-(CH_2)_5CONH_2$	39
16	$-CH_2Ar$	35	23		21
17	$-CH_2CH=CH_2$	26, 31	24		40

^a A series of other *N*-alkyl-substituted SPO were described in the study.³¹

Table 2. 5-Substituted spironaphthooxazines of the indoline series.

SPO	R	Ref.	SPO	R	Ref.
25	$-F$	41	29	$-NO_2$	26
26	$-I$	41	30	$-NH_2$	43
27		15	31	$-NHCOMe$	15
28	$-OH$	42	32		44

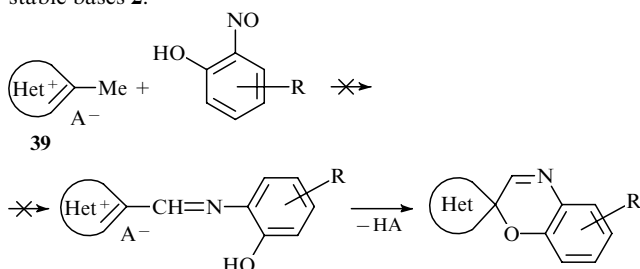
3-Substituted derivatives **33–35** (see Ref. 44) and unique bridging structures **36–38** (see Ref. 45) were synthesised.



It should be noted that substituents in the indoline fragment (particularly, at position 1) not only have an effect on the photochromic properties of SPO but also improve such important useful characteristics of SPO as solubility, affinity for polymeric matrices and photostability.

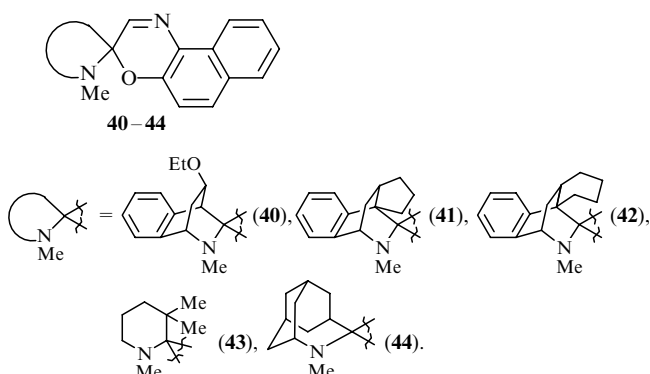
b. Spirooxazines with non-indoline heterocyclic fragments

From a synthetic standpoint, the variation in the nature of the heterocyclic fragments in SPO is among the most stubborn problems. Unlike aldehydes of the salicylaldehyde type, aromatic *o*-hydroxynitroso compounds are not involved in condensation with heterocyclic salts of type **39**, except for salts **3**, which give stable bases **2**.

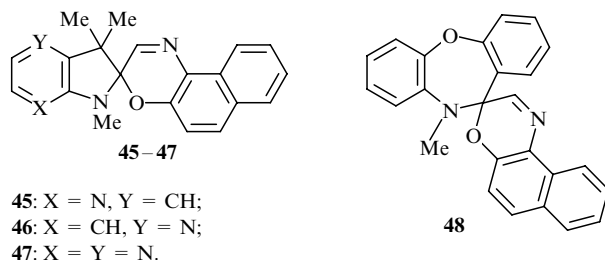


This fact practically precludes the use of a broad spectrum of oxygen- and sulfur-containing heterocycles, which are successfully employed in the synthesis of SPP.² As a result, the range of heterocyclic systems suitable for the synthesis of SPO is limited to nitrogen-containing heterocycles.

New SPO in which the indoline fragment is substituted by sterically hindered (**40–42**)^{46–49} or saturated (**43**,^{50, 51} **44**^{17, 52, 53}) azaheterocycles have been synthesised in recent years.



Besides, compounds containing azaindoline (**45–47**)^{20, 54} or dibenzooxazepine (**48**)^{18, 55–57} fragments were synthesised. It should be noted that compound **48** exhibits photochromic properties only at low temperatures (from -40 to -20 °C).

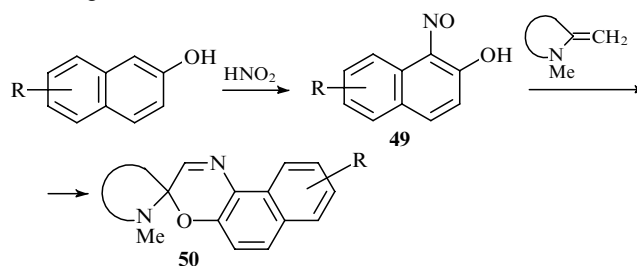


3. Modification of the oxazine fragment of spirooxazines

a. Substitution in the naphtho[2,1-*b*]oxazine fragment

Most of procedures for the structural modifications of the oxazine fragment in SPO are based on the insertion of the substituent R into the naphthalene fragment. The substituent is most commonly introduced into this fragment already in the step of the preparation of the starting 1-nitroso-2-naphthol. The general scheme of

the synthesis of SPO containing substituents in the oxazine fragment is given below.



The localisation of the nitroso and hydroxy groups at positions 1 and 2 of the starting nitrosonaphthols **49** unambiguously determines the type of the resulting oxazine fragment as naphtho[2,1-*b*][1,4]oxazine (**50**). 1-Nitroso-2-naphthols occupy a prominent place among other aromatic *o*-hydroxynitroso compounds due both to their high stability (compared, for example, to *o*-nitrosophenols) and the fact that they can be readily prepared by nitrosation of the corresponding naphthols.

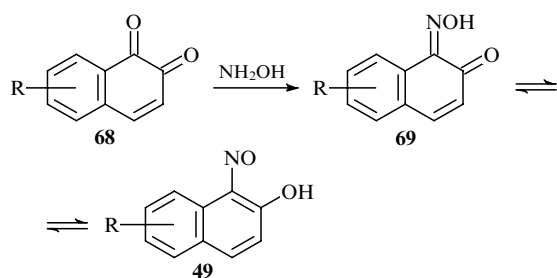
In recent years, the range of SPO of type **50** has been steadily extended due to the involvement of ever more complex nitrosonaphthols in this reaction (Table 3). This structural modification of SPO is one of the most commonly used processes, although the progress in this field is limited by the inaccessibility of some naphthols and the necessity of adapting the conditions of their nitrosation to the nature of the substituent.

Table 3. Substituted 1,3,3-trimethylspiro{indolino-2,3'-naphtho[2,1-*b*][1,4]oxazines}.

51–67					
SPO	R	Ref.	SPO	R	Ref.
51	5'-OH	28, 58, 59	60	9'-SO ₃ Na	65
52	5'-CH ₂ OH	60, 61	61	8'-CN, 9'-CN	66, 68
53	5'-CO ₂ Me	62	62	8'-OH, 9'-CO ₂ Me	69
54	5'-	59, 63	63	7', 8'-	19, 70
55	7'-NO ₂	64	64	8', 9'-	68
56	8'-OH	65	65	9'-OH	58, 65, 71, 72
57	8'-COPh	19	66	10'-Me	68, 73
58	8'-CN	29, 66	67	10'-C ₆ H ₄ Me- <i>p</i>	68, 73
59	8'-SO ₃ Na	65, 67			

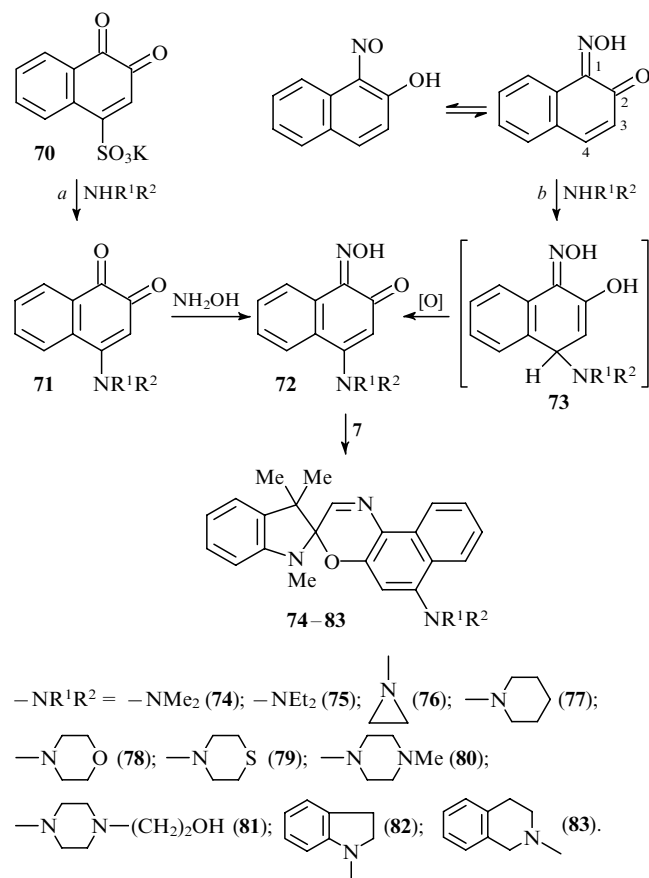
It is the difficulty to access 4-substituted 2-naphthols that accounts for the lack of 6'-substituted SPO in Table 3.

To close this gap, an original approach to 6'-substituted SPO has been developed. In this procedure, 1,2-naphthoquinones **68** rather than 2-naphthols were used as the source of 1-nitroso-2-naphthols. The reactions of compounds **68** with hydroxylamine afforded monooximes **69**, which are tautomers of nitrosonaphthols **49**.

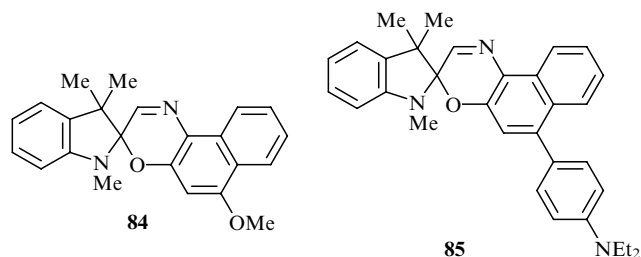


In the general case, 1,2-naphthoquinones are not more readily available compounds than naphthols. However, a number of their 4-substituted derivatives can be easily prepared by the nucleophilic substitution reaction of potassium 1,2-naphthoquinone-4-sulfonate (**70**). Thus, Rickwood and co-workers^{20, 74} used various secondary amines as nucleophiles for the preparation of 4-amino-substituted 1,2-naphthoquinones **71**, which were then employed in the synthesis of 6'-amino-substituted SPO (Scheme 3, method *a*). These authors also developed a simplified (but much less universal) approach to the synthesis of the same compounds^{20, 74, 75} on the basis of the reaction of 1-nitroso-2-naphthol, secondary amine and Fischer's base **7** without isolation of substituted nitronaphthol **72** (Scheme 3, method *b*). However, the mechanism of the insertion of the amino group is not entirely known. It was assumed²⁰ that the reaction involves the nucleophilic addition of secondary amine at position 4 of the quinone oxime tautomer of 1-nitroso-2-naphthol. Subsequent oxidation of intermediate **73** can occur under the action of the second 1-nitroso-2-naphthol molecule, which partially accounts for low yields.

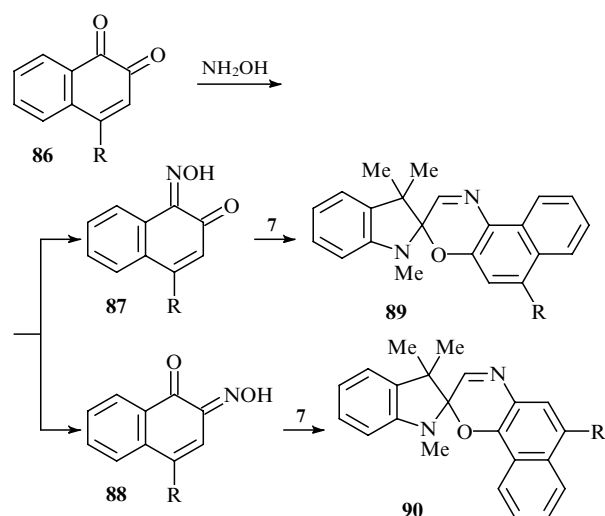
Scheme 3



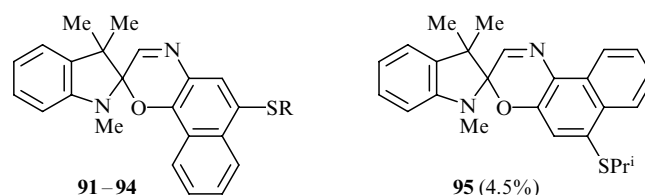
By combining both approaches, Rickwood and co-workers^{20, 76} prepared a large series of 6'-amino-substituted SPO (**74–83**). Using the synthesis of SPO **84** (see Ref. 20) and **85** (see Ref. 76) according to the method *a* as examples, the authors demonstrated that O- and C-nucleophiles can be employed as nucleophilic reagents.



This scheme has been substantially refined in subsequent studies. In particular, NMR spectroscopic studies demonstrated that the reaction of 4-substituted naphthoquinones **86** with hydroxylamine is non-regioselective and affords, in the general case, a mixture of oximes **87** and **88**, which are difficult to separate.^{16, 29, 77} The use of this mixture in the reaction with Fischer's base provides a possibility for the generation of two types of SPO, viz., naphtho[2,1-*b*][1,4]oxazines **89** and naphtho[1,2-*b*][1,4]oxazines **90**.

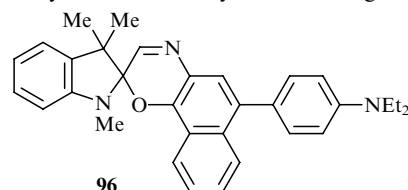


The predominance of a particular type of SPO depends on the ratio of the oximes in the mixture and their relative reactivities to Fischer's base. Thus, due to the low reactivities, 4-amino-substituted oximes **88** give the corresponding SPO **90** only in trace amounts.²⁹ However, if sulfur-containing substituents are inserted at position 4, compounds of type **90** (for example, **91–94**) rather than compounds of type **89** (for example, **95**) are generated as the major products in mixtures of SPO.¹⁶



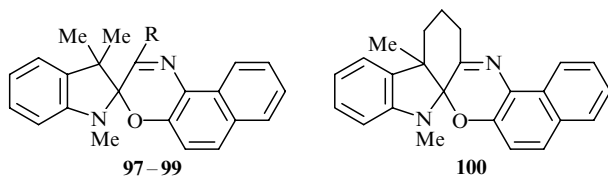
R = Prⁱ (**91**, 25.5%), C₆H₁₁ (**92**),
Ph (**93**), C₆H₄OMe-*p* (**94**).

Apparently, these results have stimulated the researchers to revise the structure of compound **85**. In the recent patent,⁷⁸ structure **96** was assigned to this compound based on the results of X-ray diffraction study of the starting oxime.



It should be noted that the synthetic efforts to prepare 6'-substituted SPO were compensated by good photochromic characteristics of most of these compounds, primarily, by high colourability and unusual spectral features.

A special type of the modification of the naphtho[2,1-*b*]oxazine fragment involves the insertion of substituents at position 2'. For example, 2'-substituted SPO **97–100** were synthesised.^{44, 79–81}



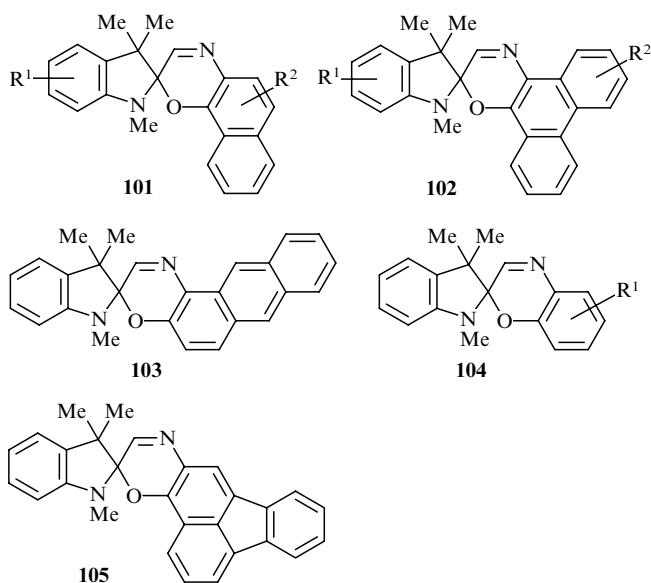
R = Me (**97**), Pr (**98**), Ph (**99**).

Unlike structurally similar SPP, SPO of this type do not exhibit photochromic properties at room temperature although short-lived coloured forms of some of these compounds were detected upon laser flash photolysis with nanosecond time resolution.⁸⁰

b. Aromatic annelation and heteroannelation

The need for the extension of the gamma of the photochromic characteristics of SPO provides a steady impetus to the synthesis of new types of SPO whose structures differ from the classical naphtho[2,1-*b*]oxazine structure **50**. This aim can be achieved by synthesising SPO with the use of aromatic and heterocyclic *o*-hydroxynitroso derivatives, for example, nitrosophenols, nitrosophenanthrols, *o*-hydroxynitrosoquinolines, *etc.*, instead of 1-nitroso-2-naphthols. This type of structural modifications, which has received considerable attention already in early studies,^{4, 6} was further developed in recent years.

In particular, new derivatives belonging to the class of SPO characterised by aromatic annelation, such as naphtho[1,2-*b*]oxazines (**101**),^{16, 82–84} phenanthro[9,10-*b*]oxazines (**102**),^{81, 85} anthra[2,1-*b*]oxazines (**103**)²³ and benzooxazines (**104**),^{44, 86} were synthesised. A procedure for the synthesis of a new representative of this type of SPO, *viz.*, spirofluoroanthene[3,2-*b*]oxazine (**105**), was covered by a patent.⁸⁷



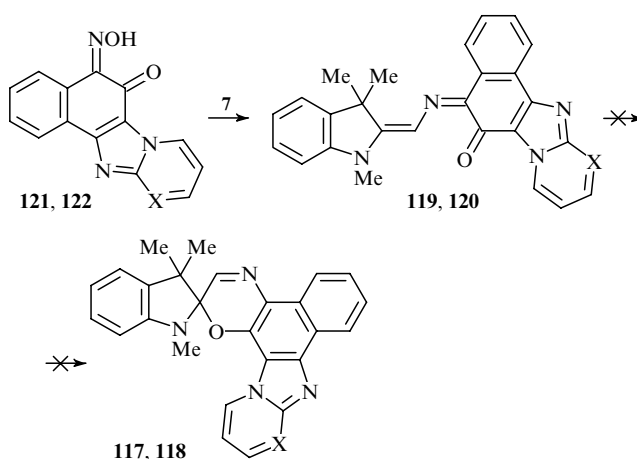
Heteroannelation of the benzooxazine fragment was particularly widely reflected in recent patents and publications. New compounds of this type are listed in Table 4.

Interesting results were obtained by Lareginie *et al.*⁷⁷ In attempting to synthesise SPO **117** and **118** containing the anne-

Table 4. Heteroannelated SPO of the indoline series.

SPO	X	Y	Ref.	SPO	X	Y	Ref.
106		—	88	112	—		83
107		—	24, 89	113			29
108		—	24, 90	114			77
109		—	91	115			85, 95, 96
110		—	92–94	116			85
111	—		83				

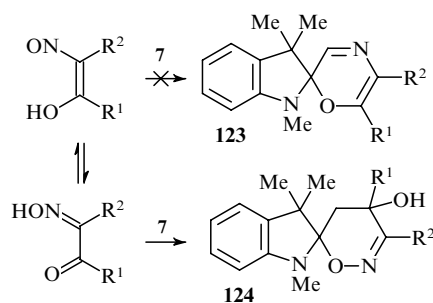
lated imidazo[1,2-*a*]pyridine and imidazo[1,2-*a*]pyrimidine rings, respectively, compounds **119** and **120** having open merocyanine structures were prepared instead of the expected compounds with spirocyclic structures.



X = CH (**117**, **119**, **121**), N (**118**, **120**, **122**).

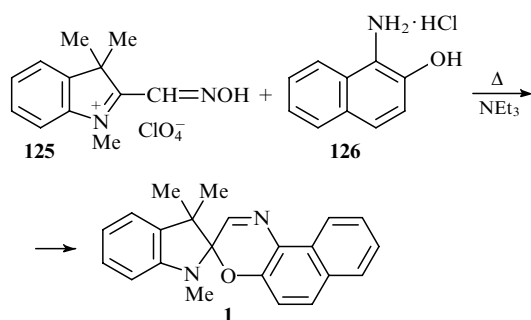
Compounds **119** and **120** are the only known examples of stable merocyanines of the spirooxazine series. Physicochemical and X-ray diffraction studies of these compounds provided valuable information on the probable three-dimensional and electronic structures of the short-lived coloured forms of SPO, which can usually be obtained only by indirect methods.^{97–99}

In conclusion of this section, let us mention an interesting attempt to synthesise SPO **123**, which contains no nuclei annelated to the oxazine ring.²⁸ Unfortunately, the synthesis afforded 1,2-oxazines **124**, which do not exhibit photochromic properties.

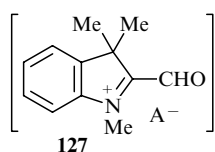


III. Synthesis of spirooxazines from 1-amino-2-naphthols and related compounds

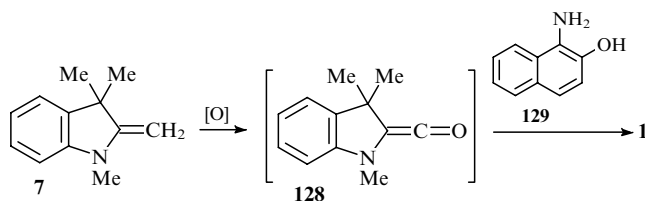
As early as 1971, when analysing various hypothetical approaches to spirocyclic photochromic compounds, Bertelson² noted that the oxazine ring of SPO could be, in principle, constructed by the reactions of carbonyl compounds with amines. The first step forward in this direction was made by Japanese scientists¹⁰⁰ who demonstrated that SPO **1** can be prepared by the reaction of 2-hydroxyiminomethyl-1,3,3-trimethylindoleninium perchlorate (**125**) with 1-amino-2-naphthol hydrochloride (**126**) in the presence of triethylamine.



Although the mechanism of this reaction remains to be studied, it seems rather probable that the reaction produces a carbonyl-containing intermediate of type **127**, which then interacts with the amino group.



Minkin and co-workers^{85, 101} have made an essential contribution to the development of this field of investigation. The Russian researchers found that the carbonyl-containing intermediate (to which the structure of ketene **128** was assigned), which can react with 1-amino-2-naphthol (**129**) to give SPO **1**, can be prepared by mild oxidation of Fischer's base **7**.¹⁰¹

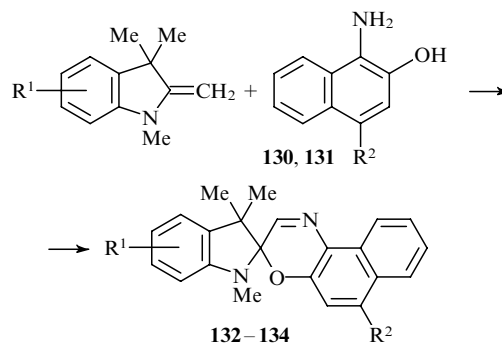


Selenium dioxide and pyridinium chlorochromate were successfully tested as oxidising agents. However, the best results were obtained with the use of dimethyl sulfoxide promoted by the addition of sodium bicarbonate. The advantages of this approach over the classical 'nitroso' method are that it affords the reaction

products in higher yields and gives rise to smaller amounts of impurities, which substantially facilitates the chromatographic purification of the products.

The use of annelated analogues of 1-amino-2-naphthols, such as 9-amino-10-phenanthrols and 1-amino-2-anthrol, instead of 1-amino-2-naphthols themselves, made it possible to prepare SPO of types **102** and **103**.^{85, 101}

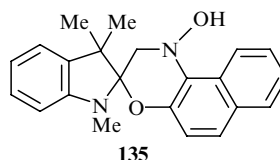
Additional advantages of the procedure under consideration were revealed in the study.¹⁵ In particular, this procedure was employed for preparing SPO **132–134** starting from readily accessible aminonaphthols **130** and **131**.^{102–104} These products contain strong electron-withdrawing substituents at position 6' and possess good photochromic characteristics.



$\text{R}^1 = \text{H}$ (**132**, **133**), 5-OMe (**134**);
 $\text{R}^2 = \text{CN}$ (**130**, **132**, **134**), $\text{SO}_2\text{C}_6\text{H}_4\text{Me-}p$ (**131**, **133**).

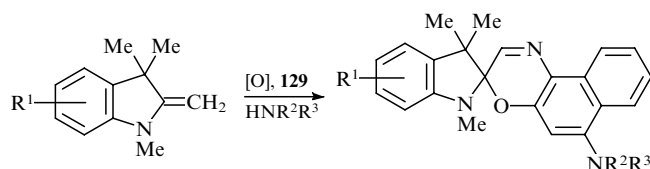
Yet another important advantage of this procedure is that the reactions can be carried out under much milder conditions. This made it possible to increase the yields of SPO **43** and **44**, which were prepared from bases of type **2** unstable under the reaction conditions (prolonged heating).¹⁵

These mild reaction conditions allowed the Russian researchers⁸ to isolate stable intermediate **135** whose structure was established by NMR spectroscopy.



Compound **135** is rapidly converted into SPO **1** upon heating in different solvents. It is not inconceivable that this compound is also the direct precursor of SPO **1** in the 'nitroso' method (see structure **5**, Scheme 1), but this hypothesis calls for an additional verification.

Within the framework of this method, yet another unexpected result was obtained.¹⁰⁵ It appeared that oxidation of Fischer's base in the presence of secondary amines afforded (in much higher yields) 6'-amino-substituted SPO analogous to those prepared according to Scheme 3.



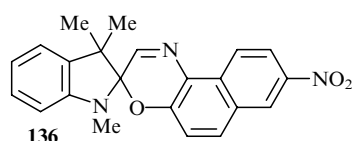
Since 1-amino-2-naphthol (**129**), unlike 1-nitroso-2-naphthol, cannot react with secondary amine by the Michael addition mechanism (Scheme 3, method *b*), the step in which the amino group is inserted into the molecule remains an open question.

IV. Chemical reactions of spirooxazines

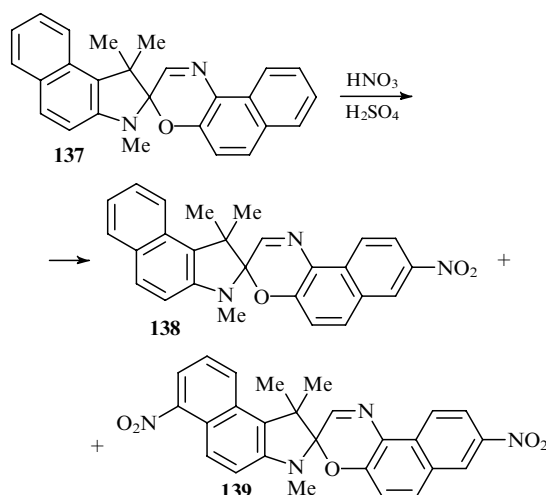
The syntheses of the first spirooxazines have presented difficulties due to which SPO had an unjust reputation of chemically unstable compounds.⁴ However, these compounds can be subjected to various chemical transformation in spite of a certain instability, particularly, in the presence of water and acids. These transformations are considered below.

1. Electrophilic substitution of the hydrogen atom

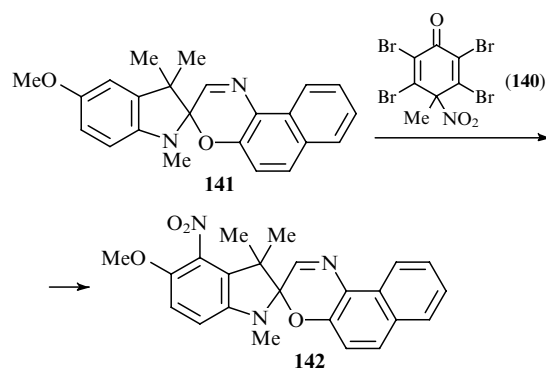
Russian scientists made an essential contribution to investigation of this type of reactions of SPO.^{64, 106, 107} In particular, they demonstrated that nitration of SPO **1** with nitric acid ($d = 1.35 \text{ kg m}^{-3}$) in concentrated sulfuric acid afforded 8'-nitro-substituted derivative **136**.



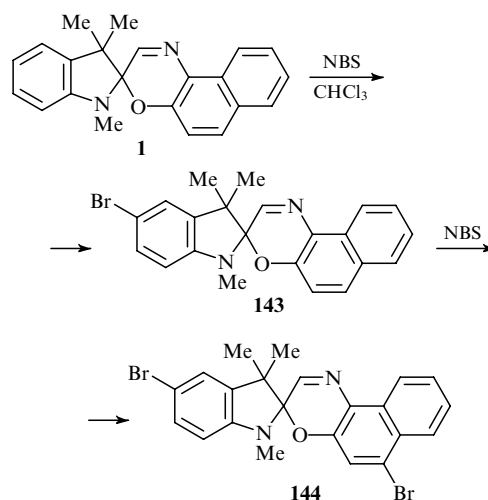
However, nitration of benzoannulated compound **137** under the same conditions gave rise to dinitro compound **139** along with the expected 8'-nitro derivative **138**.¹⁰⁶



Attempts to use a softer nitrating agent, *viz.*, 2,3,5,6-tetra-bromo-4-methyl-4-nitrocyclohexa-2,5-dien-1-one (**140**), failed.²⁹ However, the reaction of this reagent with SPO **141** containing the activated indoline fragment gave rise to 4-nitro derivative **142**.



Bromination of SPO **1** with *N*-bromosuccinimide (NBS) proceeded initially at position 5 of the indoline ring. Further bromination of the resulting SPO **143** yielded 5,6'-dibromo derivative **144** in a mixture with by-products.¹⁰⁷



2. Synthesis of esters, amides and ethers

a. Acylation and alkylation of hydroxy-substituted SPO

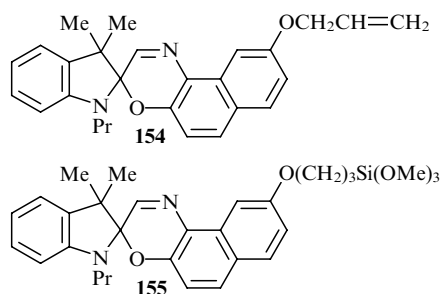
Acylation of 9'-hydroxy-containing SPO **65** and its derivatives is the most widespread reaction of SPO. Acid chlorides^{60, 71, 72, 108} or acid anhydrides¹⁰⁹ can be employed as acylating agents, which are most often prepared *in situ* from the corresponding acids and dicyclohexylcarbodiimide (DCC).^{40, 110–112} A series of acyl derivatives of SPO **65** are given in Table 5.

Analogous approaches are used for acylation of the hydroxy groups at positions 5 (see Refs 42 and 112) and 8' (see Ref. 69).

Alkylation of the HO groups of hydroxy-containing SPO is less well studied. Dürr *et al.*⁷² synthesised SPO **154** and **155** by the treatment of the corresponding hydroxy derivatives with alkyl halides in anhydrous acetonitrile in the presence of potassium carbonate.

Table 5. Acyl derivatives of 9'-hydroxy-substituted SPO **65**.

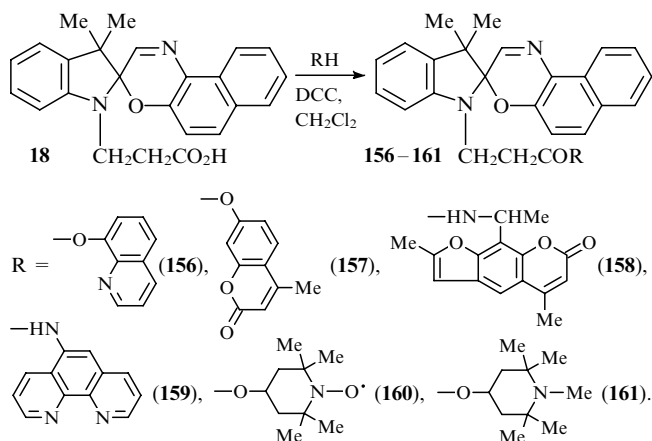
SPO	R	Ref.
145	$-\text{COC}(\text{Me})=\text{CH}_2$	60, 72
146	$-\text{CO}(\text{CH}_2)_3\text{CO}_2\text{H}$	109
147	$-\text{CO}-\text{C}_4\text{H}_3\text{S}$	40
148	$-\text{CO}-\text{H}_2\text{C}-\text{C}_4\text{H}_3\text{S}$	40
149	$-\text{CO}-\text{HC}=\text{HC}-\text{C}_4\text{H}_3\text{S}$	40
150	$-\text{CO}-\text{C}_4\text{H}_4\text{N}$	108
151	$-\text{CO}-\text{C}_6\text{H}_4-\text{C}_6\text{H}_4-\text{O}(\text{CH}_2)_{11}-\text{O}-\text{C}_6\text{H}_{11}$	112
152	$-\text{CO}-\text{C}_6\text{H}_4-\text{O}-\text{C}(\text{CF}_3)_2=\text{C}(\text{CF}_3)_2$	71
153	$-\text{CH}_2-\text{CO}-\text{C}_6\text{H}_4-\text{C}_6\text{H}_4-\text{C}_6\text{H}_4-\text{S}$	111



Dimethyl sulfate was successfully used for methylation of the hydroxy groups at positions 5' and 8'.^{59,69}

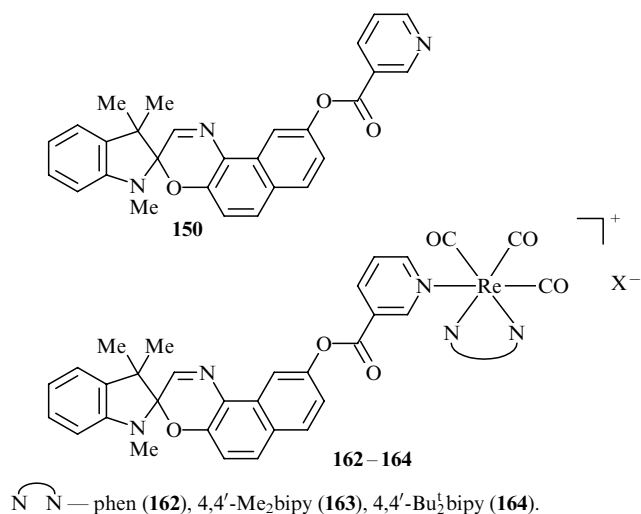
b. Reactions of carboxy-substituted SPO

N-Carboxyethyl-substituted SPO **18**, which was synthesised for the first time by Ono,⁹ is a convenient reagent for the preparation of esters and amides. Various compounds of this type (**156–161**) containing luminescent, complex-forming or antioxidant fragments were synthesised by Chinese researchers.^{36,113}



3. Synthesis of coordination compounds

Recently, Chinese researchers¹⁰⁸ reported the preparation of stable crystalline complexes of SPO **150** with Re(I) salts with compositions [Re(CO)₃(phen)(SPO)]ClO₄ (**162**), [Re(CO)₃(4,4'-Me₂bipy)(SPO)]ClO₄ (**163**) and [Re(CO)₃(4,4'-Bu₂bipy)(SPO)]·PF₆ (**164**) (phen is 1,10-phenanthroline, bipy is 2,2'-bipyridyl).



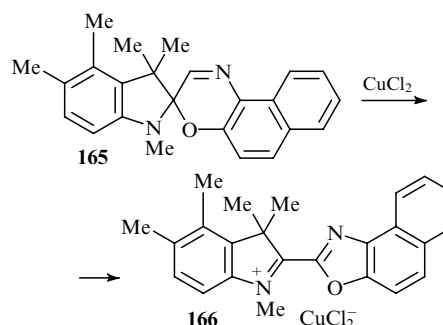
The structures of compounds **162–164** were confirmed by spectroscopic methods. In addition, the structure of compound **164** was established by X-ray diffraction analysis. Photocolouration

of SPO was observed upon irradiation of compounds **162–164** in the absorption band of the organometallic fragment (~420 nm), which was attributed to the intramolecular energy transfer.

The synthesis of stable complexes of SPO of type **115** with Ru(bipy)₂Cl₂ was described in the earlier study.⁸⁵ However, attempts to isolate these compounds in the solid state failed.

In the studies,^{114,115} the formation of stable luminescent adducts of the coloured form of SPO with metal salts in solution has been reported. In some cases, these reactions proceeded even without irradiation.⁶² Nevertheless, the conclusions about the coordination nature of these compounds should be made with caution.

Indeed, Malatesta and co-workers^{116,117} showed that SPO (for example, SPO **165**) can react with metal salts, for example, with CuCl₂, on heating through the redox mechanism to give compounds of type **166**.



Apparently, the naphthooxazole fragment, which is present both in molecule **166** and products of its transformations,¹¹⁷ is responsible for the fluorescence observed.

Recently, analogous transformations have been found in the reactions of SPO **1** with silver salts¹¹⁸ and lead salts.¹¹⁹

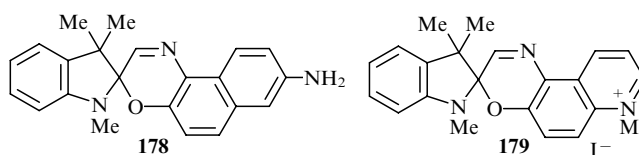
4. Reactions of hydroxymethyl- and formyl-substituted SPO

Hydroxymethyl derivative **52** proved to be very useful in studies of chemical transformations of SPO. French researchers^{61,120} used this compound for the preparation of numerous SPO derivatives (Scheme 4), which are of interest not only as photochromes but also as precursors for the preparation of biphotochromic compounds (see below).

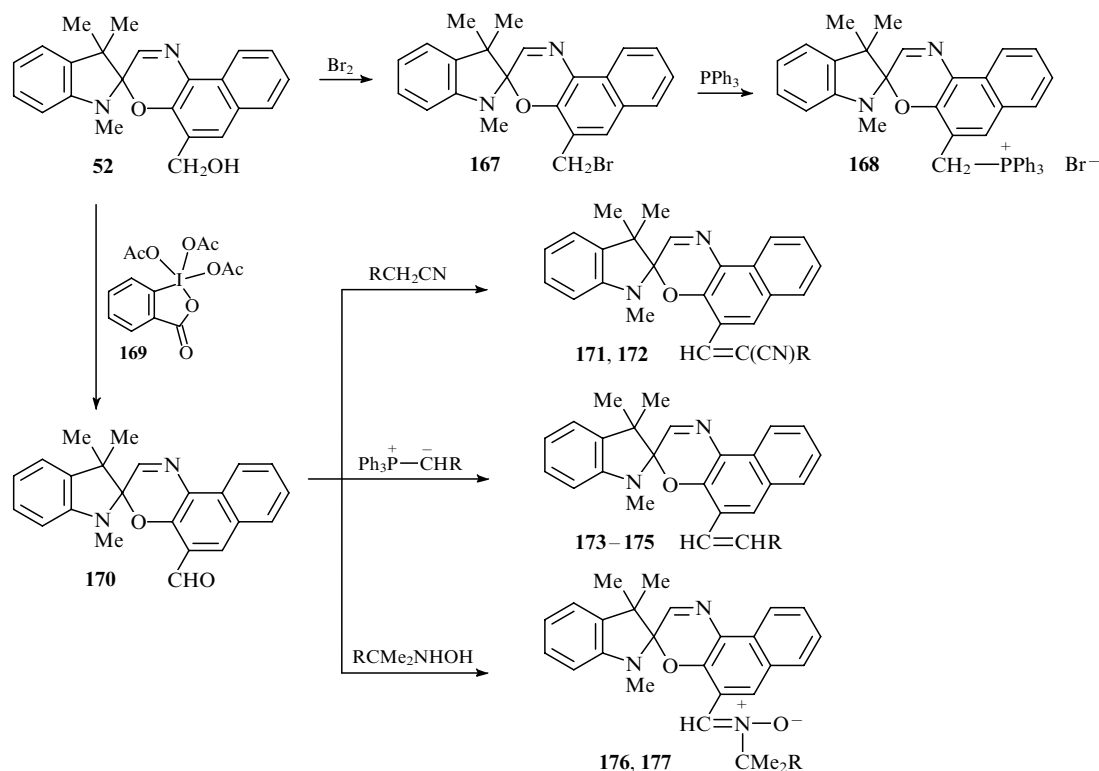
The key reaction in Scheme 4 involves mild oxidation of SPO **52** with periodinane **169** (Dess–Martin reagent) to give formyl derivative **170**. Compound **170** can be involved in different reactions at the aldehyde group, for example, in the Wittig and Knoevenagel reactions, which made it possible to prepare a series of vinyl derivatives **171–175**, which have an extended conjugation system and, as a consequence, possess unique photochromic characteristics.¹²⁰ The same formyl-substituted SPO **170** was used as the starting compound in the synthesis of compounds **176** and **177**, which contain substituents possessing properties of spin traps.^{121,122}

5. Other reactions

Of other SPO transformations, reduction of nitro derivative **136** with hydrazine hydrate in the presence of Raney nickel giving rise to amino derivative **178**¹²³ and the preparation of salt-like SPO **179**, which unexpectedly exhibits photochromic properties in the crystalline state,¹²⁴ deserve notice.



Scheme 4



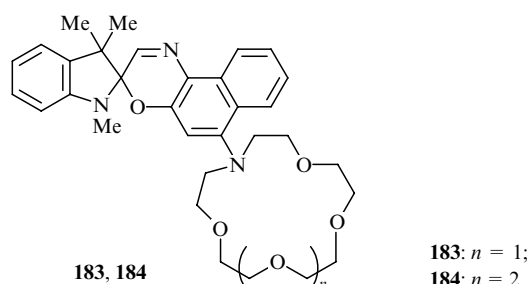
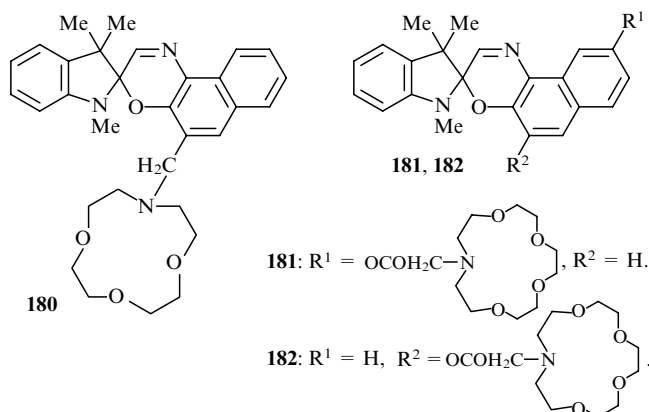
R = CO₂Et (**171**), CN (**172**, **175**), CO₂Me (**173**), CHO (**174**), Me (**176**), PO(OEt)₂ (**177**).

V. Spirooxazine-containing molecular systems

The synthesis of complex molecular systems involving covalently bound photochromic fragments is a promising field of the chemistry of SPO. These systems are increasingly employed as photomodulators, which can change their physicochemical characteristics under irradiation, thus influencing the structure and properties of their chemical environment.

1. Spirooxazine-containing crown ethers

The first compound of this type, *viz.*, SPO **180**, was prepared by Japanese scientists.^{125, 126} They introduced a macrocyclic fragment into the starting 3-hydroxymethyl-2-naphthol. Other approaches were used by the Russian–French research team,^{58, 127–129} who have actively developed this area of investigation in recent years. In particular, compounds **181** and **182** were prepared by acylation of hydroxy-containing SPO **51** and **65**, respectively. The synthesis of SPO **183** and **184** was carried out according to a procedure shown in Scheme 3 (method *b*).

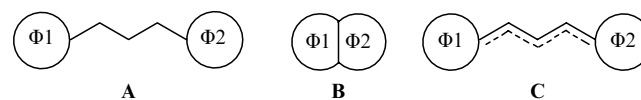


Substantial changes in the parameters of the photochromic transformations of crown-containing SPO in the presence of some metal cations were observed in virtually all studies. The recent comprehensive study¹³⁰ showed that the complex formation is a very complicated process.

2. Spirooxazine-containing biphotochromic systems

The term ‘biphotochrome’ was introduced by Dürr¹³¹ to describe molecules containing two covalently bound photochromic units of the same or different types.

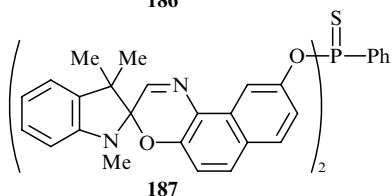
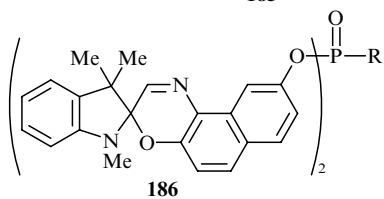
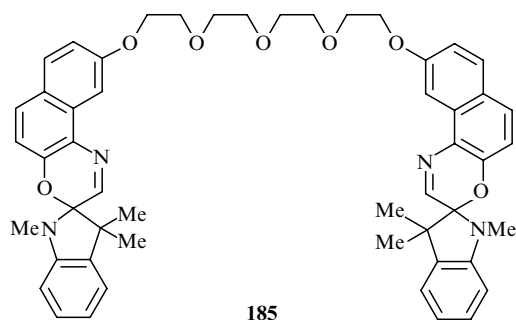
Depending on the mode of binding of two fragments, such compounds can be arbitrarily divided into three types, all having representatives of the spirooxazine series.



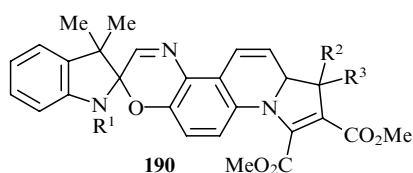
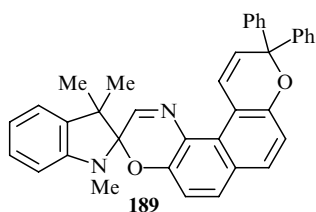
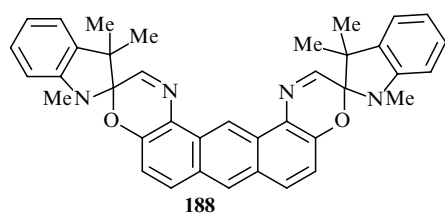
Φ1 and Φ2 are identical or different photochromic molecules.

The properties of compounds of the type **A** in which the photochromic units are linked *via* a non-conjugated chain are determined, to a large extent, by the type of the bridge. Thus, the polyether chain in compound **185** ensures the photomodulated affinity for Na⁺ ions,¹³² whereas the phosphorus-containing

groups in SPO of types **186** and **187** enhance, in the authors' opinion,¹³³ their photostability.

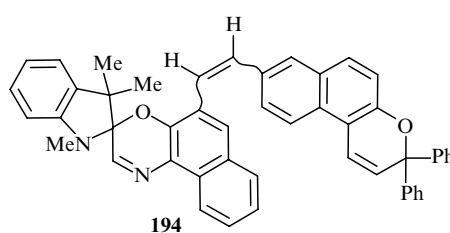
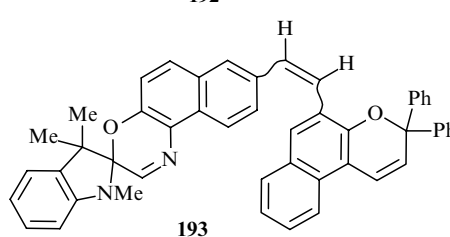
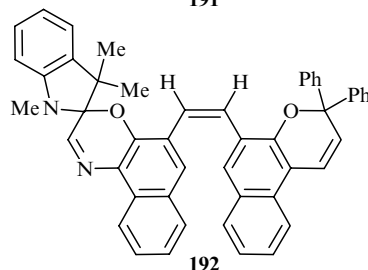
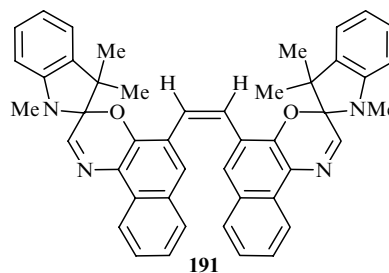


The major impetus for the synthesis of annelated biphotochromes of the type **B** containing common aromatic nuclei was the desired preparation of coloured forms possessing unusual spectral characteristics. However, since the photochromic fragments in these compounds are not independent, their simultaneous photoexcitation presents problems. Of three biphotochromic compounds of the type **B** considered below, *viz.*, SPO–SPO **188**,^{134,135} SPO–chromene **189** (see Ref. 29) and SPO–dihydroindolizines of type **190**,¹³⁶ simultaneous excitation of both photochromic fragments was observed only for compounds **190**. As a result, the absorption spectra of the coloured forms of these compounds are shifted to the IR region.

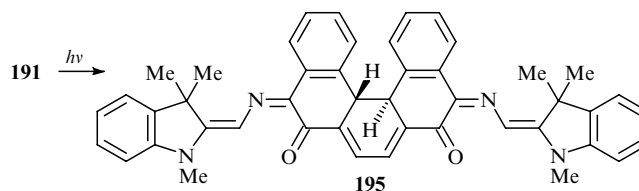


A series of biphotochromes of the type **C** in which the photochromic fragments are conjugated through the vinyl bridges have been described in the recent study.⁶¹

Compounds **191–194** containing the spirooxazine and chromene fragments were prepared from functionally substituted photochromes **168** and **170** by the Wittig reaction.



The photochromic behaviour of the above-mentioned compounds, which has been thoroughly studied later,^{137–140} proved to be very complex. For example, not only successive opening of both oxazine rings but also the *Z* → *E* isomerisation and electrocyclic cyclisation to form compound **195** were observed for SPO **191** obtained in the *Z* configuration.¹⁴⁰

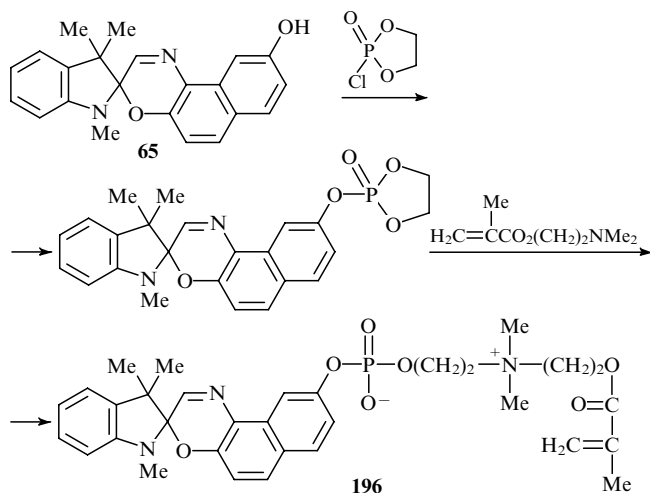


3. Spirooxazine-containing polymers

Most polymeric photochromic SPO-based materials are solutions of photochromes in the corresponding polymers. This procedure for the preparation of polymeric photochromic materials is much simpler than that proceeding *via* the covalent binding of SPO with polymers. However, the latter method has considerable advantages, in particular it:

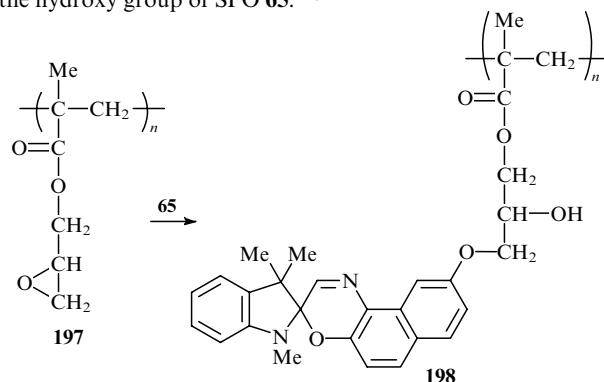
- provides a higher concentration of the photochrome;
- hinders diffusion of the photochrome thus reducing the toxic risk in the course of the *in vivo* functioning of the material (for example, in contact lenses);
- improves the 'photomodulating' influence of the photochrome on the structure and characteristics of the polymer.

Most of the above-described spirooxazine-containing polymers belong to the class of polyacrylates. The corresponding monomers, for example, SPO **145**, are generally prepared by acylation of hydroxy-containing SPO.^{60, 72, 112, 141} However, it is also possible to introduce functional groups capable of being polymerised into the indoline precursors.^{142–144} A more complicated approach was used for the preparation of phosphorus-containing methacrylate monomer **196**. The polymer, which was prepared on the basis of this monomer, mimics the structure of phospholipid membranes.¹⁴⁵



In addition to polymerisation (generally, radical) of spirooxazine-containing monomers, spirooxazine-containing polymers are also synthesised by the introduction of SPO into an available polymer containing functional groups. An example of this approach is the preparation of polymer **198** through the oxirane-

ring opening of poly(glycidyl methacrylate) **197** under the action of the hydroxy group of SPO **65**.¹⁴⁶



Polysiloxanes belong to another large class of spirooxazine-containing polymers. Studies of these polymers were initiated in the beginning of the 1990s by Krongauz and co-workers¹⁴² and are being carried out actively by this research team^{147–149} as well as by Japanese scientists.^{84, 150, 151} The main approaches to the synthesis of the polymers of type **200** are given in Scheme 5.

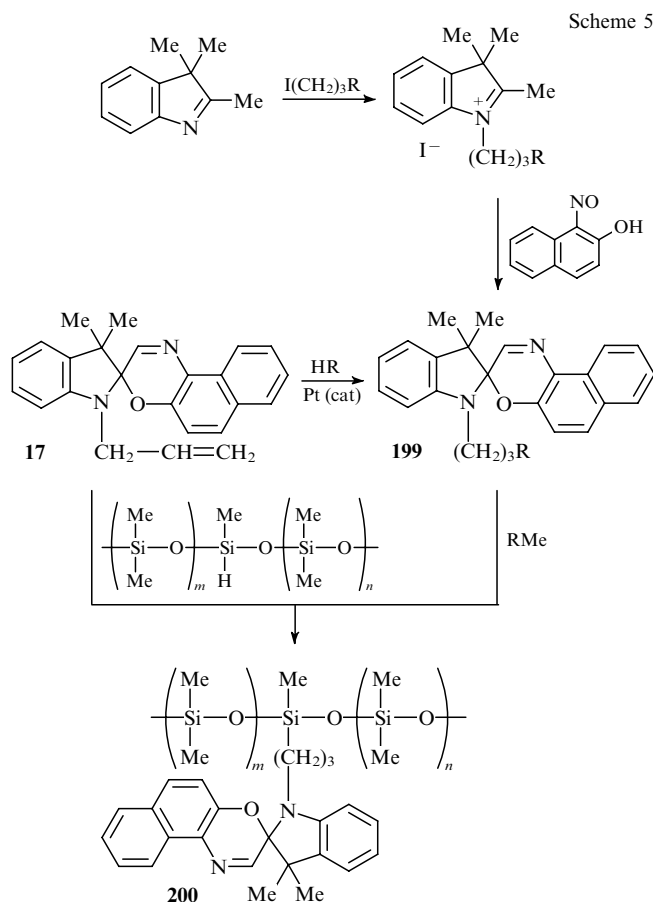
The synthesis of spirooxazine-containing polysulfones⁴³ starting from amino-substituted SPO **30** was also described.

VI. Structures of isomeric forms of spirooxazines and their interconversions in the ground state (solvatochromism and thermochromism)

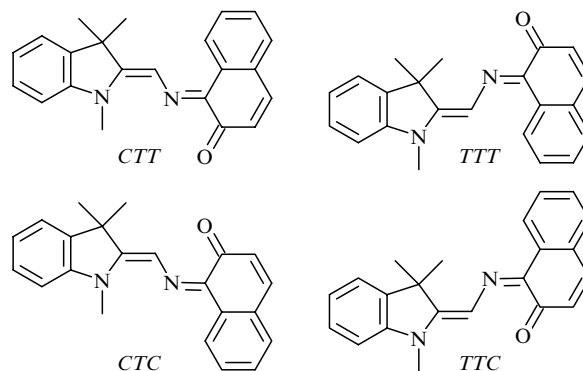
The structures of spirooxazines were comprehensively studied by ¹H NMR spectroscopy, Raman spectroscopy,¹⁵² quantum-chemical methods^{98, 153, 154} and X-ray diffraction analysis.^{16, 70, 77, 155–160}

The NMR spectra of spirooxazines are informative and allow one, with rare exception (for example, in the case of SPO **85** and **96**), to establish reliably the structures of the resulting compounds. Numerous publications^{15, 35, 40, 58, 61, 106, 107, 161} and a special-purpose study¹⁶² included the detailed assignments of the signals for protons and carbon atoms in the ¹H and ¹³C NMR spectra of a broad spectrum of SPO. It should be noted that an unexpected correlation between the chemical shift of the 2'-carbon atom of SPO in the ¹³C NMR spectra and the positions of the absorption maxima of their coloured forms was found in the study.¹⁶³

According to the results of Hartree–Fock quantum-chemical calculations (HF 6-31G**/3-21G),^{153, 154} four possible acyclic isomers of SPO, which are responsible for thermal and photo-induced colouration, adopt transoid configurations, viz., *cis-trans-trans* (CTT), *trans-trans-trans* (TTT), *cis-trans-cis* (CTC) and *trans-trans-cis* (TTC), the TTC isomer being most stable.



R = Si(OEt)₂Me.

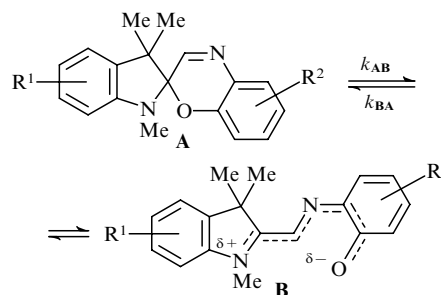


The X-ray diffraction data on the thermally unstable merocyanine form of SPO are scarce. The results of ¹H NMR spectroscopic study and X-ray diffraction analysis of open form **120**,

which was obtained in the synthesis of SPO **118**,⁷⁷ provided evidence for its *TTC* configuration.

In the ¹H NMR spectroscopic study of SPO **1**,⁹⁹ which was carried out directly on irradiation giving rise to the 90% conversion of the cyclic form, it was demonstrated that the *CTC* isomer can be formed in a small amount along with the most stable *TTC* isomer.

The tautomeric equilibrium between the cyclic **A** and merocyanine **B** forms in the ground state is typical of SPO in solutions. The **A** ⇌ **B** equilibrium was studied by ¹H NMR spectroscopy,^{85, 95, 96} circular dichroism spectroscopy^{164, 165} and spectrophotometry.^{13, 96, 166–169}

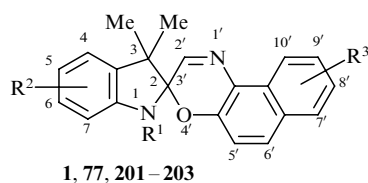


If the concentrations of the equilibrium forms **A** and **B** are sufficiently high that they can be reliably identified by NMR

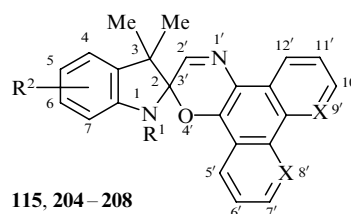
Table 6. Equilibrium constants (K_e), standard enthalpies (ΔH°), free energies (ΔG°), entropies (ΔS°) of the equilibrium **A** ⇌ **B** and rate constants (k_{AB}) and activation energies (E_a^{AB}) of the thermal colouration reaction **A** → **B**.

Compound	Solvent	$10^{-2} K_e$	ΔH° /kJ mol ⁻¹	ΔG° /kJ mol ⁻¹	ΔS° /J mol ⁻¹ K ⁻¹	$10^{-2} k_{AB}$ /s ⁻¹	E_a^{AB} /kJ mol ⁻¹	Ref.
1 ^a	toluene	0.0012	21.7	28.0	-21.0	0.00028	69.0	166
	ethanol	0.011	20.9	22.6	-5.6	0.0025	102.0	166
77 ^a	toluene	0.06	18.0	18.4	-1.3	0.0021	82.4	166
	ethanol	0.58	15.0	12.8	7.4	0.336	56.0	166
201 ^a	"	0.061	17.4	18.4	-3.3	0.017	92.0	168
202 ^a	"	0.04	20.5	19.4	3.7	0.0012	100.0	168
203 ^a	"	0.24	17.4	14.9	8.4	0.0017	118.0	168
204 ^a	toluene	0.51	9.6	13.1	-11.7	0.07	76.1	166
	ethanol	1.1	10.9	11.2	-1.0	3.52	76.5	166
	"	0.8	10.9	12.0	-3.7	3.5	77.0	168
205 ^a	"	0.1	13.7	11.4	7.7	3.2	86.0	168
115 ^b	toluene	2.4	12.1	9.1	6.8	0.39	—	96
	ethanol	7.8	10.8	6.3	15.2	0.90	—	96
	methanol	8.8	8.5	6.0	8.4	1.02	85.7	96
	acetonitrile	9.0	4.3	5.9	-5.4	5.25	—	96
206 ^b	toluene	8.4	3.6	6.1	-8.4	0.87	—	96
	ethanol	28.1	2.5	3.1	-2.0	2.65	—	96
	methanol	34.1	1.0	2.6	-5.5	3.28	79.3	96
	acetonitrile	23.3	1.1	3.6	-8.4	12.51	—	96
207 ^b	heptane	2.5	11.7	9.1	8.8	0.25	83.9	96
	toluene	7.5	8.4	6.4	6.8	0.97	74.5	96
	ethanol	30.6	3.6	2.9	2.3	0.58	100.5	96
	methanol	43.2	1.8	2.1	-1.2	0.75	101.5	96
	acetonitrile	44.6	0	2.0	-6.8	3.74	83.8	96
208 ^b	heptane	2.3	13.4	9.3	13.9	0.25	89.8	96
	toluene	8.6	8.1	6.0	6.8	1.24	78.6	96
	ethanol	33.8	2.7	2.7	0.1	0.59	102.4	96
	methanol	45.3	1.6	1.9	-1.2	0.82	115.3	96
	acetonitrile	49.3	0	1.7	-5.7	3.96	83.9	96

^a For these SPO, K_e and k_{AB} were determined at 298 K. ^b For these SPO, K_e and k_{AB} were determined at 296 K.



1, 77, 201–203



spectroscopy, the equilibrium constants can be determined (K_e). Due to the presence of the prochiral sp^3 -hybridised carbon atom in the indoline ring, the kinetics of the reaction $A \rightleftharpoons B$ can be studied by dynamic ^1H or ^{13}C NMR spectroscopy (from the shapes of the signals of the diastereotopic methyl groups bound to this carbon atom). The potential barrier is determined by the energy of the $C_{\text{spiro}}-O$ bond cleavage.

For most of SPO, the equilibrium $A \rightleftharpoons B$ is substantially shifted to the cyclic isomers **A**. In these cases, it is most convenient to monitor the equilibrium by spectrophotometry, which enables one to detect the coloured form at very low concentrations (lower than 1%). If the molar extinction coefficients (MEC) of acyclic isomers are known, the equilibrium constant and thermodynamic parameters of the equilibrium can also be determined.

The available published data allow one to follow the influence of the molecular structure of various indolinospirooxazines on the quantitative characteristics of the equilibrium $A \rightleftharpoons B$ (Table 6). In the series of SPO containing aromatic or heterocyclic fragments annelated to the oxazine nucleus, the equilibrium constant increases on going from naphthalene to phenanthrene and phenanthroline. The insertion of electron-donating groups (Oalk) at position 5 of the indoline fragment leads to an increase in the equilibrium concentration of the merocyanine form in solutions of SPO.

The equilibrium position is sensitive to the changes in the polar properties of the solvents and temperature of the solutions. In polar solvents, the equilibrium is shifted to acyclic isomers. The equilibrium constant increases as the temperature is raised. The temperature dependence of the equilibrium constant enables one to determine the thermodynamic characteristics of the equilibrium, *viz.*, the standard enthalpy (ΔH°), free energy (ΔG°) and entropy (ΔS°) (see Table 6).

The phenomenon related to the changes in the positions and sometimes in the intensities of the bands in the electronic absorption or fluorescence spectra of solutions due to changes in the properties of the solvent (polarity, tendency to be involved in specific interactions) is called solvatochromism.¹⁷⁰ The solvatochromism of spirooxazines is associated with the influence of the nature of the solvent on the position of the equilibrium $A \rightleftharpoons B$. The solvatochromic effect of SPO can be estimated from the change in the equilibrium constant in passing from one solvent to another (at the same temperature). As can be seen from Table 6, the largest changes in the equilibrium constant on going from weakly polar to polar solvents are observed for SPO of the phenanthroline series. The strong solvatochromic effect is observed also for 5-alkyloxy-substituted compounds **207** and **208**.

Thermochromism is a reversible change in colour of a compound due to a change in temperature in the range limited by the boiling point of the solvent (for solutions) or melting point (for solids).¹⁷¹ Apparently, the temperature dependence of the equilibrium constant between the cyclic and merocyanine forms of SPO in solutions is an indication that the corresponding SPO are thermochromes, *viz.*, compounds exhibiting thermochromism, and the thermochromic effect can be estimated from the standard enthalpy of the equilibrium. How fast the colour changes following the change in temperature, in particular, how fast solutions of SPO become coloured with increasing temperature, depends on the rate of attainment of the equilibrium. For SPO, $k_{BA} > k_{AB}$, *i.e.*, thermal colouration is the rate-limiting process for the attainment of the equilibrium. Hence, the activation energy (E_a^{AB}) of the process $A \rightarrow B$ can be rather accurately determined from the temperature dependence of the rate constant of colouration k_{AB} . If the preexponential factors in the Arrhenius equation have close values, the larger is E_a^{AB} , the more pronounced is the temperature dependence of k_{AB} for SPO. Hence, the thermochromic effect in SPO of the phenanthroline series is more pronounced in non-polar solvents, whereas the rate of the colour change with temperature is higher in alcohols (see Table 6).

VII. Spectral properties of spirooxazines

1. Electronic absorption spectra of cyclic forms of spirooxazines

Electronic absorption spectra of spirooxazines are characterised by long-wavelength absorption with maxima predominantly in the region of 330–380 nm and molar extinction coefficients (MEC) of 4000–20 000 litre mol⁻¹ cm⁻¹ (Fig. 1, Table 7). The effect of the substituents on the spectral characteristics of spirooxazines is associated with the structural features of SPO molecules, *viz.*, with the presence of two acoplanar fragments, heterocyclic and oxazine responsible for photochromism.

The structural simulation showed that the electronic absorption spectra of SPP, which are structural analogues of SPO, can be considered with a certain degree of approximation as linear combinations of the absorption spectra of the constituent fragments. This approximation is possible because the fragments weakly interact with each other due to acoplanarity. The long-wavelength absorption bands are assigned to the photochemically ‘active’ pyran moiety, whereas the short-wavelength bands are assigned to the heterocyclic moiety.¹⁷³ An analogous approach was used^{13, 166} for the interpretation of the absorption spectra of SPO. In particular, the absorption spectrum of SPO **1** in ethanol has a group of long-wavelength bands with maxima at 345 and 317 nm, which were assigned to electron transfers in the naphthooxazine moiety, and bands with maxima at 297 and 235 nm, which were assigned to transitions in the heterocyclic fragment.¹³

The validity of this assignment was confirmed by a comparison of the absorption spectra of solutions of SPO containing substituents in the heterocyclic and oxazine fragments, respectively. As can be seen from Table 7, the substituents in the oxazine fragment of spiroindolinonaphthooxazines exert a more substantial effect on the positions of the long-wavelength absorption bands than the substituents in the indoline moiety. The spectral range of changes in the positions of the long-wavelength absorption maxima of SPO containing substituents in the naphthooxazine moiety with respect to unsubstituted SPO **1** is ~40 nm, whereas this range for SPO containing substituents in the indoline fragment is only 3 nm (cyclohexane).

The effect of substituents in the oxazine moiety of SPO on the positions of the absorption maxima is determined by their electron-donating and electron-withdrawing properties. Compounds containing electron-donating groups at positions 5' and 9' are characterised by short-wavelength (with respect to unsubstituted SPO **1**) shifts of the maxima of the long-wavelength absorption bands, whereas compounds containing electron-donating groups at positions 6' and 8' are characterised by the corresponding long-wavelength shifts. Electron-withdrawing sub-

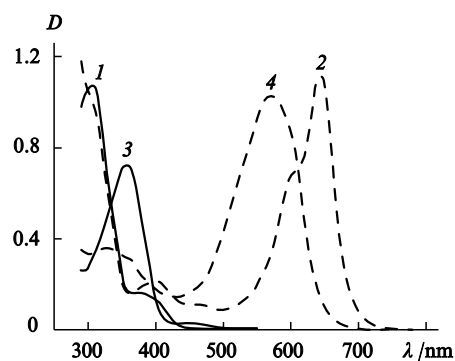
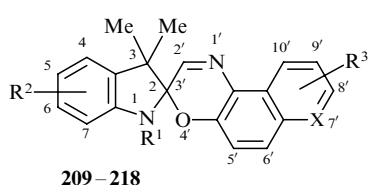


Figure 1. Electronic absorption spectra of SPO **217** in ethanol ($c = 1.1 \times 10^{-4}$ mol litre⁻¹, $T = 293$ K) (1, 2) and SPO **29** in toluene ($c = 3.4 \times 10^{-5}$ mol litre⁻¹, $T = 293$ K) (3, 4). Curves 1, 3 were measured before irradiation; curves 2, 4 were recorded after irradiation with light at $\lambda = 365$ nm.

Table 7. Positions of the absorption maxima ($\lambda_{\max}$) and molar extinction coefficients ($\epsilon_{\max}$) of the cyclic isomers **A** of spirooxazines.

Com- pound	$\lambda_{\max}$ /nm ($\epsilon_{\max}$ /litre mol ⁻¹ cm ⁻¹)					Ref.	Com- pound	$\lambda_{\max}$ /nm ($\epsilon_{\max}$ /litre mol ⁻¹ cm ⁻¹)					Ref.
	cyclo- hexane	toluene	ethanol	methanol	aceto- nitrile			cyclo- hexane	toluene	ethanol	methanol	aceto- nitrile	
1	320 (7600)	319 (7640)	318 (6450)	318 (6800)	317 (6600)	172	212	336 (5200)	337 (6020)	334 (6010)	334 (7580)	337 (5520)	172
	349 (5020)	348 (5410)	347 (4550)	347 (4710)	347 (4480)			372sh (2610)	376sh (2890)	375 (3660)	375sh (3920)	372sh (2540)	
141	318 (10330)	318 (11130)	317 (10640)	316 (9280)	316 (8900)	66	133	366 (9320)	368 (8612)	367 (9450)	366 (14690)	366 (8460)	66
	346 (5780)	347 (6280)	348 (6060)	347 (5180)	346 (4810)		132	367 (7710)	368 (7300)	369 (7850)	369 (7560)	368 (7370)	66
29	347 (21910)	356 (21490)	364 (21650)	—	367 (20210)	66	134	369 (8560)	372 (7770)	371 (7360)	370 (7260)	369 (7950)	66
51	340 (8740)	340 (9060)	339 (9100)	337 (7740)	—	66	55	—	—	358 (3920)	—	—	64
							213	366 (3970)	367 (3940)	366 (3920)	365 (4110)	365 (3160)	172
52	323 (8990)	323 (7810)	322 (7830)	321 (9500)	319 (7140)	172	214	354 (5020)	355 (4610)	353 (4840)	342 (4200)	352 (4130)	66
209	348sh (10730)	348sh (9710)	348sh (10420)	348sh (8350)	348sh (10400)	172	58	348sh (4530)	348sh (4510)	348 (4330)	348 (4040)	348 (4890)	66
	343sh (4030)	344sh (3720)	344sh (3720)	344sh (4320)	344sh (4120)		215	348 (4420)	348 (—)	348sh (—)	348sh (3990)	348sh (4390)	66
170	386 (4030)	389 (3720)	292 (3720)	357sh (4320)	389 (4120)	66	136	356 (13300)	352 (9920)	356 (11710)	356 (12640)	356 (11970)	66
	404 (3540)	406 (3190)	389 (1870)	400sh (1780)	404 (3580)		216	336 (9810)	337 (8580)	337 (8900)	336 (8580)	334 (9500)	66
210	387 (4000)	389 (3640)	357 (3500)	357sh (4340)	389 (3660)	172	217	321 (10780)	323 (9780)	322 (9260)	323 (10030)	321 (11530)	66
	405 (3450)	406sh (3190)	400 (2460)	400sh (2130)	—		61	363 (—)	364 (4370)	365 (—)	365 (4560)	363 (4490)	172
174	311 (21560)	316 (22440)	319 (25600)	317 (23240)	314 (26080)	172		379 (—)	382 (3990)	379 (—)	379 (4090)	379 (4070)	
	389sh (2830)	389sh (3460)	400 (2740)	420 (2470)	400 (2570)		218	346 (5150)	347 (4890)	345 (4400)	346 (4440)	345 (4630)	172
53	385 (4340)	382 (4020)	402 (6470)	398 (5210)	403 (5360)	66		365 (3740)	364sh (3590)	359 (3500)	360sh (3530)	360sh (3590)	
	407sh (3760)	412 (3090)					204	298 (14370)	299 (13280)	285 (17890)	285 (16310)	296 (10520)	172
175	389 (2840)	386 (2930)	378 (3010)	378 (2740)	374 (2930)	172		344 (7130)	344 (7120)	344 (6950)	342 (6280)	342 (5760)	
211	376 (2980)	378 (3100)	376 (3430)	374 (3060)	372 (3250)	66		375 (4970)	375 (5090)	373 (5000)	373 (4480)	374 (3990)	
172	349 (20260)	354 (20890)	348 (19750)	345 (19010)	344 (18720)	172	115	—	344 (5900)	345 (5890)	344 (5810)	343 (6030)	96
	432 (2170)	435 (2430)	432 (1990)	431 (1830)	424 (2080)		206	—	347 (5980)	347 (5710)	347 (5650)	345 (5690)	96
77	363 (10660)	364 (11710)	365 (10370)	364 (12700)	364 (10800)	66	207	345 ^a (5560)	345 (5420)	348 (5490)	348 (5790)	351 (5880)	96
							208	349 ^a (5670)	345 (5410)	350 (5400)	347 (5680)	351 (5800)	96

^a Heptane as the solvent.

Compound	R ¹	R ²	R ³	X
209	Me	5-OMe	5'-CH ₂ OH	CH
210	C ₁₆ H ₃₃	H	5'-CHO	CH
211	Me	5-OMe	5'-CH=CHCN	CH
212	Me	H	6'-SC ₆ H ₄ OMe- <i>p</i>	CH
213	Me	H	8'-OMe	CH
214	Me	H	8'-Br	CH
215	Me	5-OMe	8'-CN	CH
216	Me	H	9'-OMe	CH
217	Me	5-OMe	9'-OMe	CH
218	Me	H	H	N

stituents at positions 5', 6', 7', 8' and 9' cause long-wavelength shifts of the absorption maxima in the spectra of solutions of SPO.

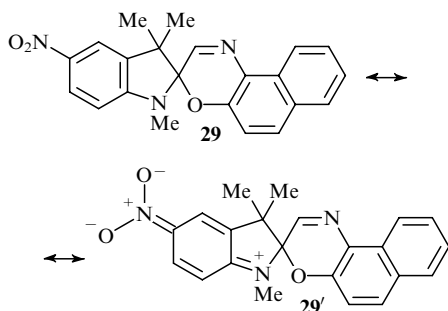
The electronic absorption spectrum of SPO **172** is characterised by an unusually broad long-wavelength absorption region due to a band with a weakly pronounced maximum at 430 nm. Conceivably, this absorption can be assigned to the intramolecular charge transfer from the naphthooxazine ring to the CN groups *via* the vinyl chain.

An extension of the π system of the oxazine fragment upon benzoannellation leads to a shift of the absorption boundary to the long-wavelength region. The electronic absorption spectrum of SPO **204** of the phenanthrene series has an additional maximum at 375 nm (toluene) compared to the absorption spectrum of naphtho derivative **1**, which is the manifestation of the vibrational nature of the long-wavelength absorption band belonging to the modified phenanthrene system.¹⁷⁴ This effect is even more pronounced in the case of anthracene derivative **103**. The spectrum of the latter compound has an additional long-wavelength vibrational maximum at 427 nm (heptane).¹⁷⁵

The modifications of the heterocyclic moiety of SPO by the replacement of the indoline fragment with the spatially hindered (SPO **40**¹⁷) or saturated (SPO **43**,⁵¹ **44**¹⁷) azaheterocycles lead to substantial changes in the position of the long-wavelength absorption band.

Nevertheless, substituents in the indoline fragment of SPO can exert an effect on the position of the long-wavelength absorption maximum assigned to the transfer in the oxazine fragment. This effect depends on the nature of the substituents in both moieties of SPO. For example, the insertion of the methoxy group at position 5 of the indoline fragment has virtually no effect on the position of the long-wavelength absorption band in the case of SPO devoid of substituents in the naphthooxazine fragment (*cf.* **1** and **141**, Table 7), whereas such an insertion leads to a small (1–4 nm) long-wavelength shift in the case of 6'-cyano-substituted SPO (*cf.* **132** and **134**) and a noticeable short-wavelength shift by 13 nm in the spectra of 9'-methoxy-substituted SPO (*cf.* **216** and **217**).

In most cases, the electronic absorption spectra of SPO are independent of the polarity of the solvents and their ability to be involved in specific interactions (see Table 7). In this connection, noteworthy is the spectrum of 5-nitro-substituted SPO **29**. The maximum of long-wavelength absorption in the spectra of solutions of this compound is shifted bathochromically as the polarity of the solvent is increased. Apparently, this fact is attributed to the enhancement of resonance stabilisation of bipolar structure **29'** with increasing polarity of the solvent. This shift was not observed in the spectrum of 8'-nitro-substituted SPO **136**.

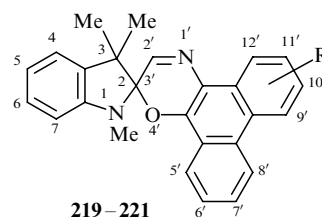


2. Electronic absorption spectra of the coloured forms of spirooxazines

The spectra of the coloured forms of SPO show absorption in a substantially longer-wavelength region than the spectra of their cyclic isomers. The maxima of the bands are observed in the region of 480–670 nm and the bands are much more intense (40 000–80 000 litre mol⁻¹ cm⁻¹; see Fig. 1, Table 8). Under normal conditions, the long-wavelength bands in the stationary absorption spectra have an asymmetrical shape, which is man-

ifested as a shoulder on the short-wavelength side (SPO **132**) or, more rarely, on the long-wavelength side (SPO **51**) relative to the maximum of the band. The position of the shoulder depends on the nature of the solvent (*cf.* SPO **29** and **216**). This effect is a consequence of the fact that the long-wavelength transition of the most stable *trans* isomer of the merocyanine form is vibrational in nature rather than results from the overlapping of bands of several stereoisomers.

The spectral characteristics of the coloured forms of SPO are sensitive to structural modifications and, unlike those of the cyclic forms, depend substantially on the substituents not only in the oxazine moiety of SPO but also in the heterocyclic fragment due to conjugation of both fragments occurring after the ring opening. The positions of the absorption maxima and the molar extinction coefficients (MEC) of the coloured forms **B** of a number of the above-considered spirooxazines and new SPO **219–221** are given in Table 8.



R = 9'-NO₂ (**219**), 10'-NO₂ (**220**), 11'-NO₂ (**221**).

The electron-donating substituents at positions 5', 6' and 9' of the naphthooxazine moiety of spiroindolinonaphthooxazines cause short-wavelength shifts of the maxima of the absorption bands of the open form, whereas the presence of such substituents at position 8' leads to long-wavelength shifts. Electron-withdrawing groups at positions 5'–9' cause a long-wavelength shift of this maximum. By contrast, the insertion of electron-donating substituents into the indoline fragment of SPO leads to a long-wavelength shift of the absorption maximum, whereas the introduction of electron-withdrawing substituents causes a short-wavelength shift. The most essential spectral changes occur upon the insertion of a substituent at position 5 of the indoline fragment and at position 6' of the naphthooxazine fragment.

Benzoannellation of the naphthooxazine fragment causes a slight shift of the absorption maximum of the coloured form. Thus, benzoannellation at positions 5', 6' (SPO **204**) leads to a short-wavelength shift, benzoannellation at positions 8', 9' (SPO **103**) causes a long-wavelength shift, whereas benzoannellation at positions 7', 8' (according to the results of the study¹⁷⁶) has virtually no effect on the absorption spectrum (it remains similar to the spectrum of the form **B** of SPO **1**).

On going from naphthalene SPO **1** and phenanthrene SPO **204** to quinoline SPO **218** and phenanthroline SPO **115**, respectively, no noticeable spectral changes occur in absorption of the merocyanine forms.

In general, the spectral changes that are observed for a series of SPO and are associated with the insertion of substituents into the acyclic isomers **B** of spiroindolinonaphthooxazines, are typical also of other SPO of the indoline series. Thus, the introduction of the NO₂ group at positions 9', 10' or 11' of phenanthrene derivatives of SPO leads to a long-wavelength shift of the absorption maximum of the coloured form.¹⁷⁷ Analogous changes occur also upon the introduction of the alkyloxy substituent at position 5 of the indoline fragment of phenanthroline-containing SPO **207** and **208** (see Table 8).

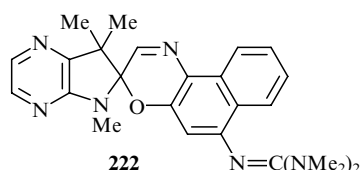
The replacements of the indoline fragment by the azabicycloalkane (SPO **40–42**),^{46–49} piperidine (SPO **43**),⁵¹ homoazaadamantane (SPO **44**)¹⁷ or dibenzooxazepine (SPO **48**)¹⁸ fragments cause short-wavelength shifts of absorption bands of acyclic isomers of SPO. In the case of SPO **40–42**, these shifts are associated with disruption of coplanarity resulting in the absence of conjugation between the lone pair of the nitrogen atom and the

Table 8. Positions of the absorption maxima ($\lambda_{\max}$) and molar extinction coefficients ($\epsilon_{\max}$) of the coloured forms **B** of spirooxazines.

Com- pound	$\lambda_{\max}$ /nm ($\epsilon_{\max}$ /litre mol ⁻¹ cm ⁻¹)					Ref.	Com- pound	$\lambda_{\max}$ /nm ($\epsilon_{\max}$ /litre mol ⁻¹ cm ⁻¹)					Ref.
	cyclo- hexane	toluene	ethanol	methanol	aceto- nitrile			cyclo- hexane	toluene	ethanol	methanol	aceto- nitrile	
1	556	596	610	613	602	172	134	647	661	651	649	654	66
	578sh	565sh	572sh	573sh	565sh			(65870)			(67150)		
141	593	612	626	623	616	66		601sh	614sh	613sh	610sh	610sh	
				(59540)			55	—	605	615	—	610 ^a	64
	567sh	578sh	585sh	579sh	573sh		213	588	608	631	632	616	172
29	537	566	605	—	577	66		565sh	584sh	598sh	600sh	561sh	
		(42780)					214	591	608	617	614	608	66
	516sh	591sh	584sh		602sh			(43740)			(44680)		
	565sh							564sh		581sh	576sh	576sh	
51	573	587	595	592	—	66	58	597	611	607	606	603	66
		(39540)						570sh					
	550sh	622sh	618sh	615sh			215	612	622	616	615	618	66
52	591	605	609	609	603	172		(65940)			(64480)		
	563sh	576sh	574sh	575sh	575sh			570sh	584	578sh	575sh	579sh	
209	607	618	623	623	615	172	136	603	617	609	607	612	66
	580sh	582sh	585sh	585sh	575sh			(59950)			(60650)		
170	617	633	638	632	633	66		574		572sh	571sh	574sh	
		(50760)		(50350)			216	556	568	608	604	601	66
	584sh	593sh	591sh	583sh	588sh			(42550)			(42600)		
210	624	635	641	635	637	172		581sh	595sh	571sh	573sh	561sh	
		(52700)		(51800)			217	593	609	617	618	612	66
	587sh		597sh	591sh	595sh			(58650)			(61800)		
174	618	632	639	636	633	172		568sh	578sh	580sh	579sh	575sh	
	589sh	593sh	597sh	594sh	590sh		61	612	620	607	606	612	172
53	596	612	626	622	617	66		(59870)			(57570)		
				(43840)				575sh	580sh	570sh	565sh	570sh	
	562sh	578sh	581sh	580sh	575sh		66	—	593	—	—	—	73
175	615	626	632	629	627	172	67	—	605	—	—	—	73
	583sh	585sh	588sh	588sh	590sh		218	556	594	597	599	597	172
211	632	645	642	641	641	66		(52680)			(57950)		
		(58780)		(60740)				577sh	563sh	561sh	558sh	559sh	
	567sh		604sh		600sh		204	568	582	598	598	589	172
172	658	668	658	657	657	172		543sh	552sh	573sh	573sh		
	615sh	625sh		611sh	618sh		219	—	585	—	—	—	174
77	543	567	592	593	572	66	220	—	604	—	—	—	174
		(56730)					221	—	592	—	—	—	174
	553sh	550sh	560sh	560sh	541sh		103	616 ^b	—	654	—	634 ^a	175
212	587	603	637	634	633	172		(63000)		(65000)		(70000)	
	624sh	637sh	606sh	601sh	596sh		115	—	584	593	592	588	96
133	623	638	642	640	638	66		(51610)	(56370)	(57700)	(55800)		
		(58600)		(58740)			206	—	588	597	596	592	96
	585sh	602sh	602sh	598sh	598sh			(52760)	(55470)	(56220)	(56360)		
132	631	645	643	642	643	66	207	588 ^b	601	611	609	604	96
		(57520)		(60840)				(59690)	(60960)	(73300)	(72900)	(59100)	
	592sh	601sh	600sh	599sh	600sh		208	588 ^b	601	611	609	604	96
								(61480)	(60670)	(78800)	(78150)	(61820)	

^a Acetone as the solvent. ^b Heptane as the solvent.

aromatic nucleus. The shortest-wavelength absorption is observed for the merocyanine forms of azaindoline-containing **SPO 45–47**. In particular, the spectrum of the form **B** of **SPO 222** (6'-substituted derivative **SPO 47**) in toluene has an absorption maximum at 478 nm.²⁰



The positions of the absorption maxima of the open forms of **SPO** depend on the polar properties of the solvents. The observed

solvatochromic effect can be both positive and negative. In the case of spiroindolinonaphthooxazines, the sign of this effect is determined by the degree of quinoidation (or bipolarity) of the merocyanine form, which depends on the electron-donating and electron-withdrawing properties of the substituents and their positions in a particular moiety of **SPO**.^{64, 66}

Analysis of the dependence of the spectral characteristics of photomerocyanines **B** on empirical Brooker's parameters (χ_R and χ_B) of the solvents enables one to estimate their polar properties.^{178–181} For 6'- and 8'-cyano-, 8',9'-dicyano- and 8'-nitro-substituted spiroindolinonaphthooxazines, there is a correlation between the frequencies of the absorption maxima of the acyclic isomers **B** and the parameters χ_B , whereas a correlation with the parameters χ_R is lacking, which is indicative of the negative

solvatochromism.⁶⁶ The above-mentioned correlation is most pronounced in the presence of an additional substituent, *viz.*, the methoxy group, at position 5. The observed effect provides evidence for a substantial charge delocalisation in the ground state of photomerocyanines resulting in stabilisation of the bipolar structure. By contrast, there is a correlation between the frequencies of the absorption maxima of the coloured forms **B** and the parameters χ_R for unsubstituted SPO **1** as well as for 6'-NC₅H₁₀-, 8'-OMe-, 9'-OMe- and 5-NO₂-substituted SPO, whereas there is no correlation with the parameters χ_B , *i.e.*, these compounds exhibit the positive solvatochromism. This effect results from a weak polarity of the ground state of the acyclic isomer, *i.e.*, from the predominantly quinoid structure of photomerocyanine **B**.

Hence, electron-withdrawing substituents in the naphthooxazine moiety of SPO would be expected to facilitate delocalisation of the negative charge on the oxygen atom giving rise to properties typical of bipolar structures. Electron-donating groups in the indoline fragment, which facilitate delocalisation of the positive charge on the nitrogen atom, exert an analogous effect. By contrast, a bipolar structure is thermodynamically unfavourable in the presence of electron-donating substituents in the naphthooxazine fragment, which facilitate an increase in the negative charge on the oxygen atom, and electron-withdrawing substituents in the indoline fragment, which lead to an increase in the positive charge on the nitrogen atom. As a consequence, the merocyanine form undergoes quinoidation. If substituents are present in both moieties of SPO, their effect would depend on which properties prevail.

There is a certain dependence of the changes in the intensities of long-wavelength absorption bands of the coloured forms of SPO on their molecular structures and properties of the solvents (see Table 8). The molar extinction coefficients of the absorption maxima of the merocyanine forms ($\epsilon_{\max}^B$) are larger for the structures exhibiting bipolar properties than for the corresponding quinoid isomers. Thus, the $\epsilon_{\max}^B$ coefficients for SPO **61**, **132**, **134**, **136**, **141**, **211** and **215** whose acyclic isomers have bipolar structures are in the range of 57 000–67 000 litre mol⁻¹ cm⁻¹, whereas these coefficients for the quinoid forms **B** of SPO **1**, **33**, **56**, **214** and **216** are in the range of 40 000–45 000 litre mol⁻¹ cm⁻¹.⁶⁶ An analogous effect is observed for indoline-containing SPO **115** and **206–208** of the phenanthroline series. The larger $\epsilon_{\max}^B$ coefficients are observed for SPO **207** and **208** containing electron-donating (OAlk) substituents in the indoline moiety of SPO, which facilitate polarisation of the merocyanine form.⁹⁶ In polar solvents, the $\epsilon_{\max}^B$ values for the absorption maxima of the coloured forms of SPO are generally larger than those in weakly polar solvents. The largest $\epsilon_{\max}^B$ coefficients are observed for SPO **207** and **208** in alcohols. This is associated with the formation of intermolecular hydrogen bonds, which can stabilise bipolar forms of acyclic isomers.

VIII. Dark decolouration of spirooxazines

As mentioned above, the thermochromism of SPO is the temperature-induced change in the equilibrium between isomers in the ground electronic state. By analogy, the photochromism can be considered as the photoinduced change in the equilibrium giving rise to a new equilibrium between the isomers in which at least one isomer, for example, the cyclic isomer (in the general case, both **A** and **B** isomers), occurs in the excited state. The equilibrium position attained under continuous irradiation is known as the photostationary state. For a quantitative analysis of the system, it is important to establish the identity (or difference) of the products of thermal and photochemical transformations of the starting SPO. Generally, products of thermal and photochemical reactions of SPO observed in stationary conditions at temperatures higher than 10 °C are spectrally identical. After termination of irradiation, the system relaxes from the photostationary state to the thermal equilibrium state occurring at this temperature. This state

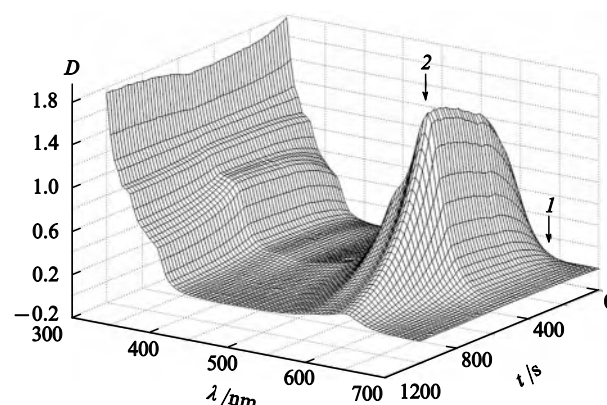


Figure 2. Evolution of the absorption spectra of SPO **58** in toluene ($c = 1.2 \times 10^{-4}$ mol litre⁻¹, $T = 293$ K) under irradiation with light at 365 nm (**1**) and after termination of irradiation (**2**).

is characterised by the rate constant, which is equal to the sum of the rate constants of the forward (k_{AB}) and reverse thermal reactions (k_{BA}) (Fig. 2). Since $k_{BA} \gg k_{AB}$ in most cases (*cf.* Tables 6 and 9), the observed relaxation process, which is referred to as a dark reaction and follows an exponential law in solutions, is described by the rate constant k_{BA} . The value, which is inversely proportional to the apparent rate constant of dark decolouration, is often used in the discussion of the practical use of photochromes and referred to as the lifetime of the coloured form (τ_B). For solutions of SPO, τ_B ranges from 10⁻¹ to 10⁴ s.

The characteristics of the dark decolouration reaction of SPO, *viz.*, the rate constant (k_{BA}) and the activation energy (E_a^{BA}), vary over wide ranges depending on the molecular structure of SPO and the nature of the solvent (Table 9).

The solvents have an ambiguous effect on the rate constant of the reverse reaction of SPO, which is determined by the electron-donating and electron-withdrawing properties of substituents in the heterocyclic and oxazine fragments. In the case of spiroindolinonaphthooxazines, certain tendencies in the change of k_{BA} can be revealed. For monosubstituted compounds containing electron-donating substituent in the naphthooxazine fragment (for example, SPO **1**, **51**, **77**, **213**, **216**) or an electron-withdrawing substituent in the indoline fragment (SPO **29**), the rate constant increases in parallel with the polarity of the solvent. By contrast, the rate constant decreases with increasing polarity of the solvent for SPO containing electron-withdrawing groups in the indoline moiety (for example, SPO **58**, **132**, **133**, **136**, **213**) or electron-donating substituents in the naphthooxazine moiety (SPO **141**, **207**, **208**). If several substituents are present in both fragments of SPO, the direction in which the rate constant of the reverse reaction changes depending on the polar properties of the solvents is determined by the relation between the electron-donating and electron-withdrawing properties of the substituents in the indoline and naphthooxazine fragments. Therefore, the revealed correlations reflect to a certain extent the polarity of merocyanines. It should be noted that the rate constant of the reverse thermal reaction in solvents, which have specific interactions (such as alcohols) and can form intermolecular hydrogen bonds with photoinduced forms of SPO, can change stepwise rather than in parallel with the polar properties of the solvents, which are determined, for example, by the dielectric permeability (see Table 9).

In considering the effect of the molecular structure of SPO on the rate constant of the dark reaction, it is necessary to take into account the above-mentioned opposite relationships between the rate constant and the polar properties of the solvents. Nevertheless, there are general regularities, which persist regardless of the nature of the solvent. The introduction of electron-withdrawing substituents into the naphthooxazine moiety of spiroindoli-

Table 9. Characteristics of thermal recyclisation, *viz.*, rate constants (k_{BA}) and activation energies (E_{a}^{BA}).

Com- pound	$10^{-2} k_{\text{BA}} / \text{s}^{-1}$ ($E_{\text{a}}^{\text{BA}} / \text{kJ mol}^{-1}$)					Ref.	Com- pound	$10^{-2} k_{\text{BA}} / \text{s}^{-1}$ ($E_{\text{a}}^{\text{BA}} / \text{kJ mol}^{-1}$)					Ref.
	cyclo- hexane	toluene	ethanol	methanol	aceto- nitrile			cyclo- hexane	toluene	ethanol	methanol	aceto- nitrile	
1	18.2 (68.4)	19.1 (62.8)	26.5 (85.9)	27.2 (83.3)	112.2 (86.1)	172	132	13.9 (70.6)	5.9 (97.0)	0.29 (93.6)	0.34 (86.2)	1.5 (94.2)	66
141	21.1 (67.8)	19.5 (66.8)	4.4 (94.2)	4.3 (94.3)	24.2 (88.8)	66	134	4.1 (86.5)	1.2 (95.3)	0.02 (99.5)	0.03 (96.1)	0.17 (99.8)	66
29	5.6 (64.5)	7.5 (80.0)	311.0	—	31.1 (67.1)	66	213	14.5 (77.0)	16.5 (69.2)	—	110.9 (85.0)	252.1 (61.5)	172
51	12.5 (71.6)	16.4 (77.5)	23.5 (83.0)	24.4 (80.1)	—	66	214	23.8 (71.0)	20.3 (67.0)	7.5 (91.4)	7.7 (90.3)	30.8 (81.1)	66
52	21.5 (72.3)	25.2 (72.2)	31.3 (78.2)	40.1 (82.8)	80.5 (67.7)	172	58	12.6 (77.8)	6.0 (88.1)	0.5 (99.1)	0.5 (97.0)	2.5 (95.9)	66
209	14.2 (68.1)	18.1 (82.1)	7.4 (96.2)	7.9 (93.7)	18.4 (87.5)	172	215	4.1 (86.3)	1.3 (94.0)	0.05 (105.7)	0.06 (103.5)	0.38 (97.8)	66
170	23.0 (71.4)	16.1 (83.7)	2.3 (90.0)	5.6 (72.1)	8.9 (88.3)	66	136	8.4 (80.0)	3.4 (93.5)	0.22 (99.7)	0.27 (97.0)	1.2 (95.3)	66
210	11.6 (77.5)	13.0 (84.5)	2.3 (88.8)	4.9 (72.8)	10.8 (86.8)	172	216	16.1 (77.5)	15.3 (69.0)	18.5 (88.7)	19.5 (85.2)	57.9 (73.6)	66
174	19.4 (72.1)	19.8 (79.7)	7.3 (87.4)	10.0 (84.3)	21.0 (90.4)	172	217	13.9 (73.0)	15.4 (63.8)	3.5 (95.5)	3.1 (94.4)	17.3 (71.5)	66
53	62.3 (70.5)	31.9 (72.9)	6.2 (83.5)	6.6 (89.5)	25.4 (84.0)	66	61	1.2 (69.2)	0.19 (99.0)	0.02 (94.4)	0.03 (91.6)	0.11 (97.8)	172
175	17.6 (76.7)	19.8 (78.3)	5.8 (92.0)	7.5 (92.5)	16.5 (88.8)	172	218^a	21.4 (80.3)	16.7 (79.0)	—	1.4 (96.2)	17.5 (90.3)	172
211	14.7 (74.6)	5.9 (86.0)	1.0 (98.0)	1.1 (93.4)	3.0 (88.5)	66	204^a	6.5 (73.6)	9.0 (73.3)	271.9 (56.3)	342.9 (46.4)	172.0 (77.4)	172
172	7.6 (79.0)	4.0 (88.7)	0.67 (92.4)	1.6 (77.7)	2.3 (92.3)	172	115^b	—	16.3	11.5	11.7 (77.5)	58.3	96
77	3.6 (71.9)	4.7 (76.4)	275.0 (68.3)	410.7 (92.5)	45.1 (73.3)	66	206^b	—	10.3	9.4	9.6 (78.5)	53.7	96
212	3.8 (75.4)	21.4 (67.5)	20.8 (76.6)	29.9 (78.8)	22.4 (86.4)	172	207^b	9.8 ^c (72.1)	12.9 (66.0)	1.9 (96.8)	1.7 (99.7)	8.4 (83.7)	96
133	28.3 (68.2)	7.8 (97.3)	0.32 (97.4)	0.37 (92.0)	1.9 (95.0)	66	208^b	10.8 ^c (76.6)	14.5 (70.5)	1.7 (100.3)	1.8 (114.0)	8.0 (83.9)	96

^a For these SPO, k_{BA} and E_{a}^{BA} were determined at 298 K. ^b For SPO of the phenanthroline series, k_{BA} and E_{a}^{BA} were determined at 296 K. ^c Heptane as the solvent.

nonaphthooxazines leads to a decrease in the rate constant of the reverse thermal reaction, the simultaneous insertion of electron-donating groups at position 5 of the indoline fragment substantially enhancing this effect. The presence of electron-donating substituents at position 5 of the indoline fragment exerts an analogous effect in other spiroindolinooxazines, for example, in SPO of the phenanthroline series. The steric effect of bulky substituents on thermal decolouration of SPO is manifested in a decrease in the rate constant (*cf.*, for example, SPO **170** and **210**, **115** and **206**, Table 9).

The temperature dependence of the rate constant of the dark reaction characterised by the activation energy has a tendency to be enhanced in polar solvents, particularly, in alcohols (see Table 9). Conceivably, a strengthening of intermolecular interactions between the alcohol molecules and merocyanine forms of SPO through hydrogen bonding leads to an increase in the activation barrier to the recyclisation reaction. There is no rather strict relationship between the activation barrier to the dark reaction and the molecular structure of SPO. However, it should be noted that spiroindolinonaphthooxazines containing electron-withdrawing substituents in the oxazine fragment are characterised by higher E_{a}^{BA} compared to the compounds with electron-donating substituents.

IX. Photochemical properties of spirooxazines

The efficiency of photoreactions is estimated from the quantum yields. However, the determination of the quantum yields for photochromic systems presents difficulties associated primarily with the determination of the molar extinction coefficients of the coloured forms. This is the reason why many researchers use more readily available parameters, such as the colourability⁹⁵ or photochromic response.⁶

In the general case, by the colourability is meant a certain value, which is either proportional or equal to the product of the quantum yield of the photoreaction (Φ_{col}) by the molar extinction coefficient at the absorption maximum of the photoproduct (ϵ_{B}). For instance, the optical density at the induced absorption maximum measured directly after the flash of a photolytic lamp was taken as the colourability (A_0) in the study.¹⁷⁹ Since the energy of photolysing radiation remained stable in the course of the experiment, the authors of the cited study believed that it is reasonable to compare the efficiency of photoprocesses involving structurally similar photochromes in solutions with the same concentration.

In another study,⁶⁸ the colourability (A_{∞}) was assigned the equilibrium value of the optical density at the absorption maximum of the photoproducts formed in solutions of SPO with the same concentration in the photostationary state. Sometimes, ϵ_{app} {the apparent molar extinction coefficient numerically equal to the ratio $A_0/([A]I)$, where $[A]$ is the initial concentration of the

photochrome and l is the optical path length} is used instead of A_0 .¹⁸⁰

The photochromic responses for several groups of SPO were given in the review.⁶ The authors noted that an estimating comparison of the efficiency of photocolouration of photochromes belonging to the same group of SPO can be performed, whereas a comparison of photochromes belonging to different groups is impermissible. A more strict approach to the estimation of the efficiency of photoreactions was proposed in the study.¹⁸¹ In the cited study, the product $\Phi_{\text{col}}\varepsilon_{\text{B}}$ was determined taking into account the fraction of light absorbed by the initial form. In this case, the colourability is independent of the conditions of irradiation. However, the uncertainty in the estimation of the photochemical activity of molecular systems associated with the determination of ε_{B} persists.

The universal character of the quantum yields (unlike the colourability) enables one to compare the photochemical properties of compounds with different structures in various media and in a wide temperature range. The correctness of the determination of the quantum yields of phototransformations depends on how much the molar extinction coefficients of the coloured forms determined by a particular method differ from the true values.

One method for the determination of the molar extinction coefficients, which is based on stabilisation and accumulation of photoproducts, involves the photocolouration reaction at low temperatures excluding the reverse[†] thermal reaction.^{13, 166, 175, 182} It is assumed that low-temperature photolysis affords only one stable isomer of the coloured form.

In alternative methods for the determination of the molar extinction coefficients, the coloured form is stabilised by the reactions with acids (protonation) or metal ions (complex formation). Actually, the starting form is completely consumed in these reactions, *i.e.*, the complete conversion $\text{A} \rightarrow \text{B}$ takes place. However, the resulting compounds have spectral characteristics, which differ from those of the photoproducts, and the assumption that their molar extinction coefficients have similar values seems to be unjustified.

A method for the determination of the molar extinction coefficients of the coloured forms with the use of the quantitative analysis of the equilibrium $\text{A} \rightleftharpoons \text{B}$ by NMR spectroscopy and spectrophotometry is quite rigorous, but the application of this method is limited to a narrow range of compounds for which the content of the coloured form in the equilibrium mixture is sufficient for NMR spectroscopic study.^{95, 96}

Good results were obtained with the use of a photokinetic method by analysing the kinetic curves, which are measured under continuous irradiation.¹⁸³ However, this method places stringent requirements on the planning and execution of the experiment as well as on the accuracy of the determination of the initial parameters (initial concentration of the photochromic compound, intensity of incident light, temperature, *etc.*). Thermal and photochemical processes, which occur in the systems within the framework of the assumed model, are described by a differential equation system including the molar extinction coefficients of the initial forms and final products, quantum yields of forward and reverse photoreactions and rate constants of thermal processes. A solution of this differential equation system enables one to obtain model characteristics of photochromic systems. However, even in the simplest case, the model includes four processes (forward and reverse thermal and photochemical reactions) involving two forms of SPO (initial cyclic and merocyanine) and, hence, the differential equation system cannot be solved analytically. To solve such systems, researchers have to use various approximations, in which particular processes are ignored.

[†] The occurrence of the reverse photoreaction leads to the attainment of a photostationary state rather than to the complete conversion $\text{A} \rightarrow \text{B}$ and, as a consequence, to the error in the determination of the molar extinction coefficients.

For example, in one of the first studies¹⁸⁴ devoted to the detailed investigation of the kinetics of photoinduced processes in SPO molecules, the authors considered spiroindolinonaphthooxazines containing electron-donating substituents at position 6' and concluded that the reverse photoreaction could be ignored because the ratio of the quantum yields of the reverse and forward photoreactions is in the range of 0.03–0.07. In more recent studies^{166, 168, 185} of the kinetics of photoinduced reactions of SPO, whose molecular structures differ from those studied earlier, the authors also ignored the reverse photoreaction with the unjustified reference to the results of the study.¹⁸⁴

An approach which involves the numerical integration of differential equations using the Runge–Kutta method and an iteration procedure using the Powell minimisation algorithm shows more promise. In this approach, the calculated and experimental photokinetic curves are compared and the modification of the parameters of the photochromic system is terminated once the discrepancy between the curves reaches the specified minimum value. The results obtained with the use of this method (in particular, for SPO)^{66, 96} are characterised by high stability and are independent of a particular experimental apparatus.

The quantum yields of photocolouration (Φ_{AB}) of SPO are higher than those of photodecolouration (Φ_{BA}), but the differences do not always reach the value given in the study.¹⁸⁴ As can be seen from Table 10, the quantum yield ratio $\Phi_{\text{BA}}/\Phi_{\text{AB}}$ varies from 0.001 to 0.5 depending on the structure of SPO and the nature of the solvents.

The efficiency of the forward photoreaction decreases in the presence of electron-withdrawing substituents in the naphthooxazine fragment and, by contrast, the presence of electron-donating groups in this moiety of SPO does not lead to changes (or increases) in the yields of the coloured isomers compared to unsubstituted SPO **1**. The introduction of electron-donating groups at position 5 of the indoline fragment leads to a noticeable decrease in the quantum yield of the forward photoreaction.

The quantum yields of photodecolouration upon the above-mentioned structural modifications are changed in the opposite order. For SPO containing electron-withdrawing substituents in the naphthooxazine fragment, Φ_{BA} are higher than those for SPO containing electron-donating substituents. In most cases, the introduction of the alkoxy groups at position 5 of the indoline fragment facilitates photorecyclisation.

The dependences of the quantum yields of the forward and reverse photoreactions of SPO on the nature of the solvent are opposite in character, *i.e.*, the quantum yields of photocolouration are lower in polar solvents and alcohols, whereas the efficiency of photodecolouration is lower in non-polar solvents (see Table 10).

The influence of the molecular structure and properties of the solvents on the efficiency of photoprocesses in SPO molecules correlates with their effect on the activation energy of thermal recyclisation because of the characteristic features of the structural and energy mechanisms of photoinduced reactions in SPO molecules.

The formation of the coloured product proceeds in two steps involving the $\text{C}_{\text{spiro}}-\text{O}$ bond cleavage followed by *cis*–*trans* isomerisation to the stable merocyanine form. Picosecond^{188–190} and femtosecond^{191, 192} photolysis revealed the existence of a short-lived cisoid¹⁹⁰ intermediate generated in the course of the $\text{A} \rightarrow \text{B}$ transformation. In these studies, an important conclusion concerning the energy mechanism of SPO photocolouration was made. It was established that only singlet excited states are involved in the photoinduced transformations of SPO.

The excitation of SPO molecules to the S_1 state is accompanied by the adiabatic $\text{C}_{\text{spiro}}-\text{O}$ bond cleavage and the formation of the cisoid isomer of the merocyanine form, which is then transformed into the ground state. Isomerisation gives rise to the metastable *TTC* isomer. This accounts for the fact that an increase in the potential barrier E_{a}^{AB} can lead to a decrease in the observed yield of the coloured product **B**. For the reverse photoreaction

Table 10. Quantum yields of photocoloration (Φ_{AB}) and photodecoloration (Φ_{BA}) of spirooxazines.

Compound	Solvent	Φ_{AB}	Φ_{BA}	Ref.	Compound	Solvent	Φ_{AB}	Φ_{BA}	Ref.
1	toluene	0.23	—	184	215	toluene	0.14	0.017	66
	"	0.22	—	186		methanol	0.09	0.037	66
	methylcyclohexane	0.41	—	168, 185	136	toluene	0.58	0.014	66
	ethanol	0.32	—	168, 185		"	0.70	—	187
201	methanol	0.19	—	186	216	methanol	0.35	0.037	66
	methylcyclohexane	0.46	—	168		methylcyclohexane	1.10	—	168
165	ethanol	0.42	—	168		ethanol	0.72	—	168
	methylcyclohexane	0.25	—	185	217	toluene	0.36	0.012	66
141	ethanol	0.18	—	185		methanol	0.35	0.013	66
	methanol	0.13	0.025	66	218	toluene	0.14	0.012	66
29	toluene	0.62	0.016	66		methanol	0.11	0.027	66
51	"	0.38	0.001	66	61	toluene	0.16	0.029	172
170	"	0.35	0.007	66		methanol	0.08	0.046	172
	methanol	0.13	0.023	66	218	toluene	0.19	0.011	172
210	toluene	0.34	0.009	172		"	0.14	—	186
	methanol	0.12	0.023	172	204	methanol	0.15	0.026	172
53	"	0.13	0.019	66		"	0.10	—	186
211	toluene	0.12	0.009	66	205	methylcyclohexane	0.49	—	168, 185
	methanol	0.06	0.019	66		ethanol	0.29	—	168, 185
77	toluene	0.48	0.004	66	115	methylcyclohexane	0.51	—	168
	"	0.50	—	187		ethanol	0.85	—	168
78	"	0.42	—	184	206	toluene	0.26	0.005	96
	methylcyclohexane	0.55	—	185		ethanol	0.24	0.016	96
82	ethanol	0.65	—	185		methanol	0.24	0.022	96
	toluene	0.50	—	187	207	acetonitrile	0.26	0.011	96
133	"	0.20	—	184		toluene	0.25	0.002	96
	"	0.20	0.009	66	208	ethanol	0.25	0.012	96
132	methanol	0.12	0.029	66		methanol	0.24	0.015	96
	toluene	0.17	0.011	66	209	acetonitrile	0.16	0.014	96
134	methanol	0.11	0.027	66		heptane	0.12	0.003	96
	toluene	0.11	0.016	66	210	toluene	0.15	0.003	96
214	methanol	0.05	0.024	66		ethanol	0.09	0.025	96
	toluene	0.32	0.018	66	211	methanol	0.09	0.032	96
202	methanol	0.28	0.031	66		acetonitrile	0.12	0.019	96
	methylcyclohexane	0.35	—	168, 185	212	heptane	0.14	0.003	96
203	ethanol	0.36	—	168, 185		toluene	0.18	0.002	96
	methylcyclohexane	0.14	—	168	213	ethanol	0.11	0.026	96
	ethanol	0.23	—	168		methanol	0.09	0.030	96
						acetonitrile	0.11	0.019	96

(assuming that it proceeds through the same cisoid intermediate), an increase in the barrier E_a^{BA} leads to an increase in probability of recyclisation.

Apparently, high quantum yields of photocoloration of nitro-substituted spiroindolinonaphthooxazines are associated with the triplet reaction mechanism.¹⁸⁷ This assumption is indirectly supported by low photostability of 5-nitro-substituted spiroindolinonaphthooxazine **29**.¹⁹³

The resistance of photochromes to photodegradation depends also on the involvement of the triplet states of the starting, intermediate and final forms in phototransformations of the photochromes because the molecules in the triplet state possess higher reactivity and can interact with dissolved oxygen and solvent molecules as well as can undergo irreversible intramolecular rearrangements. The degrees of photodegradation of SPO are lower than those of their structural analogues, *viz.*, spiropyran,¹⁹³ which is in good agreement with the singlet mechanism of phototransformations found for a series of SPO.

Destruction of spirooxazines was considered in the review.¹¹⁶

X. Conclusion

On the basis of the above-considered published data, it can be stated that a qualitative and quantitative leap forward has been made in the chemistry of SPO. Particularly considerable progress

has been achieved in the synthesis and functionalisation of spirooxazines. Numerous investigations revealed the structural factors, which exert an effect on the spectral characteristics, thermodynamic parameters of equilibria, kinetics of relaxation processes and efficiency of SPO phototransformations.

Due to the preparation of a large number of new SPO, the field of their practical application has been substantially extended. In particular, the possibilities of the use of spirooxazines in materials for recording information, optical switches¹⁹⁴ and photochromic chemosensors^{195, 196} were considered.

However, a series of practically important properties of spirooxazines are as yet insufficiently known, which leaves a wide sphere of research activity. In particular, photochromic processes in the solid phase were poorly studied.^{124, 197} Data on the fluorescence properties of spirooxazines are scarce.¹⁹⁸ Data on cross-sections of two-photon light absorption of cyclic and merocyanine forms of SPO are lacking. The latter parameter is of importance in using SPO for the construction of media for the three-dimensional recording systems (molecular memory) and photomodulated biomaterials. For spiropyran, this parameter reaches $10^{-48} \text{ cm}^4 \text{ s}$ (which is a large value for organic molecules; see Ref. 199). For structurally similar spirooxazines, this parameter would be expected to assume values of the same order of magnitude. Finally, there are only scarce data on the supra-molecular effects exhibited by spirooxazines. The first evidence²⁰⁰

for the formation of stable aggregates of merocyanine forms in solutions of spirooxazines, which are characterised by narrow absorption bands and are of interest for multifrequency systems,²⁰¹ have been published only recently.

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Norbornadiene – quadricyclane as an abiotic system for the storage of solar energy

A D Dubonosov, V A Bren, V A Chernov Ivanov

Contents

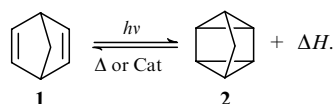
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Abstract. Data on the valence isomerisation of norbornadiene and its derivatives into the corresponding quadricyclanes published between 1990 and 2001 are considered and described systematically. The applicability of this reaction for the storage of solar energy is discussed. The bibliography includes 112 references.

I. Introduction

About ten years have passed since the publication of our review¹ in which the norbornadiene–quadricyclane system was considered as a promising accumulator and converter for solar energy. However, the interest in the problem of solar energy accumulation has not slackened. This results from the fact that irreplaceable natural energy sources, *i.e.*, coal, oil and natural gas, are still being consumed almost without control;^{2–4} furthermore, the problems related to climate changes on the Earth due to the emission of enormous amounts of carbon dioxide, as well as products of incomplete combustion of natural fuel, into the atmosphere are becoming ever more critical.⁵

The possible ways to utilise solar energy are extremely diverse.^{6,7} They include the use of solar energy to perform various photocatalytic processes,^{8–10} photodecomposition of water and photolytic production of hydrogen,^{11,12} as well as various photo-biological processes, including artificial photosynthesis.^{13–15} An alternative abiotic approach to the transformation of solar energy is to accumulate it as the strain energy in metastable photoinduced isomers of organic compounds. The norbornadiene–quadricyclane system is most promising for this purpose.^{16,17} Its advantage is that the valence isomerisation of bicyclo[2.2.1]hepta-2,5-diene (norbornadiene, NBD) (**1**) into tetracyclo[3.2.0.0^{2,7}.0^{4,6}]heptane (quadricyclane, Q) (**2**) better fits the requirements for organic photochromes intended as solar energy accumulators.¹



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The photoisomerisation of NBD results in a metastable quadricyclane structure containing highly strained cyclobutane and two cyclopropane fragments. As a result, the reverse thermal or catalytic reaction **2** → **1** is characterised by a considerable thermal effect ($\Delta H = -89 \text{ kJ mol}^{-1}$) (see Ref. 18), which is greater than the ΔH value for other photochromic systems. There is a wide range of homo- and heterogeneous catalysts that enable this reaction to be performed and hence thermal energy to be evolved,^{1,16} but the high activation barrier to the thermal transformation **2** → **1** (even at 140 °C, the half-life period of quadricyclane **2** is 14 h)¹⁹ makes it possible to store the accumulated solar energy for a long time.

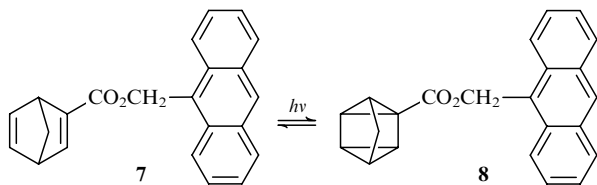
However, the system **1** → **2** has a number of considerable drawbacks. First, the longwave absorption edge of non-substituted NBD **1** (λ_{ae} , $\epsilon = 1 \text{ litre mol}^{-1} \text{ cm}^{-1}$) is no higher than 300 nm.²⁰ Second, the quantum yield (Φ) of the valence isomerisation **1** → **2** in the absence of sensitising agents is ~ 0.05 (see Refs 20, 21). In order that this system could be used on industrial scale as a solar energy accumulator, one has to chemically modify NBD for shifting the values of λ_{ae} towards the maximum of the light energy of the Sun (400–600 nm) and at the same time for increasing the photoisomerisation quantum yield. This review presents a generalisation of the studies that dealt with this problem and were carried out between 1990 and 2001. The following general directions can be distinguished: (1) the use of sensitisers for the valence isomerisation **1** → **2**, including those chemically bound to the NBD molecule; (2) modification of the structure of the starting NBD to increase λ_{ae} and Φ ; (3) the use of various polymeric systems containing NBD (or its derivatives) in the lateral or main chain of the macromolecule, as well as polymer-bound sensitisers.

II. Photosensitisation of the valence isomerisation of norbornadiene into quadricyclane

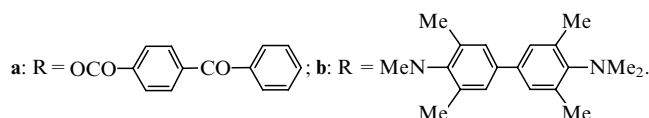
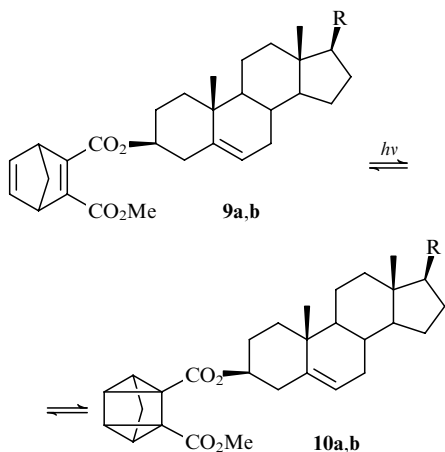
As a rule, the isomerisation **1** → **2** involves the triplet state of NBD.^{22–25} Therefore, at the initial stage of the studies under discussion, the photosensitisation was performed mostly by various carbonyl compounds (acetophenone, propiophenone, benzophenone, acridinone, Michler's ketone and some others) known as triplet sensitisers (S).^{24–27} Since the energy of the triplet state (E_T) of NBD is very high ($\sim 257 \text{ kJ mol}^{-1}$),^{22,28} only a small number of sensitisers with high E_T fit the classical triplet–triplet transfer scheme:



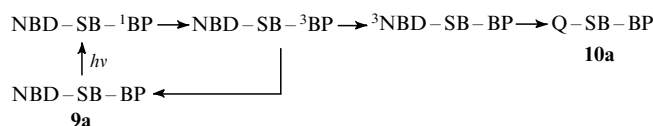
The intramolecular energy transfer from the second triplet (via the T_2 state) of the anthracene fragment to the norbornadiene moiety of compound **7** causes its isomerisation to quadricyclane **8**.⁴⁴ This mechanism was proven using two-photon flash-photolysis ($\lambda_{\text{exc}}^1 = 260\text{--}290\text{ nm}$, $\lambda_{\text{exc}}^2 > 410\text{ nm}$); the quantum yield of the photoreaction in benzene is 0.022.



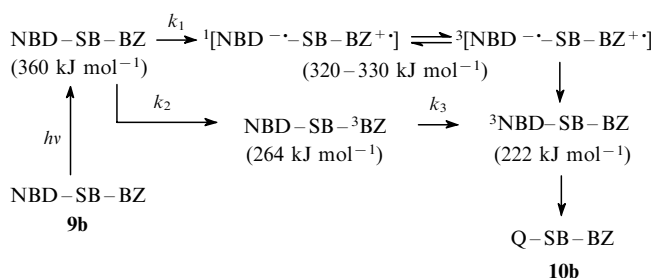
In the past decade, intense studies were carried out on the photophysical and photochemical features of intramolecular processes of energy or electron transfer through a rigid steroid bridge (SB), which links benzophenone (BP) or benzidine (BZ) with a norbornadiene molecule.^{45–48} For example, the dichromophoric 3 β -{[2-(methoxycarbonyl)bicyclo-[2.2.1]hepta-2,5-dien-3-yl]carbonyloxy}androst-5-en-17 β -ylbenzophenone-4-carboxylate (**9a**, NBD–SB–BP) undergoes isomerisation upon steady-state irradiation ($\lambda_{\text{irr}} > 350\text{ nm}$) to give a photo-product **10a** (Q–SB–BP) with a quantum yield $\Phi = 0.038$.



It should be noted that only the benzophenone chromophore can absorb irradiation under these conditions. Singlet-excited benzophenone forms the triplet state ^3BP by fast and efficient intersystem crossing. The main pathway of ^3BP deactivation involves triplet–triplet energy transfer to the norbornadiene fragment through the system of σ -bonds of the steroid bridge.



The quantum yield of isomerisation of 3 β -{[2-methoxycarbonyl]bicyclo[2.2.1]hepta-2,5-dien-3-yl]carbonyloxy}androst-5-en-17 β -yl-2,2',6,6',N,N',N'-heptamethylbenzidine (**9b**, NBD–SB–BZ) in cyclohexane is 0.07 ($\lambda_{\text{irr}} > 300\text{ nm}$), with quantitative formation of the photo-product **10b** and with no side reactions. In this case, the isomerisation scheme suggested by Tung *et al.*⁴⁵ involves not only the triplet–triplet energy transfer but also the formation of a triplet radical-ion state, which then undergoes recombination to the triplet-excited state of NBD.

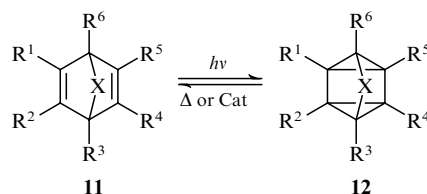


The rate constants for the corresponding steps are as follows: $k_1 = 1.1 \times 10^7\text{ s}^{-1}$, $k_2 = 5.2 \times 10^7\text{ s}^{-1}$, $k_3 = 5.2 \times 10^5\text{ s}^{-1}$ (the values in parentheses correspond to the energies of the states with respect to the ground state of compound **9b**).

The latter examples of valence isomerisation open a new approach to sensitisation, in which a coloured chromophore sensitizer that is remote from the norbornadiene fragment can undergo photoexcitation.

III. 'Donor–acceptor' norbornadienes

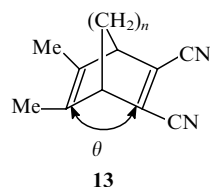
Non-substituted NBD is a formally non-conjugated, non-planar, strained diene. The steric strain in its molecule allows through-space interaction of the C=C bond π -orbitals.^{49–51} As a result, non-substituted NBD absorbs light in a longer-wave spectrum region than two isolated C=C bonds. The systems **11** in which the interaction of electron-donating substituents at one of the carbon–carbon double bonds in the molecule with electron-withdrawing substituents at another bond results in a low-intensity charge transfer band ($\epsilon < 10^2\text{ litre mol}^{-1}\text{ cm}^{-1}$) were called 'donor–acceptor' NBD.⁵² The long-wave absorption edge of these compounds (λ_{ae}) can be as high as 500–560 nm.



X = CH₂, CMe₂; R¹, R² = H, Me, Ph, 4-MeOC₆H₄;

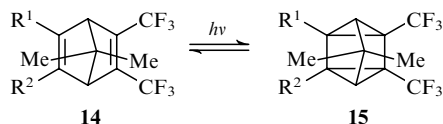
R⁴, R⁵ = CN, CO₂Me, CO₂Et, CONHPh; R³, R⁶ = H, Me.

The geometrical structure and electronic absorption spectrum of norbornadiene were studied^{53–55} with consideration of indirect conjugation of double bonds and π , σ -interaction. This interaction was observed experimentally when studying the electronic absorption spectra of bicyclo[2.2.*n*]alka-2,5-dienes **13**.⁵²



When *n* changes from 3 to 1, the angle θ decreases gradually. This is accompanied by a bathochromic shift of the long-wave absorption band (λ_{max}) from 305 to 338 nm with simultaneous increase in the molar extinction coefficient (ϵ_{max}) from 178 to 200 litre mol^{−1} cm^{−1}. The value of λ_{ae} in the spectra of norbornadienes **11** can be as high as 560 nm, while the quantum yields of the photoreaction **11** → **12** are high ($\Phi = 0.26\text{--}0.75$). However, despite high Φ values, the applicability of compounds **11** for the storage of solar energy is limited due to the following factors: (1) the low extinction coefficient ($\epsilon_{\text{max}} \approx 1000\text{ litre mol}^{-1}\text{ s}^{-1}$) makes the efficiency of the **11** → **12** process low and requires prolonged exposure to light; (2) many quadricyclanes **12** are unstable at room temperature and undergo spontaneous rear-

rangement to the original NBD **11**. Although some attempts to increase the thermal stabilities of quadricyclanes by introduction of perfluoroalkyl substituents have been undertaken a long time ago,⁵⁶ it is only in recent years that reliable methods for the synthesis of the 'donor–acceptor' NBD **14** have been developed; the latter are not only thermally stable at room temperature but also absorb solar energy quite efficiently (Table 1).^{57, 58}



R¹, R² = 4-MeOC₆H₄, 4-Me₂NC₆H₄, 2-benzofuryl, 2-thienyl.

Table 1. Spectral characteristics of norbornadienes **14** and thermal stabilities of quadricyclanes **15**.^{57, 58}

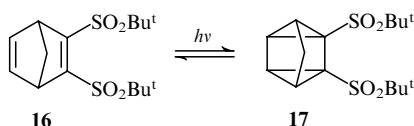
Com- pound 14	R ¹	R ²	$\lambda_{\max}$ /nm ($10^{-4} \epsilon_{\max}$ /litre mol ⁻¹ cm ⁻¹)	λ_{ae} /nm	$\tau_{1/2}^a$ /h
a	4-MeOC ₆ H ₄	4-MeOC ₆ H ₄	346 (0.51)	440	see b
b	4-Me ₂ NC ₆ H ₄	4-Me ₂ NC ₆ H ₄	390 (0.85)	510	9600
c	4-Me ₂ NC ₆ H ₄	4-MeOC ₆ H ₄	374 (0.85)	500	see b
d	4-Me ₂ NC ₆ H ₄	2-thienyl	385 (0.78)	520	500
e	2-benzofuryl	2-benzofuryl	414 (2.00)	480	72
f	4-Me ₂ NC ₆ H ₄	2-benzofuryl	407 (1.29)	580	31

^a Half-life of quadricyclane. ^b Quadricyclane is stable at 20 °C.

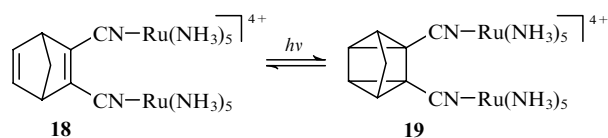
Unlike compounds **11**, norbornadienes **14** have high values of $\epsilon_{\max}$ ranging from 5000 to 20 000 litre mol⁻¹ cm⁻¹. Their absorption edge increases as the electron-donating properties of the substituents R¹ and R² increase; in fact, λ_{ae} = 580 nm for norbornadiene **14a**. The thermal stabilities of quadricyclanes **15** are sufficiently high for the practical storage of solar energy; the number of cycles **14** ⇌ **15** reaches 10³ without considerable destruction of the starting compound.

IV. 2,3-Disubstituted norbornadienes

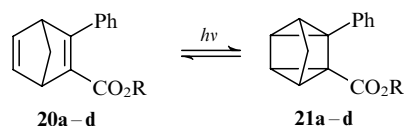
The synthesis of 'donor–acceptor' norbornadienes faces considerable difficulties: polysubstituted cyclopentadiene derivatives and disubstituted acetylene derivatives are first synthesised and then brought into the Diels–Alder reaction. 2,3-Disubstituted norbornadienes can also be synthesised from non-substituted cyclopentadiene and 1,2-disubstituted acetylene. The studies carried out over the past ten years have shown that in many cases, the presence of an electron-donating substituent and an electron-withdrawing substituent at one of the two double bonds of the norbornadiene molecule is sufficient for their spectral and photochemical characteristics not to be inferior, and sometimes even to be superior, to the corresponding parameters of the 'donor–acceptor' NBD. Two substituents of the same nature shift the λ_{ae} value only slightly towards the solar radiation maximum.^{59, 60} For example, the absorption of 2,3-di(*tert*-butylsulfonyl)norbornadiene (**16**) is characterised by a slight bathochromic shift with respect to the maximum absorption of non-substituted NBD **1**, although the **16** → **17** isomerisation occurs quantitatively in ether under irradiation with light with $\lambda_{\text{irr}} > 280$ nm.



The valence isomerisation of the 2,3-dicyanonorbornadiene–pentaamminoruthenium(II) complex **18** is an exception.⁶¹ The long-wave absorption maximum of norbornadiene **18** in methanol is observed around 490 nm ($\epsilon \approx 14\,000$ litre mol⁻¹ s⁻¹); the λ_{ae} is 700 nm, but the quantum yield of the formation of the quadricyclane **19** upon irradiation with light with $\lambda_{\text{irr}} = 500$ nm is as low as 8.3×10^{-4} .



Combination of an electron-withdrawing and an electron-donating substituents at one of the carbon–carbon double bonds in NBD favours an increase in the isomerisation quantum yield. The electronic absorption spectra and the quantum yields of the phototransformation of 3-phenylnorbornadiene-2-carboxylic acid (**20a**) and its esters **20b–d** are listed in Table 2.^{62, 63} Although these systems absorb in the spectral region $\lambda < 360$ nm, the fast and quantitative photoisomerisation **20** → **21**, which takes a few seconds in DMSO, acetonitrile, ethanol and THF ($c = 5 \times 10^{-5}$ mol litre⁻¹), allows us to consider the norbornadienes **20** to be an efficient system for the accumulation of solar energy.

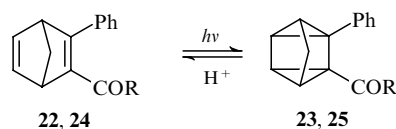


R = H (**a**), CH₂Ph (**b**), CH₂C₆H₄OMe-4 (**c**), (CH₂)₆OC₆H₄OMe-4 (**d**).

Table 2. Spectral characteristics of norbornadienes **20** and quantum yields of the photoreactions **20** → **21** in acetonitrile.^{62, 63}

Com- pound 20	R	$\lambda_{\max}$ /nm ($10^{-4} \epsilon_{\max}$ /litre mol ⁻¹ cm ⁻¹)	λ_{ae} /nm	Φ ($\lambda_{\text{irr}} = 284$ nm)
a	H	291 (1.12), 222 (0.66)	—	0.32
b	PhCH ₂	292 (0.56)	350	0.36
c	4-MeOC ₆ H ₄ CH ₂	297 (0.74), 225 (2.45)	355	0.27
d	4-MeOC ₆ H ₄ O(CH ₂) ₆	291 (0.71), 224 (1.62)	340	0.25

2-Trifluoroacetyl-3-phenylnorbornadiene (**22**) absorbs light at $\lambda_{\text{ae}} \leq 460$ nm; its photoisomerisation into the quadricyclane **23** in benzene occurs quantitatively with a quantum yield $\Phi = 0.62–0.86$ (depending on the starting concentration of norbornadiene).^{64, 65}



R = CF₃ (**22**, **23**), NHAr (**24**, **25**).

Involvement of the carbon–carbon double bond of norbornadiene in the conjugation chain Ph–C=C–CONHR affects the λ_{ae} and Φ values even more significantly.

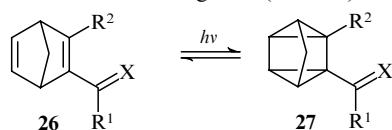
We have studied the spectral and photochemical features of 3-phenylnorbornadiene-2-carboxamides **24**.^{66, 67} Compounds **24** are characterised by absorption in the region 280–305 nm (Table 3) and $\lambda_{\text{ae}} = 375–435$ nm.^{66, 67} Irradiation with light with a wavelength corresponding to the long-wave absorption maximum ($\lambda_{\text{irr}} = 313$ nm) results in their isomerisation to give quadricyclanes **25** with high quantum yields. Electron-withdrawing substituents in the *N*-phenyl ring increase the Φ value in comparison with non-substituted 3-phenyl-2-(*N*-phenylcarbamoyl)norbornadiene **24a**, whereas electron-donor substituents decrease this

Table 3. Spectral characteristics of 3-phenylnorbornadiene-2-carboxamides **24** and quadricyclanes **25** and quantum yields of the photoreaction **24** → **25** in propan-2-ol.^{66, 67}

Compound 24	R	$\lambda_{\text{max}}/\text{nm}$ ($10^{-4} \epsilon_{\text{max}}/\text{litre mol}^{-1} \text{cm}^{-1}$)	$\lambda_{\text{ae}}(\mathbf{24})/\text{nm}$	Φ ($\lambda_{\text{irr}} = 313 \text{ nm}$)	$\lambda_{\text{ae}}(\mathbf{25})/\text{nm}$
a	Ph	233 (1.98), 280 (0.9)	375	0.53	295
b	4-MeC ₆ H ₄	232 (1.78), 285 (0.78)	380	0.46	295
c	2-MeC ₆ H ₄	229 (1.74), 280 (0.76)	380	0.49	295
d	4-MeOC ₆ H ₄	235 (1.33), 290 (0.76)	400	0.15	310
e	4-MeCOC ₆ H ₄	221 (1.30), 295 (1.28)	380	—	370
f	4-EtO ₂ CC ₆ H ₄	278 (0.93), 310 (0.74)	380	0.71	310
g	3-NO ₂ C ₆ H ₄	232 (2.28), 305 (0.87)	390	0.66	300
h	α -naphthyl	223 (1.47), 295 (0.28)	380	0.0	—
i	β -naphthyl	234 (3.78), 300 (1.00)	380	0.22	320

value. However, it should be noted that as electron-withdrawing groups are introduced, the λ_{ae} values of norbornadienes **24** become closer to those of quadricyclanes **25**, hence the efficiency of solar energy accumulation decreases. The quadricyclanes obtained upon valence isomerisation **24** → **25** are stable at room temperature and in the presence of acid catalysts. In the presence of MoO₃ as a heterogeneous catalyst, they undergo rearrangement to the original NBD with a rate constant of $k = 5 \times 10^{-2} - 10^{-3} \text{ s}^{-1}$ at 293 K.

Since the triplet mechanism of isomerisation of norbornadiene into quadricyclane can occur with high quantum yields in the presence of aromatic ketones, we studied norbornadienes **26** with one of the C=C bonds involved in the conjugation chain of the Ph–C=C–C=X fragment (Table 4).^{67–71}

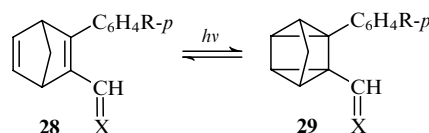


R¹ = H, Me, OMe, CH=CHPh; R² = Br, Ar; X = O, CHCOAr.

Irradiation of NBD **26** in propan-2-ol at a wavelength corresponding to the maximum absorption in the long-wave region ($\lambda_{\text{irr}} = 313$ or 365 nm) results in quadricyclane structures **27**. Absorption at the highest wavelengths is observed in the case of 2-[2-(3-nitrobenzoyl)vinyl]-3-phenylnorbornadiene (**26i**): its absorption edge approaches 500 nm while the quantum yield of isomerisation is rather high ($\Phi = 0.25$). The highest value $\Phi = 0.60$ is observed for norbornadiene **26f**. Quadricyclanes **27** are stable at 293 K; however, they readily undergo isomerisation into the original compounds under conditions of homogeneous catalysis if a small amount of trifluoroacetic acid

($10^{-2} - 10^{-3} \text{ mol litre}^{-1}$) is added to their solutions in heptane ($5 \times 10^{-5} \text{ mol litre}^{-1}$). Since heterogeneous catalysis is more suitable for practical solar energy accumulation,¹ it seemed reasonable to study the effect of oxides, viz., V₂O₅, WO₃ and MoO₃, on quadricyclanes **27**. The best catalytic activity was observed for molybdenum(VI) oxide, which is characterised by the highest metal electronegativity in this series.⁷² Stirring of solutions of quadricyclanes **27** in heptane ($5 \times 10^{-5} \text{ mol litre}^{-1}$) with MoO₃ (0.2–0.5 mg per 2 ml of a solution) results in the original norbornadienes **26** with a rate constant $k = 10^{-2} - 5 \times 10^{-3} \text{ s}^{-1}$ at 291 K. Conditions for the repeated phototransformation **26** ⇌ **27** have been determined. The calculated turnover number with the loss of the working substance not exceeding 3% is $8 \times 10^2 - 10^3$.

Elongation of a conjugation chain involving one of the double bonds in norbornadiene may be a way to increase the λ_{ae} and Φ values. In view of this, we studied the spectral and photochemical properties of 3-arylnorbornadiene-2-carbaldehyde derivatives **28**, namely, oximes, imines, hydrazones, etc. (Table 5).^{67, 69, 71, 72} By varying the electron-donating and electron-withdrawing substituents at the C=C double bond in norbornadienes **28**, it became possible to shift the values of λ_{max} to 500 nm and λ_{ae} to 620 nm. Heterogeneous catalysis with Mo(VI) oxide described above proved to be efficient for the reverse reaction of the majority of quadricyclanes **29**.



R = H, NO₂, NH₂; X = NOH, NOME, NAr, NNPh, C(CN)₂, C(CN)CO₂Et, C(CO₂Et)₂.

Table 4. Spectral characteristics of carbonyl-containing norbornadienes **26** and quadricyclanes **27** and quantum yields of the photoreaction **26** → **27** in propan-2-ol.^{67–71}

Compound 26	X	R ¹	R ²	$\lambda_{\text{max}}/\text{nm}$ ($10^{-4} \epsilon_{\text{max}}/\text{litre mol}^{-1} \text{cm}^{-1}$)	$\lambda_{\text{ae}}(\mathbf{26})/\text{nm}$	Φ^a	$\lambda_{\text{ae}}(\mathbf{27})/\text{nm}$
a	O	H	Ph	222 (1.44), 318 (0.96)	400	0.40	330
b	O	Me	Ph	250 (0.89), 297 (0.92)	400	0.34	350
c	O	Ph	Br	259 (1.02), 286 (0.39)	360	0.33	330
d	O	CH=CHPh	Ph	300 (2.48), 345 (1.10)	435	—	420
e	CHCOPh	H	Ph	231 (1.70), 377 (1.69)	450	0.10	415
f	CHCOPh	H	4-NO ₂ C ₆ H ₄	263 (2.03), 387 (2.26)	470	0.60	400
g	O	OMe	4-NO ₂ C ₆ H ₄	322 (1.53)	415	0.01	380
h	O	OMe	4-NH ₂ C ₆ H ₄	237 (1.70), 353 (2.07)	445	0.20	330
i	CHCOC ₆ H ₄ Me-4	H	Ph	375 (1.63)	470	0.12	410
j	CHCOC ₆ H ₄ Cl-4	H	Ph	258 (4.09), 380 (1.72)	475	0.15	420
k	CHCOC ₆ H ₄ Br-4	H	Ph	257 (3.76), 381 (1.68)	475	0.16	420
l	CHCOC ₆ H ₄ NO ₂ -3	H	Ph	250 (3.15), 389 (1.55)	500	0.25	420
m	CHCOC ₆ H ₄ Ph-4	H	Ph	275 (3.12), 390 (1.89)	500	0.08	440

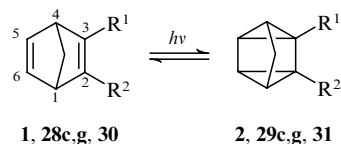
^a For compounds **26a–c, g**, $\lambda_{\text{irr}} = 313 \text{ nm}$; for compounds **26d, h**, 365 nm; for compounds **26e, f, i–m**, 436 nm.

Table 5. Spectral characteristics of norbornadienes **28** and quadricyclanes **29** and quantum yields of the photoreaction **28** → **29** in propan-2-ol.^{67, 69, 71, 72}

Compound 28	R	X	λ_{max} /nm ($10^{-4} \epsilon_{\text{max}}$ /litre mol ⁻¹ cm ⁻¹)	$\lambda_{\text{ae}}(\mathbf{28})$ /nm	Φ^a ($\lambda_{\text{irr}} = 436$ nm)	$\lambda_{\text{ae}}(\mathbf{29})$ /nm
a	H	NOH	223 (1.68), 310 (1.36)	360	0.19	310
b	H	NOMe	227 (1.70), 313 (1.48)	370	0.16	330
c	H	NPh	235 (2.16), 343 (1.66)	425	0.15	350
d	H	NC ₆ H ₄ OMe-4	238 (2.86), 365 (2.37)	465	0.12	360
e	H	NC ₆ H ₄ NMe ₂ -4	252 (1.70), 320 (1.51), 405 (2.00)	525	0.10	400
f	H	NNHPh	257 (1.67), 373 (3.06)	455	0.05	370
g	H	C(CN) ₂	251 (1.39), 303 (0.60), 382 (2.15)	480	0.74	330
h	NO ₂	C(CN) ₂	302 (1.79), 386 (2.98)	480	0.75	340
i	NH ₂	C(CN) ₂	235 (1.58), 282 (2.44), 505 (3.62)	620	0.10	380
j	H	C(CN)CO ₂ Et	249 (1.62), 298 (0.62), 376 (2.18)	490	0.69	360
k	H	C(CO ₂ Et) ₂	233 (1.75), 350 (0.76)	430	0.63	330

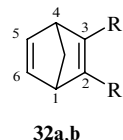
^a For compounds **28a–c, k**, $\lambda_{\text{irr}} = 365$ nm.

More complete data on the effect of substituents on the state of C=C double bonds in norbornadiene were obtained from an X-ray diffraction study of compounds **28c** and **28g** (see Ref. 73) and comparison with literature data on the structure of non-substituted NBD^{53, 74} and 2-(2,2-diphenylvinyl)norbornadiene-3-carboxylic acid **30**.⁷⁵



Compounds	R ¹	R ²
1, 2	H	H
28c, 29c	Ph	CH=NPh
28g, 29g	Ph	CH=C(CN) ₂
30, 31	CO ₂ H	CH=CPh ₂

The lengths of single bonds in the molecule **28c** have ordinary values (1.57 Å on average), but the lengths of the C(2)=C(3) (1.342 Å) and C(5)=C(6) double bonds (1.310 Å) differ markedly from the lengths of similar bonds in non-substituted NBD **1** (1.333 Å). X-Ray diffraction data suggest that the C(2)=C(3) bond is conjugated with the azomethine C=N bond and with the π -bonds in the phenyl substituents; this results in its elongation with simultaneous shortening of the C(5)=C(6) bond. In the molecule **28g**, which contains a stronger electron-withdrawing substituent, the C(2)=C(3) bond is elongated considerably [to 1.38(1) Å], whereas the C(5)=C(6) bond is shortened [to 1.29(2) Å]. The quantum yield of this photoreaction increases in the order: 0.05 (**1**) < 0.15 (**28c**) < 0.74 (**28g**). A similar pattern of changes in the lengths of double bonds was found for norbornadiene **30**;⁷⁵ the C(2)=C(3) bond in this molecule is elongated to 1.359 Å due to the conjugation with the π -systems of the substituents, while the C(5)=C(6) bond is shortened to 1.271(4) Å. The presence of two electron-withdrawing substituents at the C=C double bond in norbornadienes **32a, b** affects the distribution of the bond lengths less significantly.^{76, 77} For example, the elongation of the C(2)=C(3) bond in the molecule of 2,3-dicyanonorbornadiene (**32a**) is insignificant [to 1.339(2) Å], whereas the C(5)=C(6) bond is shortened to 1.315 Å [in the molecule **32b**,

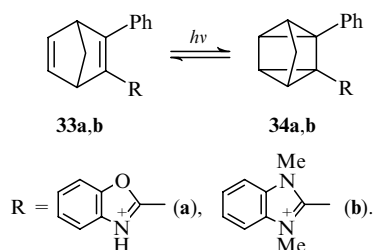


R = CN (**a**), CONH₂ (**b**).

the lengths of these bonds are 1.341(3) and 1.285(4) Å, respectively].

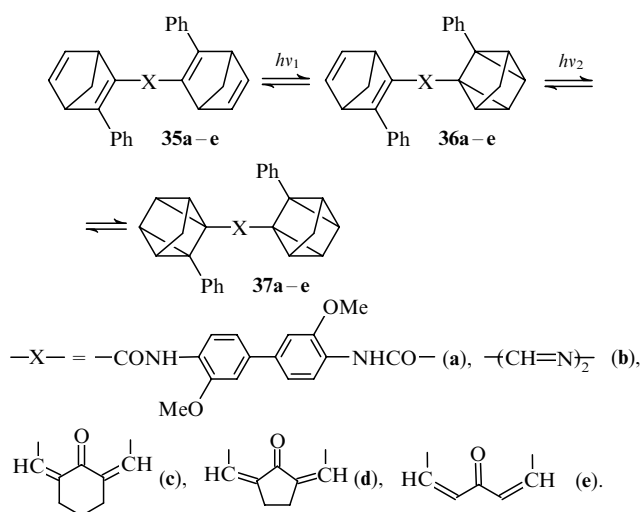
X-Ray diffraction data suggest convincingly that if one of the double bonds in norbornadiene is involved in a conjugation chain with an electron-donating and an electron-withdrawing substituents, its length increases in parallel with the λ_{ae} and Φ values.

In view of this, it seemed attractive to use organic cations as the electron-withdrawing component, although it has been shown previously^{78, 79} that the presence of pyridinium or pyrylium cations gives high values of λ_{ae} and Φ but results in irreversible opening of the cyclopropane fragment in the quadricyclanes formed. We have studied the photochemical properties of 2-benzooxazolyl and 2-benzimidazolyl derivatives of 3-phenylnorbornadiene **33a, b**.^{67, 69, 80} The benzooxazole derivative **33a** is characterised by $\lambda_{\text{ae}} = 550$ nm, but the **33a** → **34a** rearrangement occurs irreversibly. The λ_{ae} value for the benzimidazolyl derivative **33b** is 340–365 nm, depending on the type of the counter ion (I[−], ClO₄[−], BF₄[−], SbCl₆[−]), while the quantum yield of the photoreaction is 0.41–0.45. None of the known catalysts of the reverse reaction¹ affects quadricyclanes **34b**, whereas thermal initiation (343 K, solution in acetonitrile) results in the original NBD with a rate constant $k = 6 \times 10^{-4} \text{ s}^{-1}$, with complete restoration of the original spectrum. The cycle **33b** ⇌ **34b** can be repeated many times.



In order to increase the amount of accumulated solar energy per mol of the original compound, we have studied the dinorbornadiene systems **35a–e**.⁸¹ Dinorbornadienes **35a–e** absorb light in the region of 345–450 nm; the λ_{ae} values for compounds **35c–e** are as high as 530–560 nm. Irradiation of these compounds with light with a wavelength of 365 nm (**a, b**) or 436 nm (**c–e**) results in valence isomerisation into the corresponding monoquadricyclanes **36** and then into diquadricyclanes **37**. The two-step pattern of the photoreaction postulated previously for dinorbornadienyl derivatives of diamides⁸² was confirmed for 3-phenylnorbornadiene-2-carbaldazine (**35b**). The primary photoproduct **36b** is characterised by a new absorption band at 380 nm ($\lambda_{\text{irr}} = 436$ nm, $\Phi = 0.023$); its subsequent irradiation with a wavelength within this band ($\lambda_{\text{irr}} = 365$ nm, $\Phi = 0.028$) gives the diquadricyclane **37b**. The reverse transformation into the original dinorbornadienes can be carried out under conditions of homogeneous or

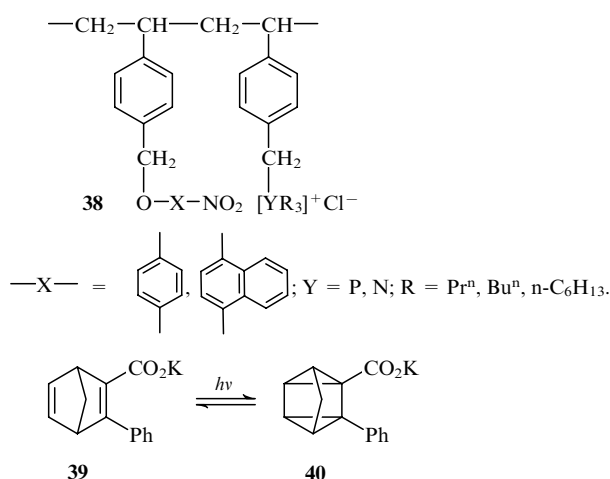
heterogeneous catalysis (addition of $\text{CF}_3\text{CO}_2\text{H}$ or MoO_3 , respectively).



V. Polymer-bound norbornadienes and sensitizers

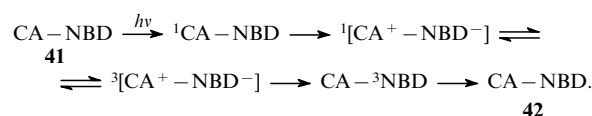
One of the leading approaches to the accumulation of solar energy developed in recent years involves the use of polymeric systems containing non-substituted NBD or its derivatives in a lateral or main chain of the macromolecule as well as polymer-bound sensitizers of the valence isomerisation $\text{NBD} \rightarrow \text{Q}$. This is primarily due to the fact that norbornadiene fragments incorporated in a polymer are more stable than free NBD molecules with the same substituents. In many cases, this makes it possible to avoid side reactions and to increase the quantum yield of $\text{NBD} \rightarrow \text{Q}$ photoisomerisation and the turnover number.

The first studies along this direction were aimed at the synthesis of polymer-bound benzophenone or acetophenone, but the photo-stability of such sensitizers proved to be rather low.^{83, 84} Polymeric photosensitizers of a new type (38) containing ammonium or phosphonium groups (for binding the substrate) together with sensitizing nitroaryloxy groups were used to carry out the 39 → 40 photoisomerisation.⁸⁵

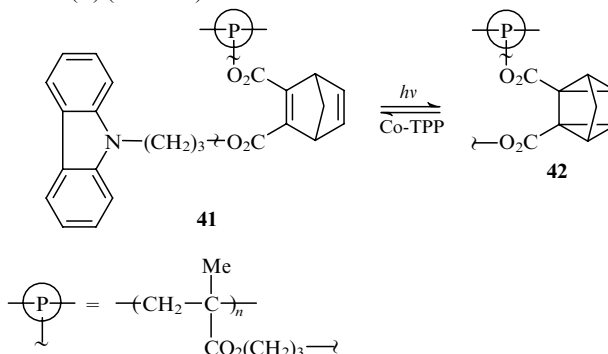


The quantum yield of this reaction was 0.19 at $\lambda_{\text{irr}} = 366 \text{ nm}$ in the absence of a sensitizer and 0.42 in the presence of the polymer 38, suggesting that intermolecular energy transfer occurred from the sensitizer (38) to the norbornadiene (39).

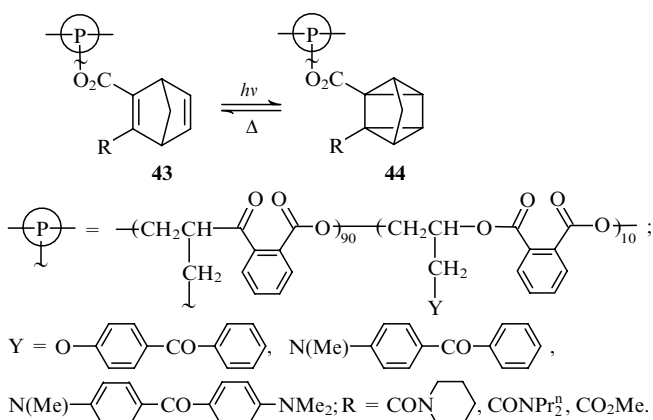
Irradiation of the polymers 41 in the visible spectral region ($\lambda_{\text{irr}} > 350 \text{ nm}$) results in their valence isomerisation into the quadricyclane derivatives 42.⁸⁶ A mechanism of this process was suggested, which involved the intramolecular electron transfer from the carbazole (CA) sensitizer to the norbornadiene fragment:



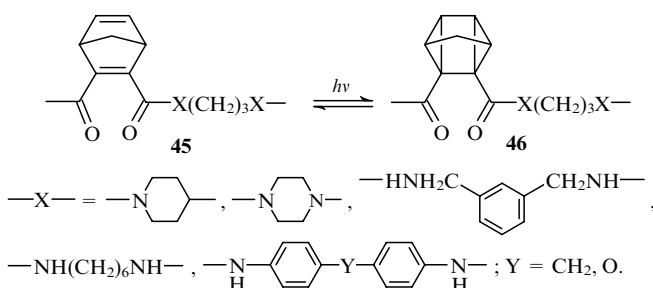
The reverse reaction occurs in the presence of catalytic amounts of (5,10,15,20-tetraphenyl-21*H*,23*H*-porphyrinato)-cobalt(II) (Co-TPP).



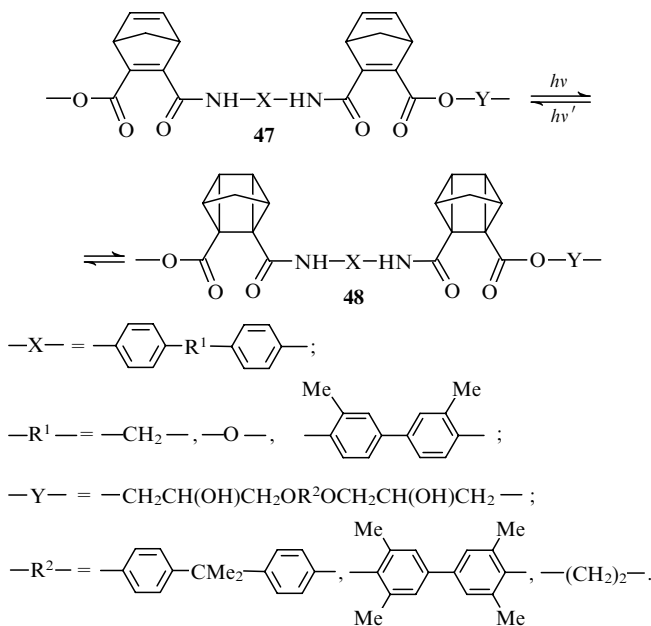
The valence isomerisation of polyesters 43 containing benzophenone and norbornadiene fragments occurs both in polymeric films and in solutions in dichloromethane ($\Phi = 0.62\text{--}0.84$) and involves a stage of efficient energy transfer from the sensitizer to NBD.⁸⁷ Compounds 44 are rather stable; the reverse reaction 44 → 43 releases $\sim 90 \text{ kJ mol}^{-1}$ of the accumulated thermal energy.



Polyamides 45 containing non-substituted norbornadiene fragments in the main chain are characterised by values $\lambda_{\text{ae}} \leq 440 \text{ nm}$.^{88–90} Irradiation of these compounds in this spectral region results in the selective isomerisation of NBD into quadricyclanes without side reactions. Incorporation of a sensitizer, e.g., Michler's ketone or 4-(*N,N*-dimethylamino)benzophenone, in the polymer increases the efficiency of the 45 → 46 process. The reverse transformation occurs upon addition of Co-TPP to a solution of the polyamide 46 in dichloromethane or upon irradiation of polymeric films of 46 with light with $\lambda_{\text{irr}} = 235\text{--}260 \text{ nm}$.

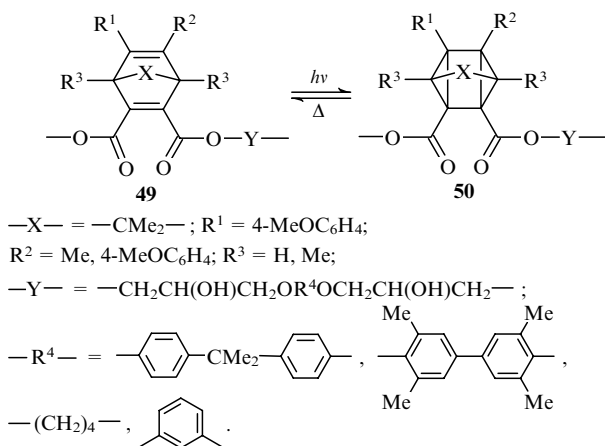


Polyesters **47** with similar composition also readily undergo photoisomerisation on exposure to sunlight in polymeric films or as solutions in THF to give quadricyclane derivatives **48**.⁹¹

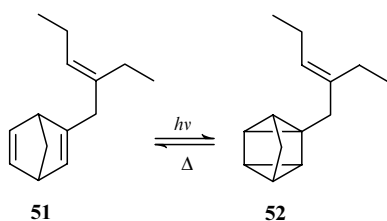


The reverse transformation of solid polymers **48** occurs efficiently under irradiation with light with $\lambda_{\text{irr}} = 272$ nm and is accompanied by liberation of heat (~ 84 kJ mol⁻¹).

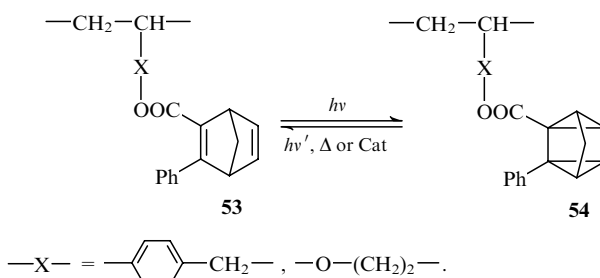
'Donor-acceptor' NBD can also be incorporated in the main chain of a polymeric molecule.^{92,93} Owing to the existence of a charge transfer band, polyesters **49** have $\lambda_{\text{ae}} \leq 500$ nm. Irradiation of polymeric films of compound **49** with visible light yields isomeric compounds **50**; the reverse reaction occurs slowly at room temperature.



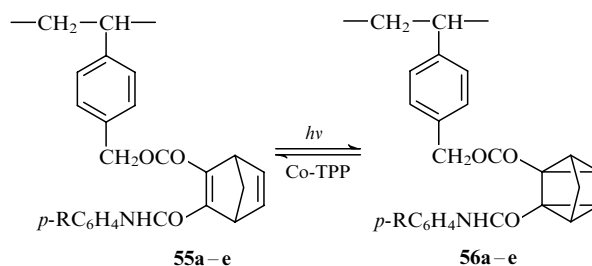
The majority of studies in this field deal with polymers in which the NBD residues are 'attached' to the main chain of the macromolecule.^{5,94-103} For example, polyisoprene **51** is isomerised in a benzene solution in the presence of $(\text{PPh}_3)_2\text{CuBr}$ as the sensitiser.⁹⁴ The reaction **52** $\rightarrow$ **51** is thermally reversible on heating of the polymer to 180 °C.



Irradiation of polymers **53**, which contain the residue of 3-phenylnorbornadiene-2-carboxylic acid, with light with $\lambda_{\text{irr}} = 313$ nm results in their isomerisation into quadricyclanes **54**.^{95,96} The reverse transformation is performed upon irradiation at $\lambda_{\text{irr}} = 248$ nm, heating to 100 °C, or adding Co-TPP to a solution of the polymer **54** in dichloromethane.

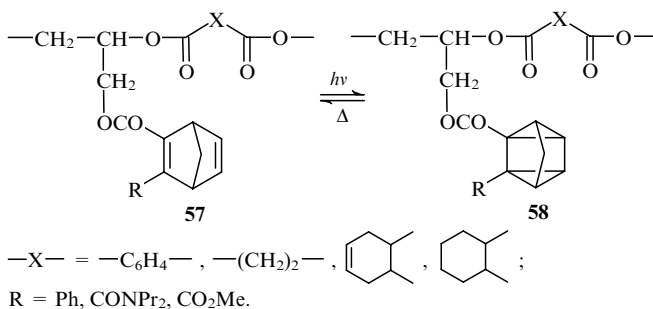


Polymer-bound amides **55a-e** were obtained in order to shift λ_{ae} to higher wavelengths; they are characterised by absorption at $\lambda_{\text{max}} = 323-351$ nm and an absorption edge at $\lambda_{\text{ae}} = 425-440$ nm.⁹⁷ Under irradiation of compounds **55a-e** with light of a mercury lamp or with sunlight, the valence isomerisation occurs readily, both in solid phase and in solutions of the polymers in THF. Its efficiency increases in the series: **55e** < **55d** < **55a** < **55b** < **55c**. Addition of Co-TPP to solutions of the quadricyclanes **56a-e** at 298 K results in their isomerisation into norbornadienes **55a-e** with a rate constant $k = (0.5-0.7) \times 10^3$ s⁻¹. The amount of the accumulated solar energy is evaluated to be 60 kJ mol⁻¹, although the presence of an *N,N*-disubstituted amide group in the norbornadiene fragment increases it to 80-86 kJ mol⁻¹ (see Ref. 98).



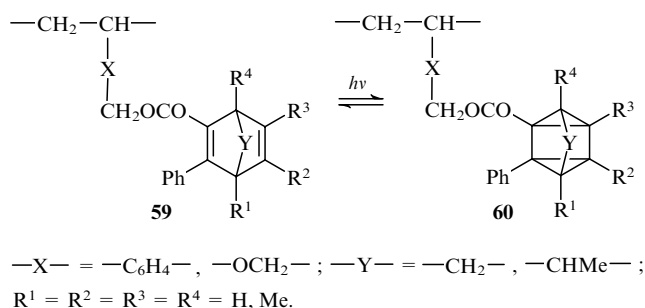
$\text{R} = \text{H (a)}, \text{Me (b)}, \text{OMe (c)}, \text{Cl (d)}, \text{COMe (e)}.$

Binding of NBD moieties with a polyester macromolecule gave photoactive systems **57**.⁵ Valence isomerisation of the latter into quadricyclanes **58** occurs readily under irradiation of the polymer at $\lambda_{\text{irr}} \leq 400$ nm, both in solid phase and in solutions in THF ($\Phi = 0.33-0.41$). The reverse transformation **58** $\rightarrow$ **57** is carried out using low-temperature initiation (62-75 °C). The amount of solar energy accumulated in this photoreaction is very high, viz., about 90 kJ mol⁻¹.

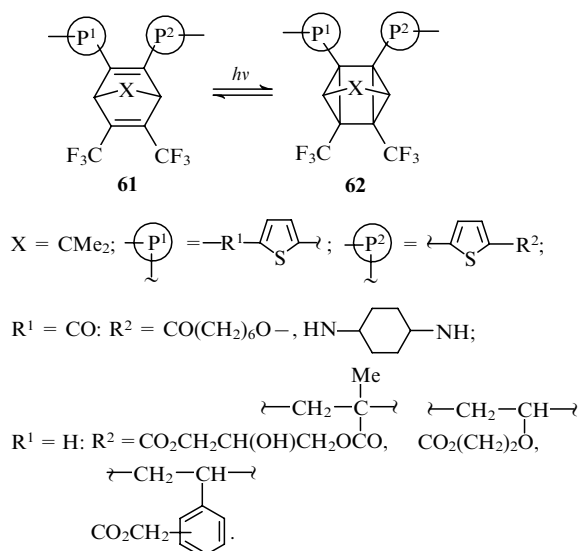


Polymers **59** with the residues of 'donor-acceptor' NBD were obtained in order to shift the λ_{ae} values farther towards the solar radiation maximum.⁹⁹ However, they were found to have $\lambda_{\text{ae}} \leq 350$ nm. Nevertheless, these compounds are characterised

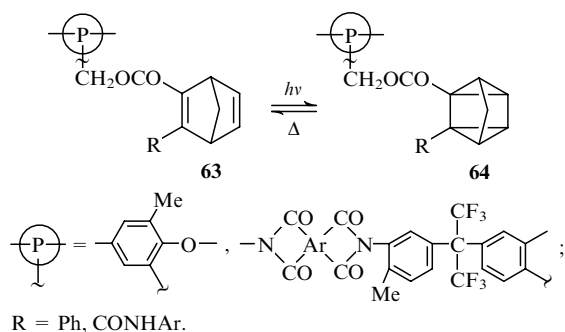
by high turnover rate of the $59 \rightleftharpoons 60$ transformation and can store 55–74 kJ mol⁻¹ of thermal energy.



Polymers **61** containing trifluoromethyl-substituted NBD present an improved version of systems of this type. Their efficient phototransformation into the isomers **62** can be carried out under irradiation in the visible spectral region (up to $\lambda_{\text{ae}} \leq 505$ nm).¹⁰⁰



The main drawback of the majority of the polymeric systems described above is their insufficient photo- and thermal stability, which limits the NBD $\rightleftharpoons$ Q turnover number. When norbornadienes **63** bound to a rigid polymeric system undergo photoisomerisation, they maintain the most important spectral and photochemical features of the NBD $\rightarrow$ Q transformation, but they have an enhanced stability in the cyclic reactions $63 \rightleftharpoons 64$.^{101, 102}



Norbornadiene-containing polystyrenes insoluble in organic solvents are even more stable.¹⁰³ Irradiation of their suspensions in dichloromethane results in isomeric quadricyclanes; in the presence of Co-TPP, the reverse reaction occurs with liberation of accumulated energy (44–77 kJ mol⁻¹).

VI. Conclusion

Analysis of recently published studies on the valence isomerisation of norbornadiene and its derivatives into the corresponding quadricyclanes revealed two major trends in relation to the accumulation of solar energy: (1) the total number of publications on this subject has decreased somewhat; (2) at the same time, we observe a significant increase in the number of studies that not only pose a certain problem but also suggest specific ways to solve it practically. In our opinion, this indicates that this problem is nearly solved rather than that the interest in the accumulation of solar energy with the use of NBD is being lost. As mentioned previously,¹ the thermal energy obtained by the method in question is more expensive than that generated by conventional methods, but cost issues will inevitably become less important as natural fuel resources are exhausted. We distinguished four main competing approaches that are used for enhancing the efficiency of isomerisation of norbornadienes into quadricyclanes. It can be concluded that considerable success has been reached along each of these directions. Efficient ways for the photosensitisation of this reaction have been developed using metal complexes or sensitizers chemically bound with the NBD molecule; in certain cases, the number of working cycles can be as high as 5000. Owing to the enhanced thermal stabilities of 'donor–acceptor' systems in which NBD molecules contain perfluoroalkyl substituents, such derivatives are promising for practical application. 2,3-Disubstituted NBD are serious competitors to these systems. This is primarily due to the facts that they are easier to synthesise and that they can absorb sunlight in the spectral region $\lambda > 400$ nm. Polymer-bound NBD can provide acceptable cyclicity and allow up to 94 kJ mol⁻¹ of solar energy to be accumulated. It is also obvious that, beside the accumulation of solar energy, the norbornadiene–quadricyclane system finds diverse new fields of application: creating molecular switches^{61, 104, 105} and optical waveguides on their basis,^{106, 107} developing new types of photochromic chemosensors for metal cations^{108, 109} and photo-switchable organic magnetic materials.^{110–112} Furthermore, NBD-containing polymers can be used as energy-boosting additives for rocket fuel.⁹⁴

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β -Telluroacroleins and tellurovinyl ketones: synthesis, reactions and structures

I D Sadekov

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Abstract. The published data on the synthesis, reactions and structures of novel organotellurium synthones, *viz.*, β -tellurovinylcarbonyl compounds, are systematised and generalised. Special attention is given to the use of these compounds in the synthesis of tellurium-containing heterocycles. The bibliography includes 57 references.

I. Introduction

β -Tellurovinylcarbonyl compounds (aldehydes and ketones) are of particular interest as starting compounds for the synthesis of various tellurium-containing heterocycles and metal chelates with the coordination sites MO_2Te_2 and MN_2Te_2 (M is metal). However, the chemistry of these compounds has not been adequately investigated. The first β -telluroacroleins and β -aryltellurovinyl ketones were prepared by nucleophilic addition of arenetelluroate anions ArTe^- to α -acetylenic aldehydes and ketones (yields 65%–75%).¹ Bis(β -acylvinyl) tellurides were synthesised in 3%–11% yields² using a similar approach, *i.e.*, by nucleophilic addition of the telluride anion Te^{2-} to α -acetylenic ketones (the reasons for the low yields of ketone will be discussed below). Two other types of β -tellurovinylcarbonyl compounds, *viz.*, aryl β -chlorotellurovinyl ketones and aryl β -trihalogenotellurovinyl ketones were prepared in the 1980's.³ The former were synthesised in four steps; the final step included the rearrangement of 3-(aryltelluro)propenoyl chlorides (yields 50%–95%).³ Aryl (β -trihalogenotellurovinyl) ketones were obtained in good yields by oxidation of tellurenyl halides with halogens.⁴

Earlier, β -tellurovinylcarbonyl compounds were used exclusively for the preparation of tellurophenes containing strong electron-withdrawing groups in position 2 (NO_2 , CHO, COMe, CO_2Et)⁵ and 1,6-dioxo-6 α -tellurapentalenes.⁶

Significant progress in the chemistry of β -telluroacroleins and β -tellurovinyl ketones has been achieved over the last 8–10 years owing to the development of methods for their synthesis. (β -Formylvinyl)(methyl)tellurium dihalides, a novel class of β -tellurovinylcarbonyl compounds, have proved to be convenient starting compounds in the synthesis of (β -halogenotellurovinyl)carbonyl

derivatives and the previously unknown β -halogenotellurovinyl aldimines. Preparative procedures for the synthesis of various tellurium-containing heterocycles based on β -tellurovinylcarbonyl compounds have been developed.

The distinguishing feature of organotellurium compounds is the formation of intramolecular hypervalent coordinative bonds between the oxygen (or nitrogen) atom and the tellurium atom [$\text{O}(\text{N}) \rightarrow \text{Te}$]; their lengths vary over a wide range, sometimes being close to the lengths of ordinary covalent bonds. Similar bond types were studied mostly for aromatic derivatives in which tellurium-centred groups [TeHal , TeOR , TeOCOR , TeSCN , TeR , $\text{Te}(\text{R})\text{Hal}_2$, TeHal_3 , *etc.*] were in the *ortho*-position relative to the substituents containing sp^2 - or sp^3 -hybridised oxygen or nitrogen atoms (CHO, COR, CO_2R , NO_2 , $\text{CH}=\text{N}$, $\text{N}=\text{N}$, CH_2NR_2).^{7–9} The intramolecular coordination $\text{O}(\text{N}) \rightarrow \text{Te}$ ensures stabilisation of various organotellurium compounds, primarily of dicoordinated tellurium derivatives, which are thermodynamically and kinetically unstable in the absence of these bonds, and significantly affects their reactivities. The preparation of pure arenetellurenyl halides,^{7–10} azides,^{8,10} acylates,^{7,8,10} and alkoxides^{8,10} is possible provided they contain the coordinative bond $\text{O}(\text{N}) \rightarrow \text{Te}$. Tellurium-centred cyclopentadienes are stable if they contain tellurium-containing substituents with *o*-formyltelluranylbenzene or their respective azomethine fragments.¹¹ However, data on X-ray diffraction analysis of β -tellurovinylcarbonyl compounds and (β -halogenotellurovinyl) aldimines containing intramolecular coordinative bonds $\text{O}(\text{N}) \rightarrow \text{Te}$ are very scarce.

II. Synthesis and reactions of β -tellurovinylcarbonyl compounds

In this review, the synthesis and reactions of β -telluroacroleins and β -tellurovinyl ketones will be considered separately for each individual group of β -tellurovinylcarbonyl compounds. Reactions typical of carbonyl groups and tellurium-containing substituents (reactions involving double bonds are still unknown) and conversions resulting in the formation of tellurium-containing heterocycles from β -tellurovinylcarbonyl compounds and their derivatives will be discussed.

1. Synthesis of β -alkyl(aryl)telluroacroleins and β -tellurovinyl ketones

Two main approaches to the synthesis of β -alkyl(aryl)telluroacroleins and β -substituted tellurovinyl ketones of the general formula $\text{RTeC}(\text{R}^1)=\text{C}(\text{R}^2)\text{COR}^3$ are known, *viz.*, nucleophilic substitution of the telluroate anions RTe^- for chlorine atoms in β -chlorovinylcarbonyl compounds and nucleophilic addition of RTe^- to the triple bonds of α -acetylenic aldehydes and ketones.

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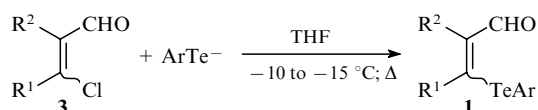
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The former approach is more general and allows the preparation of compounds containing a broad range of substituents in the carbon triad C=C–C(O). As far as the nucleophilic addition is concerned, this yields only β -tellurovinylcarbonyl derivatives devoid of α -substituents.

β -Aryltelluroacroleins (**1**) and β -aryltellurovinyl ketones (**2**) were prepared by reaction of β -chlorovinylcarbonyl compounds **3** and **4** with arenetelluroate anions^{12–15} generated in the reaction of aryllithium with tellurium powder in THF or by reduction of diaryl ditellurides with lithium in THF in the presence of catalytic amounts of naphthalene (Tables 1 and 2).

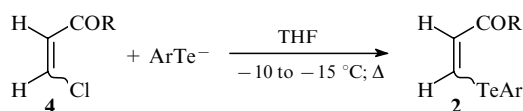
Table 1. Synthesis of β -aryltelluroacroleins **1** from β -chloroacroleins **3**.



Com- pound 1	R ¹	R ²	Ar	Yield (%)	Z : E ratio	Ref.
a	Ph	H	Ph	37	1 : 0	12–15
b	Ph	H	4-EtOC ₆ H ₄	45	1 : 0	14, 15
c	Ph	Me	Ph	60	1 : 2	14, 15
d	Ph	Me	4-EtOC ₆ H ₄	52	1 : 9	14, 15
e	Ph	Et	Ph	65	1 : 19	14, 15
f	Ph	Et	4-MeOC ₆ H ₄	58	1 : 10	14, 15
g	(CH ₂) ₄	Ph	Ph	57	1 : 0	13–15
h	(CH ₂) ₄	4-MeC ₆ H ₄	4-MeC ₆ H ₄	52	1 : 0	14–16
i	(CH ₂) ₄	4-EtOC ₆ H ₄	4-EtOC ₆ H ₄	37	1 : 0	12–16

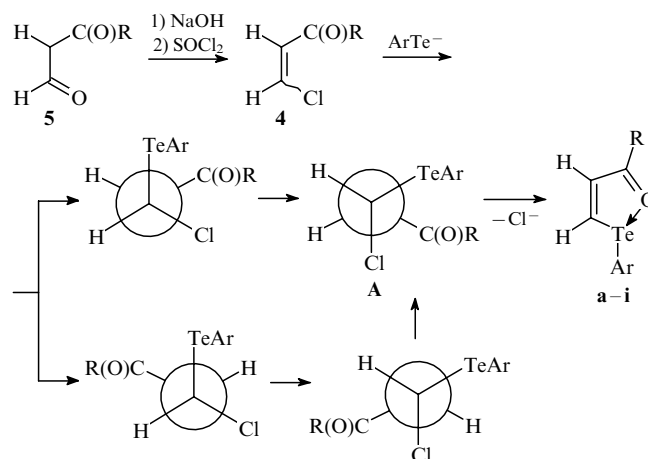
Note. The ratios of the *Z*- and *E*-isomers were determined from the ¹H NMR spectra.

Table 2. Synthesis of β -aryltellurovinyl ketones **2** from β -chlorovinyl ketones **4**.



Com- pound 2	R	Ar	Yield (%)	Ref.
a	Ph	Ph	47	12–15
b	Ph	4-MeOC ₆ H ₄	45	12, 14–16
c	Ph	4-EtOC ₆ H ₄	52	13–15
d	4-MeC ₆ H ₄	4-MeC ₆ H ₄	39	14, 15
e	4-MeC ₆ H ₄	4-EtOC ₆ H ₄	53	14–16
f	4-MeOC ₆ H ₄	4-MeC ₆ H ₄	45	12, 14, 15
g	4-MeOC ₆ H ₄	4-EtOC ₆ H ₄	39	12, 14–16
h	4-BrC ₆ H ₄	4-MeC ₆ H ₄	55	12, 14, 15
i	4-BrC ₆ H ₄	4-EtOC ₆ H ₄	47	14, 15

The stereochemistry of reactions of nucleophilic substitution of arenetelluroate anions for the chlorine atom in β -chlorovinylcarbonyl compounds was studied in the example of β -chlorovinyl ketones **4** (R = Ph, 4-MeC₆H₄, 4-BrC₆H₄, 4-MeOC₆H₄),^{12, 14, 15} since the configurations of substituents at the double bond of the starting compounds and the derived tellurovinyl ketones **2** could easily be established from the values of coupling constants of olefinic protons. Ketones **4** synthesised by treatment of sodium salts of β -oxoaldehydes **5** with SOCl₂ represent a mixture of *Z*- and *E*-isomers where the latter predominate.

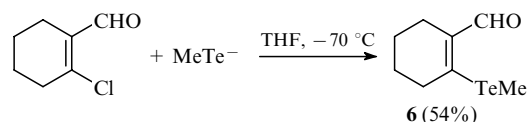


As described earlier,^{14, 15} the ratios of *Z*- and *E*-isomers in chlorovinyl ketones **4** depend on the nature of the substituent in position 4 of the phenyl ring and are equal to 0 : 1 (R = 4-BrC₆H₄), 1 : 12 (R = Ph), 1 : 5 (R = 4-MeC₆H₄), 1 : 1.5 (R = 4-MeOC₆H₄). However, aryl β -aryltellurovinyl ketones **2a–i** prepared from them represent exclusively *Z*-isomers.^{12, 14, 15} Thus, substitution of ArTe[–] for the chlorine atom results in complete reversal of the configuration of the *E*-isomers of aryl β -chlorovinyl ketones **4** and complete retention in the case of *Z*-isomers. This was rationalised in terms of a two-step vinylic nucleophilic substitution mechanism, *viz.*, vinylic substitution through addition–elimination.¹⁷ The first step of this reaction includes addition of highly nucleophilic arenetelluroate anions¹⁸ to the double bond of chlorovinyl ketones, the electrophilicity of the double bonds being enhanced owing to the presence of the oxo group. The conformers **A** stabilised by the coordinative bond O → Te certainly possess the highest stabilities compared with the other conformers existing due to the rotation of the carbanions formed around the simple bond. Subsequent elimination of the chloride ion from conformers **A** yields the *Z*-isomers of aryl β -aryltellurovinyl ketones **2a–i**, which are additionally stabilised by the coordinative bond O → Te.^{14, 15}

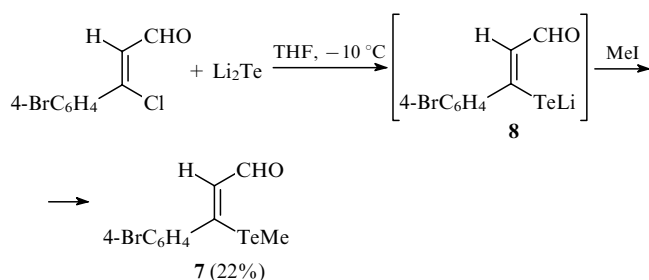
β -Chloro- β -phenylpropenal obtained as a mixture of *Z*- and *E*-isomers in a 9 : 1 ratio¹⁹ reacts with arenetelluroate anions to yield exclusively the *Z*-isomers of compounds **1a,b**.^{14, 15} The reaction of arenetelluroate anions with 2-chlorocyclohex-1-enecarbaldehyde has the same stoichiometric result, *i.e.*, exclusive formation of *Z*-isomers of compounds **1g–i** (see Table 1).^{14, 15}

In contrast to chloroacroleins and chlorovinyl ketones non-substituted in the α -position, compounds **3** (R¹ = Ph, R² = Me, Et) react with arenetelluroate anions to afford mixtures of *E*- and *Z*-isomers of compounds **1c–f**; their isomeric ratios vary widely (see Table 1). In this case, the O → Te interaction, which stabilises conformers **A**, competes with the steric repulsion of bulky phenyl and alkyl groups, as a result of which the stereospecificity of the reaction is lost.^{14, 15}

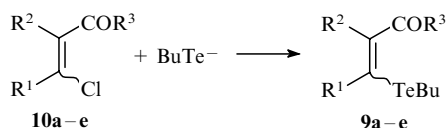
Among β -alkyltellurovinylcarbonyl compounds, β -methyltelluroacroleins were the first to be synthesised by nucleophilic substitution of the chlorine atom in β -chlorovinylcarbonyl derivatives.^{14, 15, 20} Thus 2-methyltellurocyclohex-1-enecarbaldehyde **6** was prepared by reaction of β -chlorocyclohex-1-enecarbaldehyde with lithium methanetelluroate obtained from methylithium and tellurium in tetrahydrofuran. This reaction proceeds smoothly only at -70°C .



The approach to the synthesis of β-methyltelluroacrolein **7** is based on the reaction of equimolar amounts of the corresponding β-chloroacrolein with lithium telluride with subsequent alkylation of intermediate lithium telluroate **8** with methyl iodide.²¹



β-Butyltellurovinyl ketones **9a–e** were synthesised by nucleophilic substitution of the chlorine atom in the corresponding β-chlorovinyl ketones **10** using the reaction with the butanetelluroate anion generated by reduction of dibutyl ditelluride with diisobutylaluminium hydride.²² Compounds **9a–e** were obtained as mixtures of *E*- and *Z*-isomers,²² however, their ratios were not indicated.



$\text{R}^1 = \text{R}^3 = \text{Me}$, $\text{R}^2 = \text{H}$ (**a**); $\text{R}^1\text{–R}^3 = (\text{CH}_2)_2$, $\text{R}^2 = \text{H}$ (**b**);
 $\text{R}^1\text{–R}^3 = (\text{CH}_2)_3$, $\text{R}^2 = \text{H}$ (**c**); $\text{R}^1 = \text{Me}$, $\text{R}^2\text{–R}^3 = (\text{CH}_2)_3$ (**d**);
 $\text{R}^1 = \text{Me}$, $\text{R}^2\text{–R}^3 = (\text{CH}_2)_4$ (**e**).

(β-Acylvinyl)triethylammonium chlorides **11** obtainable in high yields upon treatment of chlorovinylcarbonyl derivatives with triethylamine²³ can be used in the synthesis of β-aryltellurovinyl aldehydes **1** and ketones **2** instead of β-chlorovinylcarbonyl compounds.^{14–16} The reactions of compounds **11** with sodium tellurophenolates prepared by reduction of diaryl ditellurides with sodium borohydride are carried out in methanol with subsequent short-term boiling of the reaction mixture (Table 3).

This approach to the synthesis of β-aryltellurovinylcarbonyl compounds is more convenient than that from chlorovinylcarbonyl compounds, since ammonium salts are more storage-stable

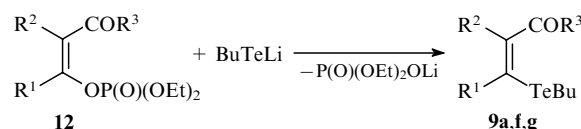
Table 3. Synthesis of β-aryltelluroacroleins and β-aryltellurovinyl ketones from β-acylvinyltriethylammonium chlorides **11**.

$$\begin{array}{c}
 \text{R}^2 \\
 \diagup \\
 \text{R}^1\text{-C=CH-COR}^3 + \text{ArTe}^- \xrightarrow{\text{MeOH, } \Delta} \text{R}^1\text{-C=CH-COR}^3 \\
 \diagdown \\
 \text{NEt}_3\text{Cl}^- \\
 \text{11} \\
 \downarrow \\
 \text{R}^1\text{-C=CH-COR}^3 \\
 \diagdown \\
 \text{TeAr} \\
 \text{1h–j, 2e,g,i,j}
 \end{array}$$

Compound	R ¹	R ²	R ³	Ar	Yield (%)	Ref.
1h	(CH ₂) ₄	H		4-MeC ₆ H ₄	71	14–16
1i	(CH ₂) ₄	H		4-EtOC ₆ H ₄	70	12–16
1j	(CH ₂) ₄	H		4-ClC ₆ H ₄	79	14–16
2e	H	H	4-MeC ₆ H ₄	4-EtOC ₆ H ₄	79	14–16
2g	H	H	4-MeOC ₆ H ₄	4-EtOC ₆ H ₄	83	12, 14–16
2i	H	H	4-BrC ₆ H ₄	4-EtOC ₆ H ₄	85	14, 15
2j	H	H	Ph	4-MeC ₆ H ₄	86	12, 14–16

than their chlorine-containing analogues. Moreover, the preparation of arenetelluroate anions is preparatively more simple, and the yields of the reaction products are usually higher.

Enol phosphates **12** were also used as starting compounds in the synthesis of β-substituted tellurovinylcarbonyl compounds.²⁴ Their reactions with lithium butanetelluroate prepared from butyllithium and tellurium powder in THF result in β-butyltellurovinyl methyl ketones **9a,f,g**.

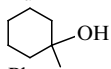


$\text{R}^1 = \text{R}^3 = \text{Me}$, $\text{R}^2 = \text{H}$ (**a**); $\text{R}^1 = \text{Ph}$, $\text{R}^2 = \text{H}$, $\text{R}^3 = \text{Me}$ (**f**);
 $\text{R}^1\text{–R}^2 = (\text{CH}_2)_3$, $\text{R}^3 = \text{Me}$ (**g**)

A large variety of telluroacroleins and tellurovinyl ketones non-substituted in the α-position were prepared by nucleophilic addition of alkane(arene)telluroate anions generated by reduction of dialkyl(aryl) ditellurides with sodium borohydride in methanol or ethanol to the triple bonds of acetylenic aldehydes or ketones **13** (Table 4).^{1, 14, 15, 25, 26} The reaction proceeds under

Table 4. Synthesis of β-alkyl(aryl)telluroacroleins and β-alkyl(aryl)tellurovinyl ketones by addition of telluroate anions to acetylenic carbonyl compounds.

$$\begin{array}{c}
 \text{R}^1\text{C}\equiv\text{CCOR}^2 + \text{R}^3\text{Te}^- \longrightarrow \text{H} \\
 \diagup \\
 \text{R}^1\text{-C=CH-COR}^2 \\
 \diagdown \\
 \text{TeR}^3 \\
 \text{13}
 \end{array}$$

Compound	R ¹	R ²	R ³	Yield (%)	<i>Z</i> : <i>E</i> ratio	Ref.
1a	Ph	H	Ph	90	1 : 0 ^a	14, 15, 25
1b	Ph	H	4-EtOC ₆ H ₄	61	1 : 0 ^a	14, 15
1k	H	H	Ph	80	1 : 0 ^b	26
1l	Ph	H	4-MeC ₆ H ₄	76	—	25
1m	Ph	H	4-MeOC ₆ H ₄	68	—	25
3b	H	Ph	4-MeC ₆ H ₄	86	1 : 0 ^b	14, 15
3c	H	Ph	4-EtOC ₆ H ₄	89	1 : 0 ^b	14, 15
3j	H	Ph	4-MeOC ₆ H ₄	71	—	1
3k	Bu	Ph	4-MeOC ₆ H ₄	68	—	1, 25
3l	Bu	Me	4-MeOC ₆ H ₄	71	—	1
3m		Ph	Ph	84	—	25
3n	Ph	Ph	Ph	86	—	25
3o	Ph	4-MeOC ₆ H ₄	Ph	74	—	1
9h	H	H	Bu	84	89 : 11	26

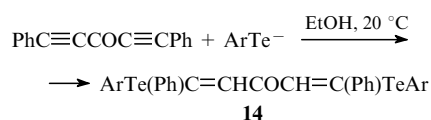
^a The assignment was made on the basis of the identity of the compounds synthesised to those prepared from β-chloroacroleins. ^b The assignment was made on the basis of coupling constants of olefinic protons in the ¹H NMR spectra.

mild conditions and results in β -alkyl(aryl)telluroacroleins and β -alkyl(aryl)tellurovinyl ketones (yields 60%–90%).

The stereochemistry of the nucleophilic addition of arenetelluroate anions to the triple bond was studied for the acetylenic derivatives **13**, where $R^1 = H$, $R^2 = H$, Ph.^{14, 15, 26} It was found that all these reactions yield *Z*-isomers in high yields. In the case of β -aryltellurovinyl phenyl ketones **2b,c**, the coupling constants for the alkene protons $^3J_{HH}$ are equal to 8.79 Hz, which corresponds to the *cis*-configuration. The *Z*-configuration of the substituents in β -phenyltelluroacrolein (**1k**) was also determined from the ^1H NMR spectra.

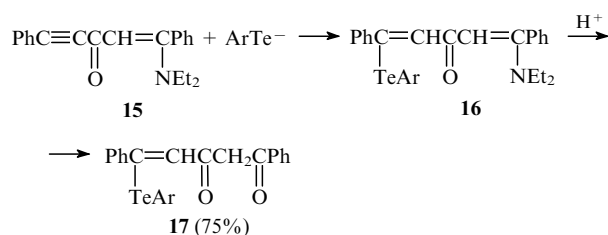
However, reaction of the butanetelluroate anion with propionaldehyde yields a mixture of *Z*- and *E*-isomers of the aldehyde **9h** in an 89 : 11 ratio.²⁶ This seems to be due to the lower electronegativity of the butyl substituent as compared with the phenyl one. Indeed, according to quantum-chemical calculations,^{27–30} the lengths and, hence, the stabilities of the intramolecular coordinative bond $O(N) \rightarrow Te(II)$ depend on the electronegativities of substituents at the tellurium atom: the higher this value the shorter the coordinative bond. Weakening of the coordinative bond on going from $R = Ph$ to $R = Bu$ results in partial cleavage of this bond in the butyl derivative and the appearance of the *E*-isomer of compound **9h** in the solution.

Arenetelluroate anions, which are the strongest nucleophiles in the series of structurally related anions ArM^- ($M = O, S, Se, Te$),¹⁸ react with symmetrical diacetylenic ketones to give only the bisadducts **14** (yields 84%–88%),²⁵ whereas alcohols and phenols add to one or both triple bonds depending on the reaction conditions.



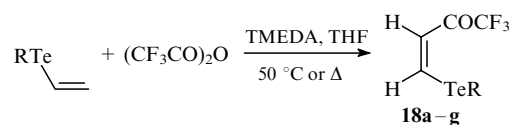
$Ar = Ph, 4-MeC_6H_4$.

Due to the relatively low electrophilicity of the triple bond in β -aminovinyl ethynyl ketones **15**, they do not react with nucleophiles, such as amines, alcohols and phenols. However, arenetelluroate anions readily add to compounds **15**. Thus ketone **16** was prepared in 68% yield.²⁵ Acid hydrolysis of this ketone results in the elimination of diethylamine and the formation of diketone **17**.²⁵



$Ar = 4-MeC_6H_4$.

A specific synthetic procedure was used to prepare β -trifluoroacetylvinyl tellurides **18a–g**.³¹ Like other heterosubstituted alkenes (vinyl sulfides, vinyl ethers, *N*-vinylamides, carbazoles, *etc.*) (see Ref. 31 and references cited therein), vinyl tellurides $RTeCH=CH_2$ react with trifluoroacetic anhydride in THF to give ketones **18a–g** (yields 50%–84%). However, in contrast to the previously mentioned heterosubstituted alkenes, the use of catalysts is necessary, among them *N,N,N',N'*-tetramethylethylenediamine (TMEDA) is the most efficient. The yields of alkylvinyl tellurides **18a–d** are higher than in the case of compounds **18e–g**.

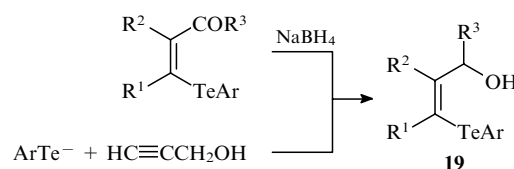


$R = Bu^n$ (**a**), Bu^i (**b**), $EtO_2C(CH_2)_2$ (**c**), $NC(CH_2)_2$ (**d**), Ph (**e**),
 $\text{O} \begin{array}{c} \diagup \diagdown \\ \text{N}CH_2CH=CH_2 \end{array}$ (**f**), $PhCH=CH$ (**g**).

It is of note that the 1,1-disubstituted vinyltelluride, *viz.*, 1-butyltelluro-1-phenylethylene, does not enter into this reaction.³¹

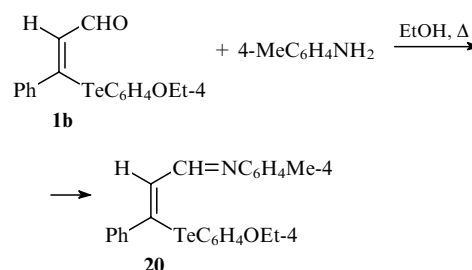
2. Reactions of β -alkyl(aryl)telluroacroleins and β -alkyl(aryl)tellurovinyl ketones

Reactions of β -alkyl(aryl)tellurovinylcarbonyl compounds have been studied relatively little. Like other aldehydes and ketones, they are reduced with sodium borohydride to 3-aryltelluroprop-2-en-1-ols **19**,¹³ which can be used as the starting compounds in the synthesis of 5*H*-1,2-oxatelluroles. Compounds **19** ($R^1 = R^2 = H$) were prepared by nucleophilic addition of arenetelluroate anions to the triple bond of propargyl alcohol.^{13, 32, 33}

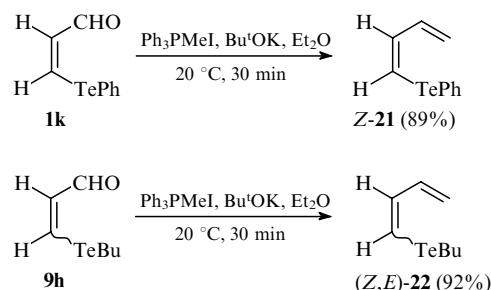


$R^1 = R^2 = H$, $R^3 = Ar = Ph$; $R^1 = Ph$, $R^2 = R^3 = H$; $Ar = Ph$,
 4- $EtOC_6H_4$; $R^1 - R^2 = (CH_2)_4$, $R^3 = H$; $Ar = Ph$, 4- $EtOC_6H_4$;
 $R^1 = R^2 = R^3 = H$; $Ar = Ph$, 4- $MeOC_6H_4$, 4- $EtOC_6H_4$.

Azomethine **20** was prepared by condensation of β -aryltelluroacrolein **1b** with *p*-toluidine.¹⁵

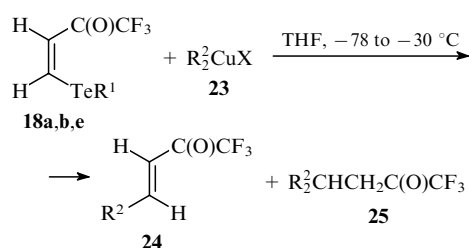


β -Alkyl(aryl)telluroacroleins, particularly compounds **1k** and **9h**, enter into the Wittig reaction with *in situ* generated methylenetriphenylphosphorane to give dienyl tellurides **21** and **22**.²⁶ The configurations of the starting alkenes are retained.



Z- β -Alkyl(aryl)tellurovinyl trifluoromethyl ketones **18a,b,e** react with zinc cuprates **23** at low temperatures (from $-78^\circ C$ to $-30^\circ C$) to give *E*-isomers of α,β -unsaturated trifluoromethyl

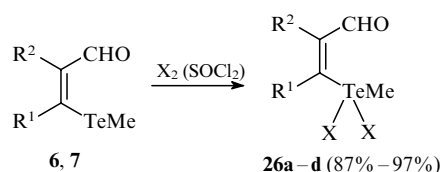
ketones **24**.³⁴ However, compounds **24** are obtained in high yields only with cuprates **23** where $R^2 = \text{Ar}$ and $\text{CH} = \text{CHPh}$. In the case of alkylzinc cuprates, the yields of ketones **24** do not exceed 70%; dialkylated ketones **25** are formed as side products (yields 11%–19%).³⁴



$R^1 = \text{Bu}^n$ (**a**), Bu^i (**b**), Ph (**e**); $R^2 = \text{Ph}$, 4-MeC₆H₄, 4-MeOC₆H₄, 4-EtOC₆H₄, PhCH=CH, C₈H₁₇, C₁₀H₂₁, C₁₂H₂₅;
X = (CN)(ZnCl)₂, ZnCl.

It is noteworthy that the reaction of organocopper derivatives Ph₂CuLi, Ph₂CuMgBr, Ph₂Cu(CN)Li₂ and Ph₂Cu(CN)(MgBr)₂ with ketones **18a,b,e** is accompanied by the predominant formation of the diphenyl derivatives **25**, whereas ketones **24** are the side products.³⁴

Only one reaction of β -alkyl(aryl)telluroacroleins involving the two-coordinate tellurium atom is presently known. Like other vinyl tellurides,³⁵ β -methyltelluroacroleins **6** and **7** are oxidised to the four-coordinate tellurium derivatives **26a–d** by halogens or thionyl chloride under mild conditions (PhH, 0–5 °C).^{15,20,21}



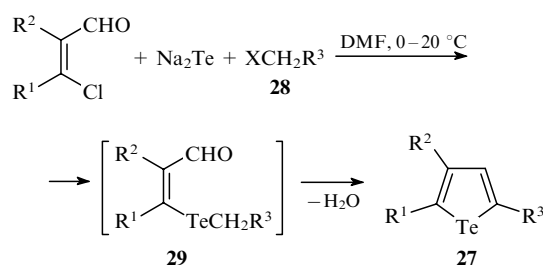
$R^1 - R^2 = (\text{CH}_2)_4$, X = Cl (**a**), Br (**b**), I (**c**); $R^1 = 4\text{-BrC}_6\text{H}_4$, $R^2 = \text{H}$, X = Br (**d**).

3. Synthesis of tellurium-containing heterocycles

a. Tellurophenes

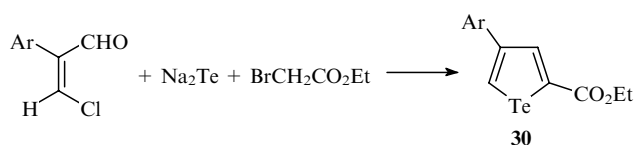
A series of substituted tellurophenes **27** containing strong electron-withdrawing groups in position 2 were synthesised by reaction of β -chloroacroleins with sodium telluride and the α -halogenomethyl derivatives **28**.^{5,36,37}

This reaction proceeds under mild conditions and results in the heterocycles **27** in 25%–30% yields. Presumably, β -substituted telluroacroleins **29** are the intermediate products in this reaction.



$R^1 = \text{Bu}^t$, $R^2 = \text{H}$; $R^3 = \text{CHO}$, COMe, CO₂Et, NO₂;
 $R^1 = 3\text{-MeOC}_6\text{H}_4$, 4-MeOC₆H₄; $R^2 = \text{H}$, $R^3 = \text{CO}_2\text{Et}$;
 $R^1 - R^2 = (\text{CH}_2)_4$; $R^3 = \text{COMe}$, CO₂Et, NO₂;
 $R^1 - R^2 = (\text{CH}_2)_5$, $R^3 = \text{CO}_2\text{Et}$; X = Cl, Br.

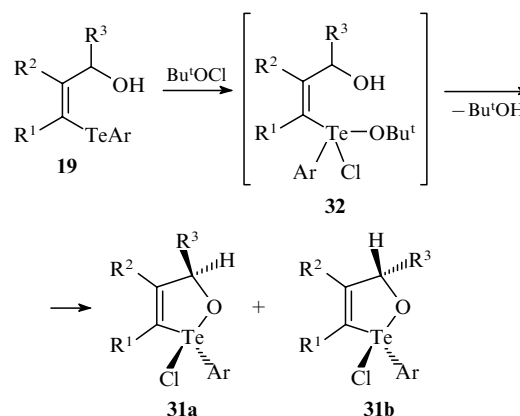
2,4-Disubstituted tellurophenes **30** were prepared from α -aryl- β -chloroacroleins.³⁸



The above-described methods for the synthesis of tellurophenes are similar to the reactions used in the synthesis of substituted thiophenes and selenophenes.

b. 2-Aryl-2-chloro-5H-1,2-oxatelluroles

3-Aryltelluroprop-2-en-1-ols **19**^{13,32,33} were used as starting compounds in the synthesis of four-coordinate derivatives of 5H-1,2-oxatellurole.^{13,33} Thus 2-aryl-2-chloro-5H-1,2-oxatelluroles **31a,b** were synthesised in 44%–82% yields by oxidation of alcohols **19** with Bu^tOCl. This reaction seems to proceed through the intermediate formation of σ -telluranes **32** which are further converted into the heterocycles **31a,b** with elimination of Bu^tOH.¹³



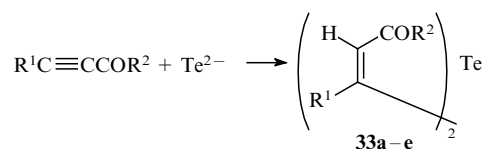
$R^1 = R^2 = R^3 = \text{H}$; Ar = Ph, 4-MeOC₆H₄, 4-EtOC₆H₄; $R^1 = R^2 = \text{H}$, $R^3 = \text{Ar} = \text{Ph}$; $R^1 = \text{Ph}$, $R^2 = R^3 = \text{H}$; Ar = Ph, 4-EtOC₆H₄.

Oxatelluroles **31** containing substituents in position 5 of the heterocycle are formed as a mixture of two isomers as can be evidenced from the ¹H NMR spectra of these compounds. Thus the signals of the methine protons of 2-chloro-2,5-diphenyl-5H-1,2-oxatelluroles are observed as two singlets at $\delta = 6.02$ and 6.27.

4. Bis(β -acylvinyl) tellurides

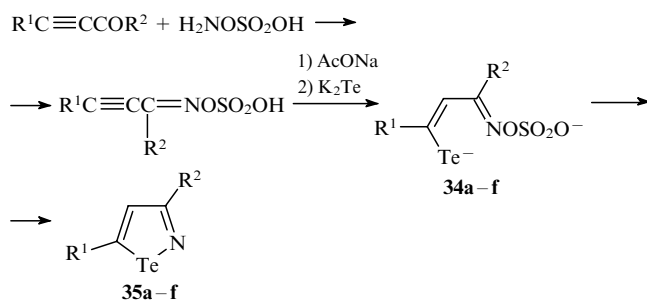
Of the methods for the synthesis of bis(β -acylvinyl) tellurides that have been studied, the data about the reactions, structures and applications of these compounds in the synthesis of tellurium-containing heterocycles are virtually absent in the literature.

The syntheses of bis(β -acylvinyl) tellurides **33a–e**, like those of β -alkyl(aryl)telluroacroleins and β -alkyl(aryl)tellurovinyl ketones, were carried out using the nucleophilic addition of potassium telluride to the triple bond of α -acetylenic ketones.² To this end, acetylenic ketones were made to react with potassium telluride and hydroxylamine-*O*-sulfonic acid in an aqueous solution of sodium acetate.



$R^1 = \text{H}$; $R^2 = \text{Me}$ (**a**, 11%), Et (**b**, 6%), Pr (**c**, 3%);
 $R^1 = R^2 = \text{Me}$ (**d**, traces); $R^1 = \text{Ph}$, $R^2 = \text{Me}$ (**e**, 3%).

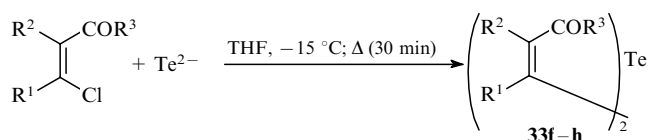
The low yields of ketones **33a–e** are due to the competing heterocyclisation of the intermediate oximes **34** into isotellurazoles **35**.^{2,39} Under these conditions, 3-mono- (**35a–c**) and 3,5-disubstituted isotellurazoles (**35d–f**) are obtained in nearly the same yields (3%–10%) as ketones **33**.



- 35: R¹ = H; R² = Me (a, 6%), Et (b, 5%), Ph (c, 4%);
 R¹ = R² = Me (d, 10%); R¹ = Ph, R² = Me (e, 7%);
 R¹ = CH₂=CH, R² = Me (f, 5%).

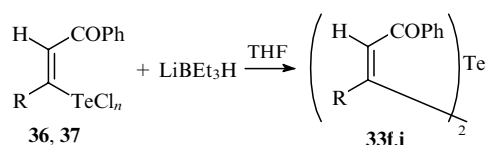
This method is inapplicable to the synthesis of isotellurazoles non-substituted in position 3, since bis(β-cyanovinyl) tellurides (NCCH=CR)₂Te (R = H and Ph), are the only reaction products (yields 20% and 14%) when α-acetylenic aldehydes are used instead of ketones.

Nucleophilic substitution of the telluride anion for the chlorine atom in β-chlorovinylcarbonyl compounds is used in the preparative synthesis of ketones and aldehydes **33**.^{14,15} Lithium telluride, prepared from lithium and elementary tellurium in THF in the presence of catalytic amounts of naphthalene, reacts with β-chloroacroleins and β-chlorovinyl ketones to give compounds **33f–h** in 39%–60% yields.^{14,15}



- R¹ = R² = H; R³ = Ph (f), 4-MeC₆H₄ (g);
 R¹–R² = (CH₂)₄, R³ = H (h).

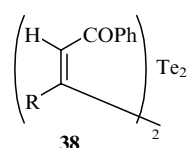
The synthesis of bis(β-benzoylvinyl) tellurides **33f,i** was carried out using β-chlorotellurovinyl phenyl ketones **36** and β-trichlorotellurovinyl phenyl ketones **37**.⁴ Reduction of the former with lithium triethylborohydride in THF affords ketones **33f,i** in 53%–92% yields; the yields in the latter case were not indicated.



- R = H (**33f**), Ph (**33i**); n = 1 (**36**), 3 (**37**).

This method obviously holds little promise for the synthesis of ketones **33f,i**, since chlorotellurium derivatives **36** are prepared in four steps from α-acetylenecarboxylates,³ and trichlorotellurovinyl ketones are produced upon their oxidation.

Special mention should be made of the unusual course of the reduction of compounds **36** and **37**. Tellurenyl halides⁴⁰ and tellurium trihalides⁴¹ devoid of the coordinative bond O(N) → Te are reduced to the corresponding ditellurides. In the case of the chlorotellurium derivatives **36**, ditellurides **38** are formed in trace amounts, apparently due to the presence of strong intramolecular coordinative bonds O → Te in the starting tellurenyl chlorides.



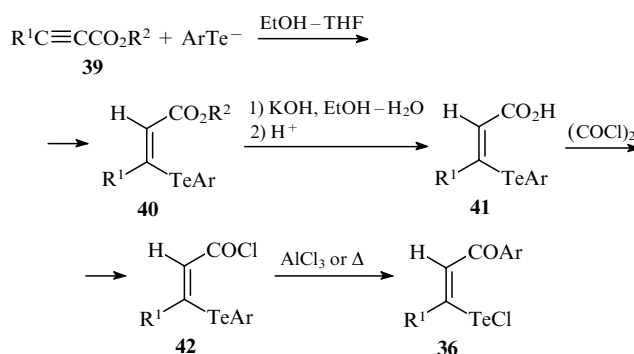
An analysis of the ¹H NMR spectrum of ketone **33f**^{14,15} [a ten-proton multiplet of aromatic protons at δ = 7.24–8.10

and an AX system (two two-proton doublets at δ = 8.36 and 9.14, ³J_{HH} = 9.67 Hz)] prompts a conclusion that the benzoylvinyl fragments of this compound exist in conformations with the *cis*-arrangement of the hydrogen atoms.

5. β-Halogenotellurocarbonyl compounds and their analogues; β-halogenotellurovinyl aldimines

a. Synthesis

Aryl β-chlorotellurovinyl ketones **36** are among the most well-studied β-tellurovinylcarbonyl compounds XTeC(R¹)=C(R²).COR³ where X is an electronegative substituent. They were prepared in four steps starting from α-acetylenecarboxylates **39**.^{3,4,42–44} The first step includes nucleophilic addition of arene telluroate anions generated by reduction of the corresponding diaryl ditellurides with sodium borohydride in EtOH–THF to esters **39**. This leads to methyl(ethyl) 3-aryltelluropropenoates **40** (predominantly, *Z*-isomers) (yields 58%–95%).³ However, ester **40** (R = H, Ar = Ph) is formed as a mixture of *Z*- and *E*-isomers (13 : 1).³ Hydrolysis of esters **40** with KOH and subsequent acidification of the reaction mixture result in β-(aryltelluro)acrylic (**41**, R = H) or β-(aryltelluro)cinnamic acids (**41**, R = Ph) (yields 68%–95%). Treatment of acids **41** with oxalyl chloride gives 3-(aryltelluro)propenoyl chlorides **42**. The latter are rearranged into ketones **36** (yields 31%–96%) on boiling in deuteriochloroform or by treatment with AlCl₃.^{3,4,42–44} Telluraflavones are formed in some cases in addition to ketones **36** (see below).⁴²



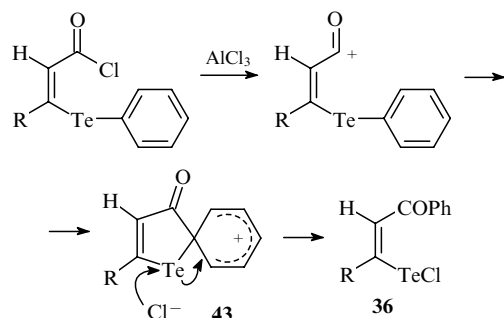
R² = Me, Et.

R ¹	Ar	Yield (%)	Ref.
H	Ph	82	3
Me	Ph	76	3, 43
Me	4-FC ₆ H ₄	—	43
Me	4-MeOC ₆ H ₄	—	43
Me	4-Me ₂ NC ₆ H ₄	31	4, 43
Ph	Ph	81	3, 4
Ph	2-MeC ₆ H ₄	75	3
Ph	3-MeC ₆ H ₄	92	42
Ph	4-MeC ₆ H ₄	92	3
Ph	4-MeOC ₆ H ₄	96	3, 4
Ph	3-FC ₆ H ₄	78	42
Ph	3-MeOC ₆ H ₄	4	42
Ph	4-MeCOC ₆ H ₄	50	3
Ph	1-C ₁₀ H ₇	82	3
4-MeOC ₆ H ₄	Ph	—	4
2,5-(MeO) ₂ C ₆ H ₃	Ph	70	44
4-Bu ^t C ₆ H ₄	Ph	—	4

The rates of both thermal and catalytic rearrangements of compounds **42** are governed by the electronic nature of *p*-substituents in the aryl nuclei.³ Thus in the case of β-(phenyltelluro)cinnamoyl chlorides, compound **42** (R = Ph, Ar = 4-MeOC₆H₄) could not be isolated at all, since it undergoes rearrangement into ketone **36** (R = Ph, Ar = 4-MeOC₆H₄) in nearly quantitative yield even at 20 °C. The half-transformation time of the acid chloride **42** (R = Ph, Ar = 4-MeC₆H₄) in boiling CDCl₃ is 1 h, whereas that for compound **42** (R = Ar = Ph) is 30 h under

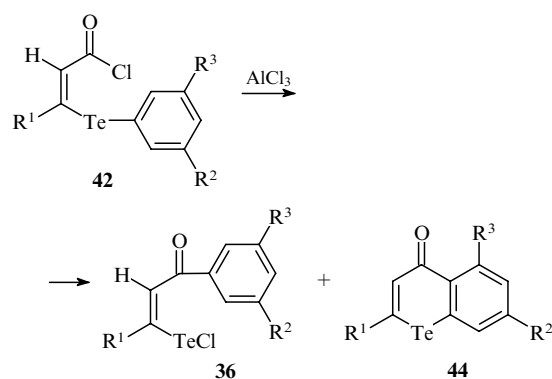
identical conditions. The presence of strong electron-withdrawing substituents (*e.g.*, Ar = 4-MeCOC₆H₄) inhibits almost completely the thermal rearrangement, the yield of ketone **36** (R = Ph, Ar = 4-MeCOC₆H₄) being < 1% on boiling in CDCl₃ for 72 h.

The putative mechanism of the catalytic rearrangements of acid chlorides **42** into compounds **36** involves an attack of the acylium cation on the aromatic carbon atom bound to tellurium (*ipso*-acylation) to yield the spirocyclic σ-complex **43**. Subsequent nucleophilic attack of the chloride ion on the tellurium atom yields ketones **36**.



It should be noted that such rearrangements were first observed for *o*-(aryltelluro)benzoyl chlorides *o*-ClCOC₆H₄TeAr (Ar = Ph, 4-MeC₆H₄, 2-C₄H₃S). Heating of these compounds with ZnCl₂ gave *o*-chlorotelluro)benzophenones *o*-ClTeC₆H₄.COAr in high yields.^{45–47}

The structures of the rearrangement products of aroyl chlorides **42** depend on the position and the nature of substituents in the ArTe fragments. In the case of *p*-substituted β-(aryltelluro)prope-noyl chlorides **42**, the only reaction products are ketones **36**.³ However, the introduction of donor substituents into the *m*-position of aryl substituents results in the activation of the *o*-positions towards electrophilic attack and prevents *ipso*-acylation, which results in either a mixture of ketones **36** and telluraflavones **44** or only the latter compounds.^{42, 44}

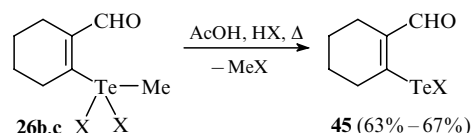


R ¹	R ²	R ³	Yield of 36 (%)	Yield of 44 (%)	Ref.
Ph	Me	H	92	0	3
Ph	F	H	78	5	3, 42
Ph	F	F	—	18	42
Ph	OMe	H	4	78	3
Ph	OMe	OMe	0	90	3
4-MeOC ₆ H ₄	OMe	H	5	44	44
3,4-(MeO) ₂ C ₆ H ₃	OMe	H	5	68	44
2,5-(MeO) ₂ C ₆ H ₃	OMe	H	5	—	44
4-MeOC ₆ H ₄	OMe	OMe	0	52	44
3,4-(MeO) ₂ C ₆ H ₃	OMe	OMe	0	57	44
2,5-(MeO) ₂ C ₆ H ₃	OMe	OMe	0	72	44

The above-described method for the synthesis of ketones **36** has certain limitations: it is a multistep procedure and affords only those aroyl derivatives that are not substituted in the α-position.

A method for the preparation of β-halogenotellurenylvinyl-carbonyl compounds based on the use of β-methyldihalogenotellurovinylcarbonyl compounds **26** is devoid of these drawbacks. Until now, such compounds were mostly employed for the preparation of 2-halogenotellurocyclohex-1-enecarbaldehydes **45**,^{15, 20} they can undoubtedly be used in the synthesis of vinyl-tellurenyl halides containing a broad range of substituents in the carbon triad.

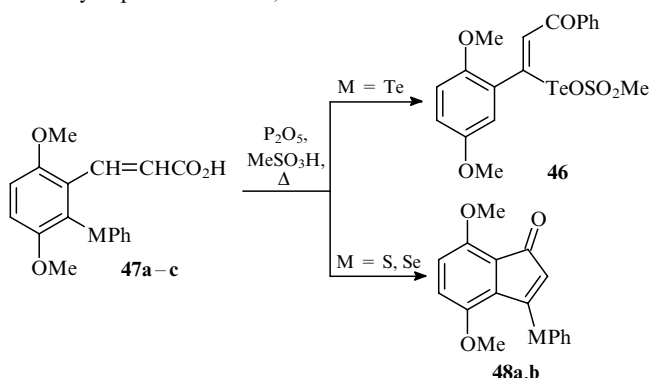
Like 2-formylphenyl(alkyl)tellurium dibromides,⁴⁸ compounds **26** (their syntheses were discussed in Section II.2) undergo reductive elimination of methyl halide upon boiling in acetic acid in the presence of catalytic amounts of the corresponding hydrohalic acids.^{15, 20}



X = Br, I.

It is noteworthy that reductive elimination of methyl halides is extremely sensitive to the admixtures present in the reagents used and is therefore poorly reproducible.

The mesylate derivative **46** is an example of tellurenyl derivatives containing electronegative substituents other than halogen atoms, which has been prepared by direct synthesis.⁴⁴ This compound is an unstable oil; it was synthesised by heating a mixture of β-(phenyltelluro)-2,5-dimethoxycinnamic acid (**47c**), phosphoric anhydride and methanesulfonic acid. It is of note that sulfur (**47a**) and selenium analogues (**47b**) undergo cyclisation into benzocyclopentenones **48a, b** under identical conditions.⁴⁴

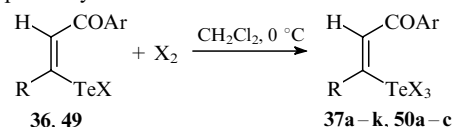


M = S (a), Se (b), Te (c).

b. Reactions

Reactions of (β-halogenotellurovinyl)carbonyl compounds characteristic of the constituent two-coordinate tellurium atom have been studied largely for aryl β-halogenotellurovinyl ketones **36**.

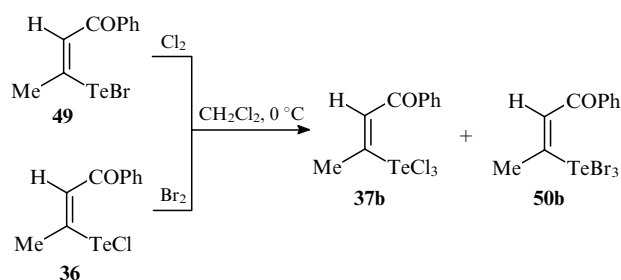
Ketones **36** enter into reduction, oxidation and exchange reactions of chlorine atoms by other anionoid substituents. Aryl β-chlorotellurovinyl ketones **36** and their bromo analogues **49** undergo oxidative addition of chlorine and bromine under mild conditions (CH₂Cl₂, 0 °C) to give aryl β-trichlorotellurovinyl ketones **37a–k** and aryl β-tribromotellurovinyl ketones **50a–c**, respectively.⁴



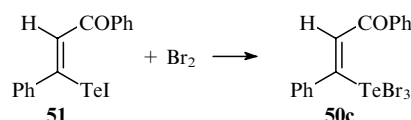
37: X = Cl; R = H, Ar = Ph (**a**, 70%); R = Me: Ar = Ph (**b**, 74%), 4-FC₆H₄ (**c**, 92%), 4-Me₂NC₆H₄ (**d**, 39%); R = Ph: Ar = Ph (**e**, 66%), 3-FC₆H₄ (**f**, 88%), 4-FC₆H₄ (**g**, 88%), 2-MeC₆H₄ (**h**, 82%), 4-MeOC₆H₄ (**i**, 55%); R = 4-MeOC₆H₄, Ar = Ph (**j**, 85%); R = 4-Bu^tC₆H₄, Ar = Ph (**k**, 79%).
50: X = Br; Ar = Ph: R = H (**a**, 52%), Me (**b**, 70%), Ph (**c**, 89%).

Iodine, possessing the weakest (in comparison with other halogens) oxidizing properties, does not oxidise tellurenyl iodides. Thus phenyl β -iodotelluro- β -phenylvinyl ketone ITeC(Ph)=CH.COPh is not converted into the corresponding tellurium triiodide in a reaction with iodine.

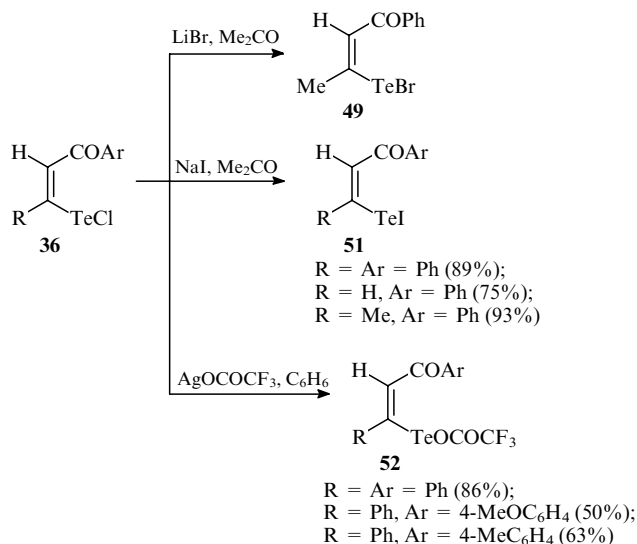
The attempts to prepare mixed tellurium trihalides were unsuccessful. Thus the reaction of tellurenyl bromide **49** ($\text{R} = \text{Me}$, $\text{Ar} = \text{Ph}$) with chlorine gave a mixture of tellurium trichloride **37b** and tellurium tribromide **50b** in a 2:1 ratio, whereas treatment of tellurenyl chloride **36** ($\text{R} = \text{Me}$, $\text{Ar} = \text{Ph}$) with bromine yields a mixture of analogous tellurium trihalides, but in a 1:2 ratio.⁴



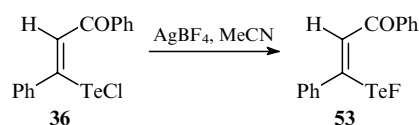
At the same time, the reaction of tellurenyl iodide **51** with bromine results in tellurium tribromide **50c**.⁴



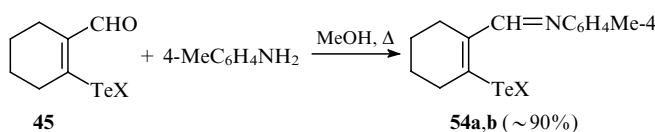
The chlorine atoms in tellurenyl chlorides **36** are highly mobile and readily exchangeable for other anions (Br^- , I^- , CF_3COO^-), which affords the tellurenyl derivatives **49**, **51**, **52** in high yields.³



Quite unexpected results were obtained in the reaction of aryl β -chlorotellurovinyl ketone **36** ($\text{R} = \text{Ar} = \text{Ph}$) with AgBF_4 (see Ref. 3). β -Fluorotellurovinyl phenyl ketone **53** was isolated instead of the expected tetrafluoroborate. Obviously, this reaction results in the decomposition of the complex ion BF_4^- , but the reasons for this decomposition have not been established.

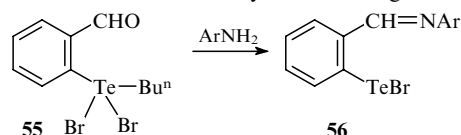


The condensation of aldehydes **45** with aromatic amines (boiling of equimolar amounts of reactants), which affords azomethines **54a,b**, is the only well-studied reaction of (β -halogenotellurovinyl)carbonyl compounds **45** involving the carbonyl group.^{15,20}



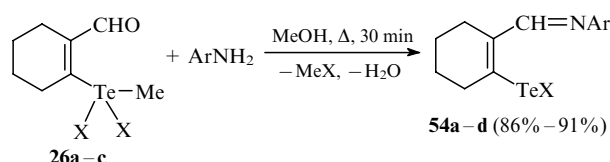
$\text{X} = \text{Br}$ (**a**), I (**b**).

Earlier,¹⁰ it was shown that the reaction of *o*-butyldibromotellurobenzaldehyde (**55**) with aromatic amines is accompanied by reductive elimination of butyl bromide to give azomethines **56**.



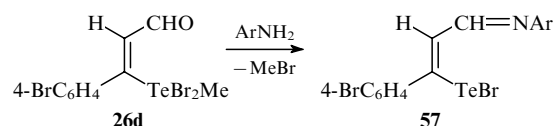
$\text{Ar} = \text{Ph}$, $4\text{-MeC}_6\text{H}_4$, $4\text{-MeOC}_6\text{H}_4$.

2-Methyldihalogenotellurocyclohex-1-enecarbaldehydes **26a–c** and aldehyde **56d** react with aromatic amines in a similar manner. The yields of azomethines **24a–d**, **57** amount to 86%–91%.^{15,20,21}



$\text{Ar} = 4\text{-MeC}_6\text{H}_4$; $\text{X} = \text{Cl}$ (**54a**), Br (**54b**), I (**54c**);

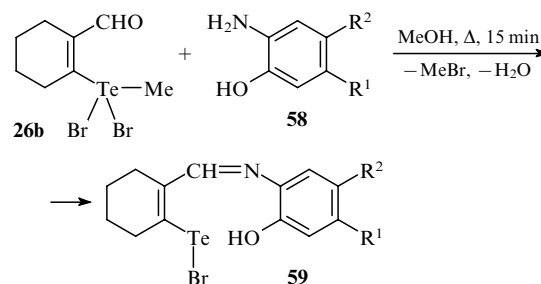
$\text{Ar} = 4\text{-MeOC}_6\text{H}_4$; $\text{X} = \text{Br}$ (**54d**).



$\text{Ar} = 4\text{-MeC}_6\text{H}_4$, $4\text{-MeOC}_6\text{H}_4$.

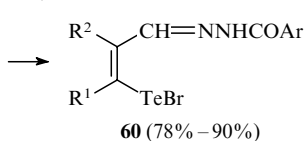
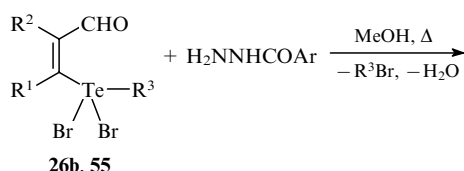
This procedure for azomethine synthesis has certain advantages over those mentioned above, since it excludes the conversion of aldehydes **26** into the tellurenyl derivatives **45**.

o-Aminophenols **58** react with aldehyde **26b** in a similar way: the yields of azomethines **59** vary from 78% to 85%.⁴⁹



$\text{R}^1 = \text{R}^2 = \text{H}$; $\text{R}^1 = \text{H}$, $\text{R}^2 = \text{Me}$; $\text{R}^1 = \text{NO}_2$, $\text{R}^2 = \text{H}$.

Reactions of 2-methyldibromotellurocyclohex-1-enecarbaldehyde **26b** and *o*-butyldibromotellurobenzaldehyde (**55**) with aromatic acid hydrazides proceeds in the same way as with aromatic amines. Short-term (10 min) boiling of equimolar amounts of the reactants results in *N*-aroylhydrazones of 2-bromotellurocyclohex-1-enecarbaldehyde or *o*-bromotellurobenzaldehyde **60**.⁵⁰



$\text{R}^1-\text{R}^2 = (\text{CH}_2)_4$, $\text{R}^3 = \text{Me}$; $\text{Ar} = 4\text{-BrC}_6\text{H}_4$, $4\text{-MeOC}_6\text{H}_4$;

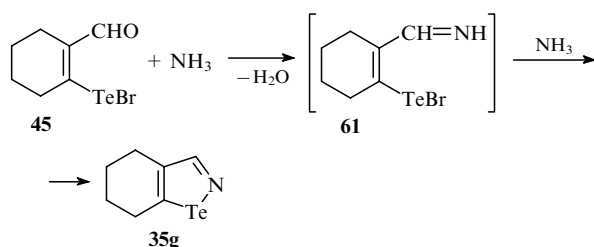
$\text{R}^1-\text{R}^2 = (\text{CH}=\text{CH})_2$, $\text{R}^3 = \text{Bu}$, $\text{Ar} = 4\text{-MeOC}_6\text{H}_4$.

6. Synthesis of tellurium-containing heterocycles

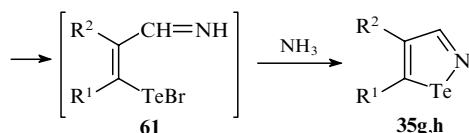
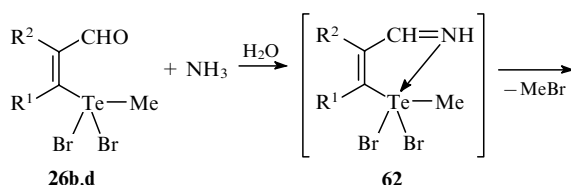
β -Halogenotellurovinylcarbonyl compounds and their aza analogues were used as starting compounds in the synthesis of tellurium-containing heterocycles comprising one or two heteroatoms in addition to the tellurium atom.

a. Isotellurazoles

The synthesis of isotellurazoles **35a–f** by the reaction of α -acetylenic ketones with hydroxylamine-*O*-sulfonic acid and potassium telluride (Section II.4) has significant disadvantages in comparison with other methods due to very low yields of isotellurazoles and the impossibility of obtaining compounds non-substituted in position 3. The procedure for the synthesis of isotellurazole from compounds of the type **45** is devoid of these drawbacks.²⁰ Thus 4,5-tetramethyleneisotellurazole **35g** was prepared in 70% yield by passage of ammonia through a solution of 2-bromotellurocyclohex-1-enecarbaldehyde **45** in benzene. The putative mechanism of this reaction involves the intermediate formation of imine **61**; dehydrobromination of the latter under the action of ammonia yields isotellurazole **35g**.²¹



The synthesis of isotellurazoles from aldehydes **26** as starting compounds is preparatively more convenient, since it excludes the conversion of aldehydes into the tellurenyl derivatives of the type **45**. Passage of ammonia through benzene solutions of tellurium dibromides **26b,d** gave isotellurazoles **35g,h** in ~70% yields.²¹ Allowing for the fact that the reaction of tellurium dibromides **26b,d** with aromatic amines proceeds through elimination of methyl bromide, a mechanism for the formation of isotellurazoles has been proposed.²¹ Its initial step includes the formation of imines **62**, which are further converted into imines **61** by elimination of methyl bromide; their cyclisation into isotellurazoles is described above.

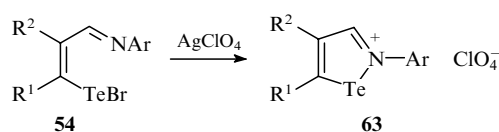


$\text{R}^1-\text{R}^2 = (\text{CH}_2)_4$ (**26b**, **35g**); $\text{R}^1 = 4\text{-BrC}_6\text{H}_4$, $\text{R}^2 = \text{H}$ (**26d**, **35h**).

This method for the synthesis of isotellurazoles is similar to that proposed by Renson for the synthesis of isoselenazoles.⁵¹ However, due to the high thermal stability of tellurodibromides **26** (σ -telluranes of the type $\text{R}^1\text{R}^2\text{TeX}_2$), the respective reactions are carried out at room temperature, while those of less stable selenium analogues should be carried out only at -78°C .

b. *N*-Arylisotellurazolium salts

N-Arylisotellurazolium perchlorates **63** were prepared in 78%–86% yields by treatment of solutions of aldimines **54** in acetone or DMF with the silver perchlorate–acetonitrile complex in acetone.²¹

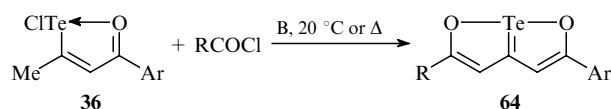


$\text{R}^1-\text{R}^2 = (\text{CH}_2)_4$; $\text{Ar} = 4\text{-MeC}_6\text{H}_4$, $4\text{-MeOC}_6\text{H}_4$;

$\text{R}^1 = 4\text{-BrC}_6\text{H}_4$, $\text{R}^2 = \text{H}$; $\text{Ar} = 4\text{-MeC}_6\text{H}_4$, $4\text{-MeOC}_6\text{H}_4$.

c. 1,6-Dioxa-6a-tellurapentalenes and 1-oxa-6-aza-6a-tellurapentalenes

Aryl β -chlorotelluro- β -methylvinyl ketones of the type **36** were used as starting compounds in the synthesis of 1,6-dioxa-6a-tellurapentalenes **64**.^{6,43} Condensation of these compounds with carboxylic acid chlorides in CH_2Cl_2 or MeCN in the presence of excess of a base (triethylamine, pyridine, 2,6-lutidine) gives heterocycles **64** (yields 11%–85%). This reaction occurs with various (saturated, unsaturated, aromatic, heterocyclic, *etc.*) acid chlorides.



$\text{Ar} = \text{Ph}$; $\text{R} = \text{Me}$, Ph , $4\text{-O}_2\text{NC}_6\text{H}_4$, $4\text{-MeOC}_6\text{H}_4$;

$\text{Ar} = 4\text{-FC}_6\text{H}_4$; $\text{R} = \text{Me}$, Ph , $4\text{-FC}_6\text{H}_4$, $4\text{-O}_2\text{NC}_6\text{H}_4$, $4\text{-NCC}_6\text{H}_4$,

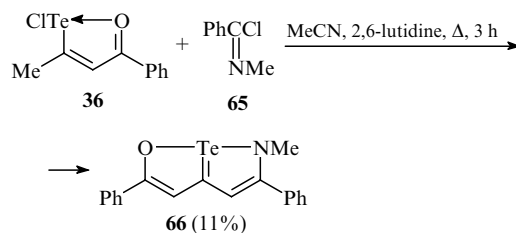
$4\text{-MeOC}_6\text{H}_4$, $2,4\text{-(NO}_2)_2\text{C}_6\text{H}_3$, $3,5\text{-(NO}_2)_2\text{C}_6\text{H}_3$, furyl-CH=CH ,

thiophenyl-CH=CH , $4\text{-MeOC}_6\text{H}_4\text{CH=CH}$;

$\text{Ar} = 4\text{-MeOC}_6\text{H}_4$; $\text{R} = \text{Me}$, $4\text{-O}_2\text{NC}_6\text{H}_4$, $4\text{-MeOC}_6\text{H}_4$;

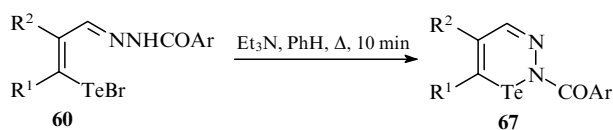
$\text{Ar} = 4\text{-Me}_2\text{NC}_6\text{H}_4$; $\text{R} = 4\text{-O}_2\text{NC}_6\text{H}_4$, $4\text{-NCC}_6\text{H}_4$.

The use of imidoyl chloride **65** instead of acid chlorides has led to 1-oxa-6-aza-6a-tellurapentalene **66**.⁴³



d. 2-Aroyl-1,2,3-telluradiazines

Dehydrobromination of aldimines is the key step in the synthesis of isotellurazoles. A similar approach was used in the synthesis of 2-aryol-1,2,3-telluradiazines **67**.⁵⁰ These heterocycles were synthesised in 76%–82% yields by treatment of benzene solutions of *N*-aryolhydrazones **60** with triethylamine.

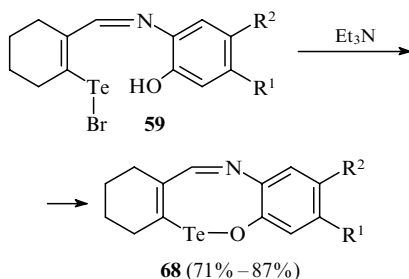


$R^1 - R^2 = (CH_2)_4$; Ar = 4-BrC₆H₄, 4-MeOC₆H₄;

$R^1 - R^2 = (CH=CH)_2$; Ar = 4-MeOC₆H₄.

e. 1,2,6-Oxatellurazocine benzo-derivatives

Benzo-1,2,6-oxatellurazocine derivatives **68** were prepared by dehydrobromination of the corresponding β-bromotellurovinylaldehydes **59** in the presence of an equimolar amount of triethylamine with subsequent short-term boiling of the reaction mixture.⁴⁹



$R^1 = R^2 = H$; $R^1 = H$, $R^2 = Me$; $R^1 = NO_2$, $R^2 = H$.

7. β-Trihalogenotellurovinylcarbonyl compounds

The only available data in the literature concerns aryl β-trihalogenotellurovinyl ketones X₃TeC(R)=CHCOAr (X = Cl, Br).

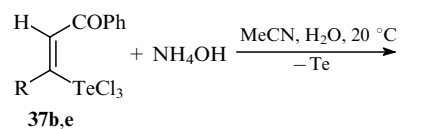
a. Synthesis

The only known method for the synthesis of aryl β-trichlorotellurovinyl ketones **37** and aryl β-tribromotellurovinyl ketones **50**, viz., the oxidative addition of chlorine and bromine to aryl β-chloro- (**36**) and aryl β-bromotellurovinyl ketones (**49**), respectively, is described in Section II.5.b.

b. Reactions

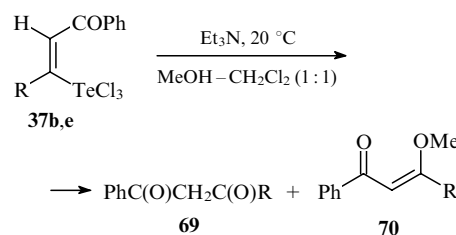
Reactions of aryl β-trihalogenotellurovinyl ketones were studied primarily for the chloro derivatives **37**. The latter are reduced to bis(β-aryolvinyl) tellurides with lithium triethylborohydride and react with various nucleophiles. It should be noted that under the action of hypophosphorous acid as reducing agent tellurotrichlorides **37b,e** are reduced to tellurenyl chlorides **36b,f**.⁴ Of special interest is the striking difference between the structures of the reaction products of aryl β-trichlorotellurovinyl ketones **37** and tellurotrichloride derivatives containing no intramolecular coordinative bonds O → Te with nucleophiles.⁴¹ Reactions of the latter with nucleophiles result in the exchange of anionoid substituents for chlorine atoms or reduction of tellurium trichlorides to ditellurides, no detelluration occurs. The Michaelis addition of nucleophiles to the enone fragment of the ketones **37** proceeds with the elimination of the tellurium atom; sometimes, the trichlorides are reduced to tellurenyl chlorides.

Reaction of tellurium trichlorides **37b,e** with aqueous ammonia yields diketones **69**, tellurenyl chlorides **36** and metallic Te.⁴



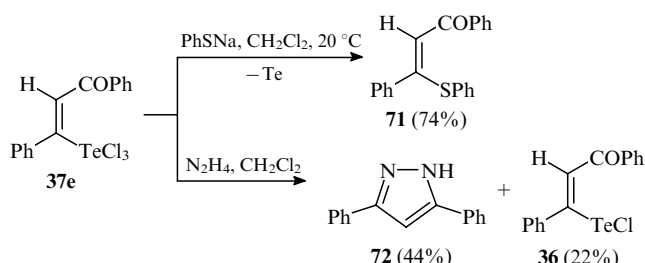
Compound 37	R	Yield of 69 (%)	Yield of 36 (%)
b	Me	56	13
e	Ph	63	36

Ketones **69** and methyl ethers of enols **70** (a mixture of *Z*- and *E*-isomers) are formed in the reaction of tellurium trichlorides **37b,e** with triethylamine.⁴



Compound 37	R	Yield of 69 (%)	Yield of 70 (%)
b	Me	38	56
e	Ph	15	80

The reaction of tellurium trichloride **37e** with sodium benzenethiolate which proceeds with elimination of the tellurium atoms yields the *Z*-isomer of β-phenyl-β-phenylthiovinyl phenyl ketone **71**. The reaction of tellurium trichloride **37e** with hydrazine gives a mixture of pyrazole **72** and tellurenyl chloride **36** (R = Ph).⁴



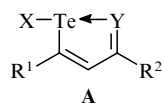
8. β-Methyldihalogenotelluroacroleins

The synthesis of β-methyldihalogenotelluroacroleins was considered in Section II.2. Reductive elimination of methyl halides from these compounds results in β-halogenotelluroacroleins. Reaction with aromatic amines and acid hydrazides yields β-halogenotellurovinylaldehydes (Section II.5.b). The use of β-methyldihalogenotelluroacroleins in the synthesis of isotellurazoles was considered in Section II.6.a.

III. Structures and spectral characteristics of β-tellurovinylcarbonyl compounds

β-Tellurovinylcarbonyl compounds are convenient objects for the study of intramolecular coordinative bonds between O or N atoms and tellurium-containing substituents and the effects of these bonds on the structural and chemical properties of compounds under study.

The molecular and crystal structures of five β-tellurovinylcarbonyl compounds of the general formula **A** have been studied^{3,4,15,31} using X-ray diffraction analysis (Tables 5 and 6).



Compounds containing two-coordinate tellurium atoms (*e.g.*, carbonyl derivatives **1b**, **18c**, **36** and azomethine **20**) possess *Z*-configuration of the C=C bond, which ensures the formation of the intramolecular coordinative bonds O → Te and N → Te. The configuration of the substituents at the Te atom in the above-mentioned compounds can be described as a slightly distorted T-shaped structure, since the value of the angle X—Te—Y is close to 180° (164.4°–170.9°). According to the N-X-L nomenclature,⁵² these compounds represent 10-Te-3-telluranes. The lengths of the C—Te bonds in the two-coordinate tellurium derivatives **1b**, **18c**, **36** and **20** (2.06–2.119 Å) and the values of the bond angles X—Te—C (93.6°–98.5°) are similar to those of other two-coordinate tellurium derivatives.^{8,9,53}

The five-membered tellurium-containing rings in compounds **1b** and **20** are virtually planar; the phenyl rings in these compounds deviate from the planes of the heterocycles by 57.3° and 60.0°, respectively.

In addition to the presence of the intramolecular coordinative bond C=O → Te, the distinguishing feature of the trifluoromethyl derivative **18c**³¹ is the interaction of the carbonyl atom of the ethoxycarbonyl group with the Te atom. However, the length of this bond (3.92 Å) exceeds the sum of the van der Waals radii of O and Te (3.70 Å⁵⁴) and can therefore be neglected in the analysis of the polyhedron of the tellurium atom in this compound.

The coordination polyhedron of the Te atom in tellurium tribromide **50c**, a four-coordinate tellurium derivative, represents a trigonal bipyramid; the intramolecular coordinative bond O → Te is not taken into account.⁴ Here, the tellurium atom, the vinyl fragment and one bromine atom lie in the equatorial plane, while the other two bromine atoms are in the axial positions. The Te—Br_{equiv.} bond (2.513 Å) is shorter than the Te—Br_{ax.} bond (the average length is 2.660 Å). Taking account of the intramolecular coordinative bond O → Te (2.362 Å), the geometry of the bonds at the tellurium atom can be regarded as an octahedron.

In addition to intramolecular interactions, the crystals of compound **50c**, like those of aryltellurium tribromides,⁵⁵ contain the intermolecular bond Te...Br (3.757 Å), which enables binding of individual molecules into polymeric chains.

Apart from bond lengths, the intramolecular coordinative bond O(N) → Te is characterised by the covalence factor (χ), which is calculated by the formula⁵⁶

$$\chi = \frac{(R_A + R_B) - d_{AB}}{(R_A + R_B) - (r_A + r_B)},$$

where *R* and *r* are the van der Waals and covalent radii of the non-bonded elements A and B and *d*_{AB} is the distance between the atoms A and B.

Obviously, the higher the value of χ the shorter the bond.

The Te—Y bond lengths in β-tellurovinylcarbonyl compounds (see Table 5, compound **18c** will be mentioned separately) depend on the nature of the substituent X and increase in the following order: Cl < Br₃ < C₆H₄OEt-4 (for Y = O) ≅ C₆H₄OEt-4 (for Y = NC₆H₄Me-4). Depending on the nature of X, similar changes in the bond lengths corroborated by the results of quantum-chemical calculations^{27–30} were observed in the case of *o*-tellurinated phenylcarbonyl derivatives and (β-halogenotellurovinyl)aldimines.^{7–9}

2-Trifluoroacetylvinyl 2-ethoxycarbonyl ethyl telluride (**18c**) presents special interest.³¹ The intramolecular coordinative bond in this compound (3.22 Å, $\chi = 0.24$) is the longest in the series of organotellurium compounds (*e.g.*, the length of the O → Te bond in aldehyde **1b** is 2.725 Å). The reason for the significant elongation of the O → Te bond in the ethoxycarbonyl derivative **18c** seems to be due to the decrease in the electron density of the oxygen atom of the trifluoroacetyl group which, in turn, is determined by specific electron-withdrawing properties of the trifluoromethyl substituent.

β-Halogenotellurenylvinyl ketones of the general formula RC(TeX)=CHCOAr were studied by ¹²⁵Te NMR spectroscopy (Table 7).^{3,57}

Two main conclusions can be drawn from the data presented in Table 7. First, the chemical shifts of the Te atoms in these halogenotellurium derivatives are primarily affected by the electronegativity of the halogen atom: the higher the electronegativity the more low-field the ¹²⁵Te signal. The nature of substituents at

Table 5. The bond lengths in compounds of the type **A** (in Å).

Compound	R ¹	R ²	X	Y	C—Te	Te—X	C(R ¹)=CH	CH—C(R ²)	C(R ²)=Y	Y → Te	χ	Ref.
1b	Ph	H	C ₆ H ₄ OEt-4	O	2.101	2.124	1.368	1.437	1.219	2.725	0.59	15
18c	H	CF ₃	(CH ₂) ₂ CO ₂ Et	O	2.06	2.14	1.34	1.42	1.24	3.22	0.24	31
36	Ph	C ₆ H ₄ OMe-4	Cl	O	2.08	2.47	1.354	1.425	1.27	2.19	0.95	3
20	Ph	H	C ₆ H ₄ OEt-4	NC ₆ H ₄ Me-4	2.119	2.138	1.336	1.442	1.278	2.771	0.58	15
50c	Ph	Ph	Br ₃	O	2.175	2.513 ^a	1.33	1.47	1.26	2.362	0.83	4

2.660^b

Note. χ is the covalence factor (see text). ^a The Te—Br_{equiv.} bond length. ^b Average length of the Te—Br_{ax.} bond.

Table 6. The values of the bond angles in compounds of the type **A** (in degrees).

Compound	R ¹	R ²	X	Y	X—Te— —C(R ¹)	Te—C(R ¹)= =CH	C(R ¹)=CH— —C(R ²)	CH—C(R ²)= =Y	C(R ²)= =Y → Te	Y → Te— —X	Ref.
1b	Ph	H	C ₆ H ₄ OEt-4	O	98.5	119.4	122.4	123.7	103.2	168.3	15
18c	H	CF ₃	(CH ₂) ₂ CO ₂ Et	O	94.1	126	112	124	—	—	31
36	Ph	C ₆ H ₄ OMe-4	Cl	O	93.6	113.7	118.6	116.8	114.2	170.9	3
20	Ph	H	C ₆ H ₄ OEt-4	NC ₆ H ₄ Me-4	95.6	120.5	125.1	120.7	104.5	164.4	15
50c	Ph	Ph	Br ₃	O	95.0 ^a	114.0	121.1	118.4	111.9	—	4

^a The Br_{equiv.}—Te—C angle.

Table 7. The ^{125}Te NMR spectra of compounds $\text{RC}(\text{TeX})=\text{CHCOAr}$ in CD_2Cl_2 .

R	Ar	X	δ /ppm	Ref.
Me	Ph	Cl	1744 ^a	3, 57
Me	Ph	Cl	1726	50
Me	Ph	Br	1691 ^a	3, 57
Me	Ph	Br	1672	50
Me	Ph	I	1510	3
Ph	Ph	Cl	1697	57
Ph	Ph	Br	1672	57
Ph	Ph	I	1501	57
Ph		Cl	1692	57
Ph		Br	1654	57
Ph	2,5-(MeO) $_2$ C $_6$ H $_3$	I	1484	57

^a Bis(diethylcarbamato)tellurium served as the standard; the $\delta^{125}\text{Te}$ values are given relative to Me_2Te , these are calculated according to the formula $\delta(\text{Me}_2\text{Te}) = \delta[\text{Te}(\text{S}_2\text{CNET}_2)_2] + 833$.

the carbon atoms only weakly affects the $\delta^{125}\text{Te}$ value (the maximum δ value does not exceed ~ 50 ppm).

IV. Conclusion

The data presented in this review suggest that the chemistry of β -tellurovinylcarbonyl compounds has progressed considerably in recent years. This can be exemplified by the development of procedures for the preparative synthesis of these compounds and azomethines prepared from them as well as by studies of the reactivity of β -tellurovinylcarbonyl compounds and the effect of the intramolecular coordinative bond $\text{O}(\text{N}) \rightarrow \text{Te}$ on the reaction features. The use of β -tellurovinylcarbonyl compounds and related aldimines has made it possible to develop preparative procedures for the synthesis of isotellurazoles, *N*-arylisotellurazolium salts and novel tellurium-containing heterocycles, such as 5*H*-1,2-oxatelluroles, 1,6-dioxa-6*a*-tellurapentalenes, 1,2,3-telluradiazines and 1,2,6-oxatellurazocines.

Further investigations in this field will presumably be carried out along the following lines:

1. Synthesis of novel β -tellurovinylcarbonyl compounds (ditellurides, telluronium ylides, tellurimides, telluronium salts).

2. In-depth studies of reactions of β -tellurovinylcarbonyl compounds which have been studied insufficiently even for known compounds.

3. Further studies of possible applications of compounds considered and newly prepared in the synthesis of miscellaneous tellurium-containing heterocycles.

4. Synthesis of complex compounds including metal chelates containing the coordinative site MN_2Te_2 from β -tellurovinyl aldimines.

5. Systemic studies of the effect of the nature of tellurium-containing substituents and donor sites (COR , $\text{CH}=\text{NR}$) on the lengths and stabilities of the intramolecular coordinative bonds $\text{O} \rightarrow \text{Te}$ and $\text{N} \rightarrow \text{Te}$.

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^a — *Russ. J. Gen. Chem. (Engl. Transl.)*

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^c — *Chem. Heterocycl. Compd. (Engl. Transl.)*

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

^e — *Mendeleev Chem. J. (Engl. Transl.)*

Rational design of metal coordination compounds with azomethine ligands

A D Garnovskii, I S Vasil'chenko

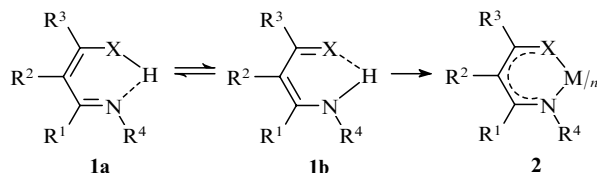
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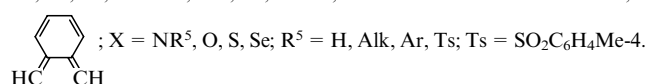
Abstract. This review surveys the state of art in the coordination chemistry of chelating azomethine systems, viz., amino(hydroxy)-azomethines, β -aminovinyl ketones, β -aminovinylimines and their sulfur- and selenium-containing analogues. Variations in the fine structure of azomethine ligands allow one to perform the targeted synthesis of chelate and molecular, mono-, bi- and polynuclear, homo- and heterometallic structures. The bibliography includes 425 references.

I. Introduction

Advances in coordination chemistry are to a large extent associated with the construction of new types of ligand systems. However, there are some well-known rather simple ligands, which can also allow progress in the chemistry of complex compounds relying on the principles of rational design (variation in the fine structure of ligand systems). Among these ligands are, for example, Schiff bases (azomethines) and their structural analogues, which are the 'oldest' ^{1,2} and most studied ^{3–24} ligands in coordination chemistry. The complexes with these ligands have attracted interest for more than 150 years primarily because the nature of substituents in azomethine ligand systems **1** can be varied over a wide range and it is possible to prepare mononuclear metal chelates **2** exhibiting various physicochemical properties and containing coordination units with different geometry.



$R^1, R^2, R^3, R^4 = \text{H, Alk, Ar, HetAr}; R^2 - R^3 = \text{CH}=\text{CH}-\text{CH}=\text{CH},$



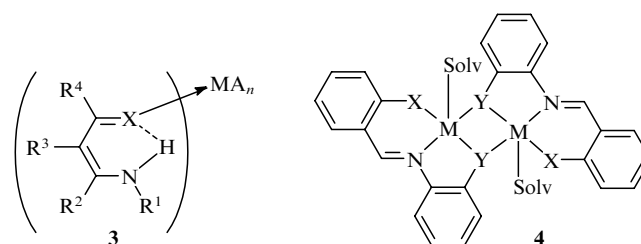
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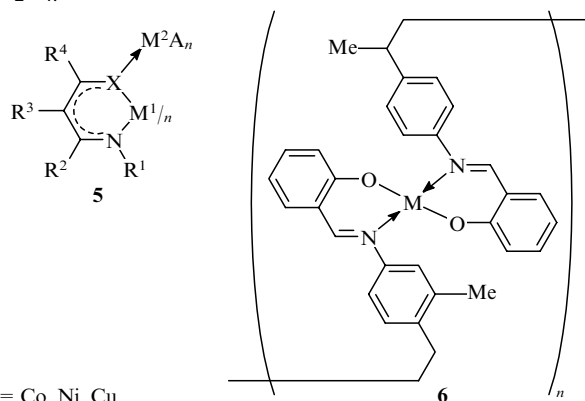
Uspekhi Khimii 71 (11) 1064–1089 (2002); translated by T N Safonova

In earlier reviews ^{2–23} and numerous more recent papers, most attention has been concentrated on azomethine-based chelate compounds. However, not only chelates **2** but also other structural types of metal complexes of chelate-forming azomethines have been much studied. ^{20, 22, 24–33}

Taking into account the classification proposed by one of the authors of the present review, ^{24–26} complex compounds of Schiff bases and their analogues can be divided into the following three types: chelates **2**; molecular complexes **3**; bi- and polynuclear compounds (**4** and **5**) and polymeric structures (**6**).



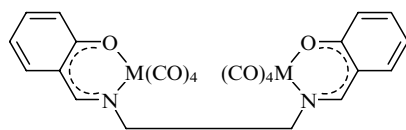
$R^1 - R^4 = \text{Alk, Ar}; X, Y = \text{NTs, O, S}; M = \text{Ni, Cu, Zn},$
 $A = \text{Hal, NO}_3; M = \text{B, Al, Sn, Ti, Zr, Hf, Th, Zn, Cd, Hg};$
 $n = 2 - 4.$



$M = \text{Co, Ni, Cu}.$

All attempts to synthesise the fourth type of complexes, viz., π -complexes, ^{24–26} with azomethine ligands failed because, apparently, of a shortage of complex-forming agents and the lack of procedures for the synthesis, which could be used for the preparation of these (predominantly organometallic ^{24, 34–36}) compounds. However, it should be noted that the reactions of N, N' -bis(salicylidene)ethylenediamine with typical π -complex-forming

agents, viz., metal hexacarbonyls, afforded chelate compounds **7**.³⁴



M = Cr, W.

7

Metal chelates involve deprotonated (anionic) di- or polydentately coordinated azomethine ligand systems. Neutral chelate-forming azomethine compounds **3**, most of which are monodentately coordinated to the metal atom, serve as ligands in molecular complexes. Chelates **4** as well as compounds **5**, which are adducts of chelate compounds **2** and Lewis acids (M^2A_n),^{24,30} and metal-containing azomethine polymers **6**^{31–33} can be assigned to bi- and polynuclear structures.

The present review surveys the data (published predominantly in the last decade) on the synthesis and structures of different types of azomethine metal complexes. Particular attention is given to the choice and modifications of ligand systems (rational design) and procedures for the synthesis of complexes of Schiff bases and their analogues, which are of importance in the preparation of compounds with the desired mode of arrangement of the coordination bond and geometry of the metallocycles as well as in the construction of complexes of different nuclearity and with different degrees of oligomerisation.

II. Azomethine metal chelates

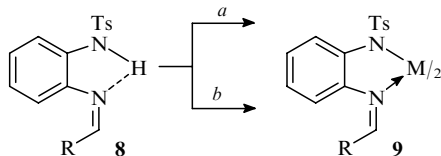
This section is devoted primarily to the employment of azomethine compounds, which have an intramolecular hydrogen bond giving rise to a five- or six-membered coordination unit and contain varying aldehyde and amine fragments, as chelating ligands. Chelate compounds based on these ligands can be prepared by reactions of ligand systems with metal salts as well as with the use of template and electrochemical synthesis methods.²⁴

1. Chelate compounds with five-membered metallocycles

a. Complexes with N,N-donor atoms

Aromatic azomethine chelates containing the five-membered MN_4 coordination unit became available in 1977.³⁷ These compounds are prepared by the reactions of Schiff bases of monotosylated *o*-phenylenediamine with metal acetates (method *a*)^{17,37–39} or metals under the conditions of electrosynthesis. The latter method involves the reactions of zero-valent metals (anode) with ligands in an electrolytic cell equipped with a platinum cathode (method *b*).^{39–43}

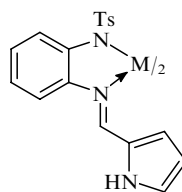
Compounds **8** contain aromatic^{37,38} and heterocyclic^{38–43} fragments as the substituent R.



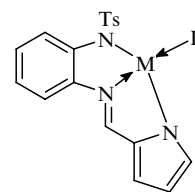
R = Ar, HetAr; M are 3d metals.

(a) $M(OAc)_2$, MeOH, Me_2CO ; (b) M^0 , $-2e^-$, MeCN.

In compounds **9**, ligands containing the pyrrole substituents, which are capable of forming additional coordination bonds, can serve as both bidentate ligand systems **10**^{40,41} and tridentate ligand systems **11**.⁴¹

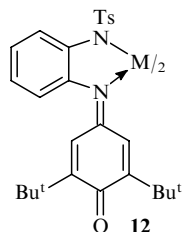


10: M = Zn, Cd.

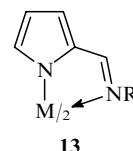


11: M = Co, Ni; L = H_2O .

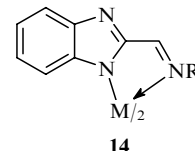
The quinone-imine groups can be involved in chelates **12** containing a five-membered coordination unit.^{44–48}



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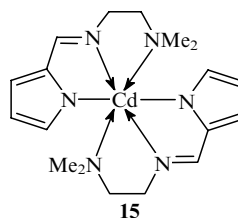


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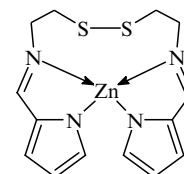


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Complexes with Schiff bases of 2-formylpyrrole **13**^{5,12,20,21,49–55} and 2-formylbenzimidazole **14**^{43,56–60} studied earlier belong to azomethine complexes containing the five-membered MN_4 coordination unit. It should be emphasised that chelates of type **13** were generated under the conditions of chemical^{5,12,20,21} and electrochemical^{49–55} syntheses, whereas chelates **14** were prepared only by the electrochemical method^{56–60} because of the rather low acidity of the N–H bond in benzimidazole. This approach was also employed in the synthesis of chelate compounds **15** and **16** with the use of pyrrole-based aldimine ligands possessing nitrogen-⁵⁵ or sulfur-containing⁶¹ fragments. Tropone imine complexes also contain the MN_4 coordination unit with the azomethine bond.²⁰



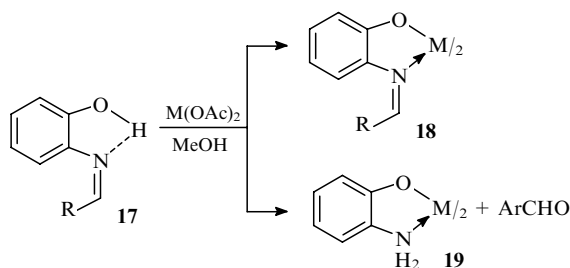
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b. Chelates with N,O-donor atoms

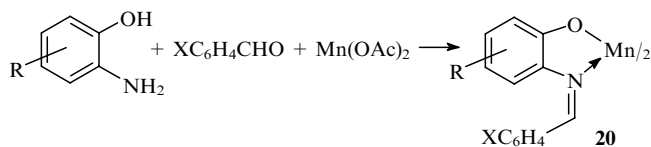
Azomethines **17**, which were derived from *o*-aminophenol and contain an intramolecular hydrogen bond, serve as bidentate ligands and form bicyclic chelate compounds **18** with the five-membered MN_2O_2 coordination unit.^{20,22,25,62,63}



R = Ar, HetAr; M = Cu, Mn, Co, Ni, Zn, Cd etc.

These reactions, particularly those used for the preparation of copper(II) chelates⁶² (**18**, M = Cu), are accompanied by partial hydrolysis of the exocyclic azomethine bond resulting in contamination of chelate compounds **18** with *o*-aminophenol complex **19**. Because of this, copper chelate **18** (R = Ph, M = Cu) was prepared in the presence of an excess of benzaldehyde.⁶²

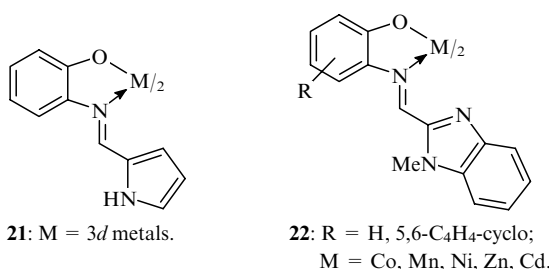
The template synthesis of manganese complexes **20**⁶⁴ is of interest.



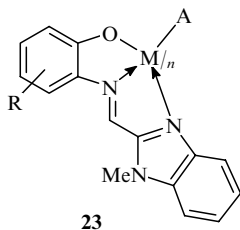
R = H, 4-NO₂; X = H, 2-NO₂, 3-NO₂, 2-MeO, 4-MeO, 4-Me₂N.

The reactions of compounds **17** with acetates of other metals (Co, Ni, Zn, Cd) in methanol afforded virtually pure complexes with composition ML₂.^{20, 22, 24, 65, 66} The exceptions are the palladium chelates PdL₂, which were prepared⁶⁶ from azomethines **17** [R = C₆H₄R¹; R¹ = H, 4-Cl, 4-NMe₂, 2,4-(OMe)₂] in an Me₂CO–MeOH mixture.

Of complexes **18** with varying substituents R, noteworthy are chelate compounds containing heterocyclic fragments, for example **21**^{67, 68} and **22**⁶⁹ prepared by chemical and electrochemical methods.

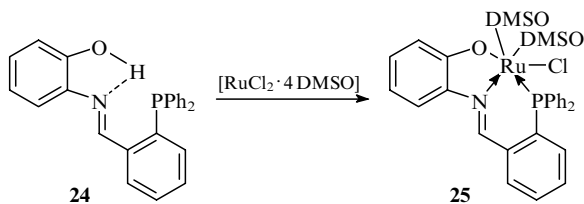


It was proposed (although this assumption was not supported by X-ray diffraction data) that complexes analogous to compounds **23**, which are generated from *o*-aminophenol and heteroaromatic aldehydes, can contain tridentate ligands.⁷⁰



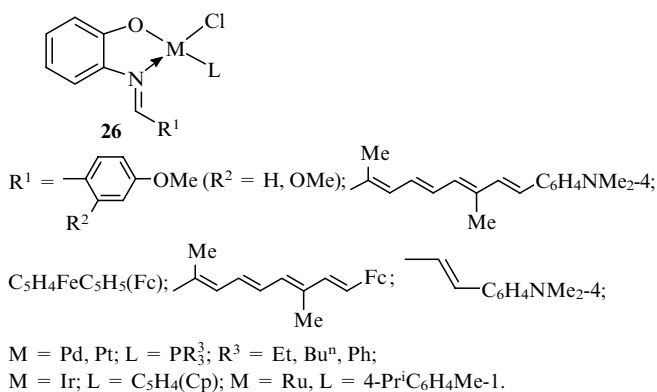
R = H, C₄H₄-cyclo; n = 1, 2; A is absent or is NO₃, OCOMe;
M = Ni, Pb, Th, UO₂.

Compounds **17** whose aldehyde fragments possess substituents capable of being involved in additional coordination can serve as tridentate ligands as well.⁷¹ Thus, the P,N,O-tridentate mode of coordination of the ligand was found in chelate **25**, which was prepared from compound **24** and the [RuCl₂·4DMSO] complex by the ligand-exchange reaction²⁴ in THF and structurally characterised.

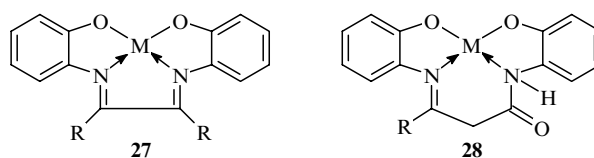


In most cases, bidentate ligands **17** are involved in tetracoordinated complexes with composition ML₂. However, monocyclic chelates **26** of the L¹L²MCl type, which are composed of one monoanion of Schiff bases of *o*-aminophenol, were also synthesised⁷² by the reactions of the corresponding ligands with the

[(R₃P)(Cl)M(μ-Cl)]₂ (M = Pd, Pt), [(η⁵-Cp)(Cl)Ir(μ-Cl)]₂ and [(4-PrⁱC₆H₄Me-I)(Cl)Ru(μ-Cl)]₂ complexes in methanol.

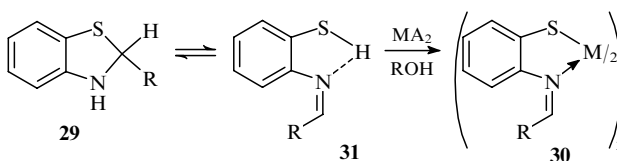


Recently,⁷³ complexes **27** and **28** containing three metallocycles each were prepared by the template synthesis.



c. Chelate compounds with N,S(Se)-donor atoms

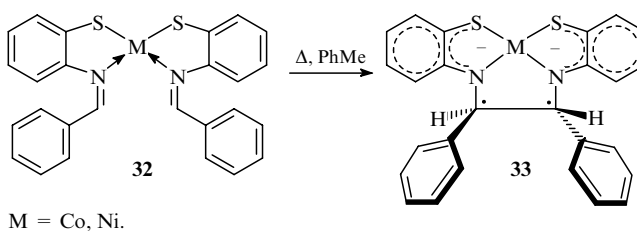
The synthesis of chelates containing the five-membered MN₂S₂ coordination unit involves the well-studied reactions of Schiff bases of *o*-mercaptoaniline with metal salts.^{20, 22, 24, 39, 74, 75}



R = Ar, HetAr, Fc; M = Co, Ni, Pt, Pd, Zn; A is an anion.

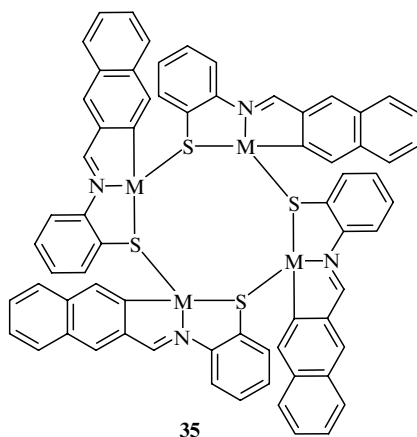
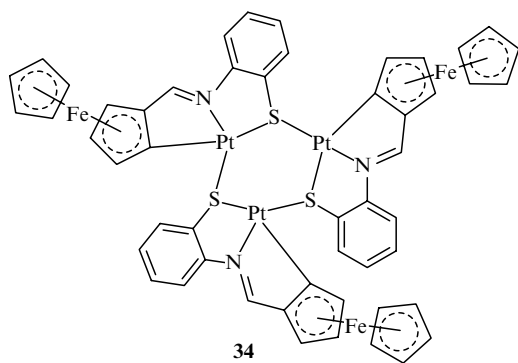
The reactions of Schiff bases of *o*-mercaptoaniline, which occur predominantly in the closed form of 2,3-dihydrobenzothiazole **29**,^{76, 77} with metal salts in alcohols (methanol, ethanol) afforded chelate compounds **30** containing the open deprotonated form of *o*-mercaptophenylazomethine **31** as the ligand system. In these chelates, aromatic^{78–87} or heterocyclic^{39, 69, 75, 88–90} as well as organometallic systems (for example, ferrocene⁷⁴) are most often involved as the substituent R.

Chelate compounds **30** exhibit a specific type of valence tautomerism.^{83, 84} For example, heating of complexes **32** in toluene over a short period of time gave rise to cobalt and nickel 2,2'-bis(1,2-diphenylethylenediimine)benzothiolates **33** through the formation of the C–C bond.

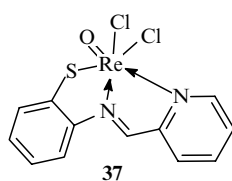
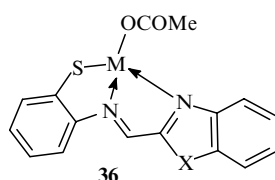


It should be noted that this transformation was not observed for chelates **30** containing the 3,5-di-*tert*-butyl-4-hydroxyphenyl fragments as the substituents R.⁸⁶

In some cases, the reactions afforded tri- (**34**)⁸⁵ and tetrameric (**35**)^{81, 82} structures along with complexes **30**.

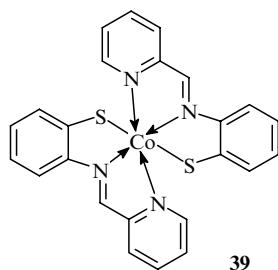
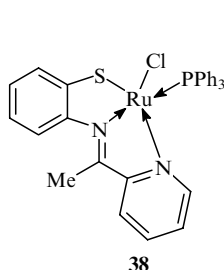


Most of chelates of tridentate azomethine ligands characterised by the N,S-ligand environment are azomethine complexes prepared from heterocyclic aldehydes.^{39, 69, 75, 89–90} Compounds **36** (X = NMe,³⁹ S⁶⁹) serve as examples of this type of chelate compounds.

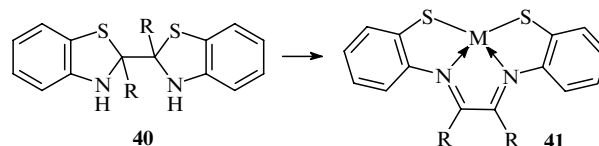


M = Pd, Zn, Cd; X = NMe, S.

2-(2-Pyridyl)-2,3-dihydrobenzothiazole⁸⁹ and 2-methyl-2-(2-pyridyl)-2,3-dihydrobenzothiazole⁷⁵ act as donor ligands of the N₂S type to give complexes **37** and **38**, respectively. 2-(2-Pyridyl)-2,3-dihydrobenzothiazole also serves as the tridentate ligand in tetracyclic chelates **39**.⁹⁰

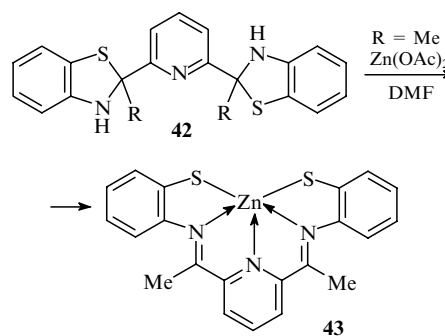


The complex formation involving bis-2,3-dihydrobenzothiazoles **40** gives rise to tricyclic chelates **41** with composition ML, in which mercaptoazomethines act as tetradentate ligands.⁹¹

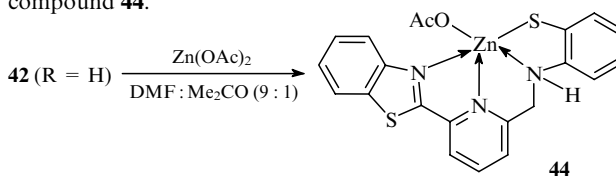


R = H, Me, Ph; M = Cd, Zn, Hg.

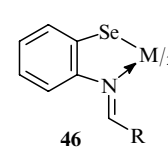
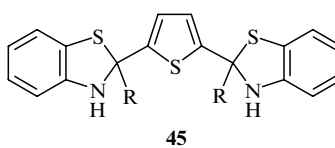
The use of 2,6-dicarbonyl derivatives of pyridine **42a,b** (LH₂ ligands) as the aldehyde (ketone) fragment made it possible to prepare chelates with pentadentate ligands.^{88, 92, 93} The structure of complex **43** was established by X-ray diffraction analysis.⁹²



If the nature of the ligand system in compounds **42** (R = H) and the reaction conditions are changed,⁹⁴ the complex formation is accompanied by a redox process with the resulting changes in the type and denticity of ligand system **42** giving rise to chelate compound **44**.



Apparently, chelate compounds prepared on the basis of 2,5-bis(2,3-dihydrobenzothiazol-2-yl)thiophene derivatives **45**⁹⁵ can also be assigned to five-membered azomethine chelates containing N,S-donor centres.



M = Zn, Cd; R = Ph,

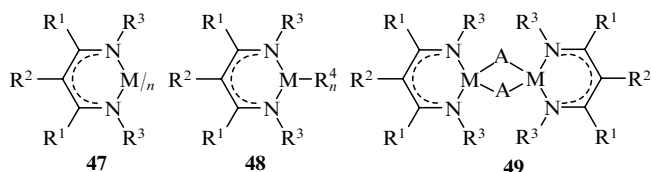
There are only a few complexes **46**, which belong to azomethine chelates containing five-membered metalocycles and the MN₂Se₂ coordination unit. These complexes were prepared by template synthesis from metal *o*-aminobenzeneselenolates and the corresponding aldehydes.⁹⁶

Similar reactions involving the *o*-aminobenzenetellurol chelate compound⁹⁷ afforded metal-free ditelluride rather than a tellurium-containing chelate analogous to complex **46**.⁹⁸

2. Chelate compounds with six-membered coordination units

a. Complexes with N,N-donor atoms

Not only numerous classical bis-β-aminovinylimines **47**^{4, 12, 17, 20, 22, 24, 99–104} but also monoanionic complexes **48**^{101, 105–116} and binuclear structures **49**^{108, 109, 112, 114, 117} are examples of six-membered metal chelates prepared on the basis of bidentate azomethine N,N-donors **1** (X = NR⁵).



A = Hal, OAc.

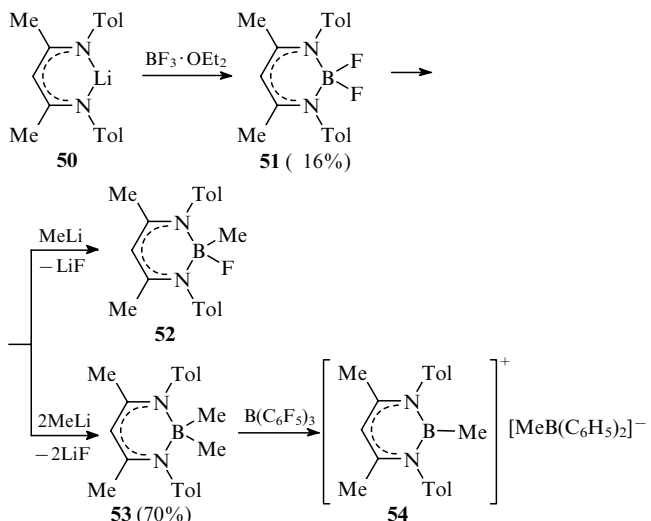
Most of chelate compounds **47** ($n = 2$) typical of β -aminovinylimines were obtained by the reactions of ligands **1** ($X = \text{NR}^5$) with metal salts in alcohols. In this connection, of particular interest is the synthesis of the first structurally characterised tris-diiminate complex **47** ($R^1 = R^3 = \text{Me}$, $R^2 = \text{H}$, $M = \text{Al}$, $n = 3$), which was prepared by the ligand-exchange reaction of 2-methylamino-4-methyliminopent-2-ene with $\text{Me}_3\text{N} \cdot \text{AlH}_3$ in toluene.¹⁰³

First publications on complexes **48** appeared in the mid-1990's. These studies were devoted primarily to the directed synthesis of chelates, in which the metal centre is shielded by bulky substituents, and were aimed at constructing new catalysts of polymerisation and other processes.

β -Aminovinylimines **1** bearing bulky substituents (predominantly, $\text{C}_6\text{H}_3\text{-2,6-Pr}_2^i$) at the nitrogen atom were used for the preparation of this type of chelate compounds with lithium,¹¹³ barium,¹¹⁸ magnesium,^{119–121} boron,¹⁰⁷ aluminium,^{110, 122–124} gallium and indium,¹¹⁰ scandium,^{125, 126} samarium and gadolinium,^{127, 128} ytterbium,¹²⁹ tin,¹³⁰ titanium,^{101, 105, 131} zirconium,^{101, 132, 133} vanadium,¹⁰⁵ chromium,^{105, 134} copper,^{106, 109, 111, 114, 115–117, 135} zinc,^{108, 112, 114} platinum¹¹⁶ and rhodium.¹³⁶

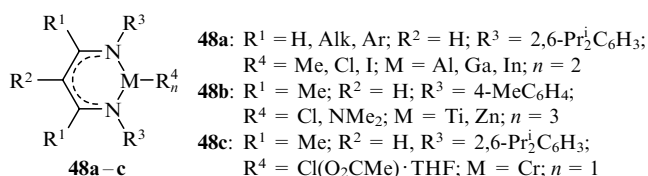
Chelates **48** were synthesised either from lithium complexes **50** (predominantly) or by the reactions of β -aminovinylimines with different complex-forming agents.

Thus, a series of boron-containing complexes of β -diketimines **51–54** were prepared.¹⁰⁷

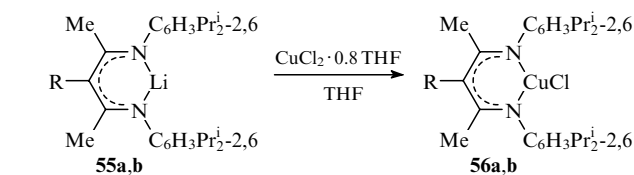


Tol = 4-MeC₆H₄.

Chelate **51**, which was used as the starting compound in the synthesis of complexes **52–54**, was prepared by the reaction of $\text{BF}_3 \cdot \text{OEt}_2$ with lithium derivative **50** and isolated from a solution in toluene. β -Aminovinylimines were used for the synthesis of complexes of aluminium, gallium and indium **48a**,¹¹⁰ titanium and zirconium **48b**¹⁰¹ and chromium **48c**.¹³⁴

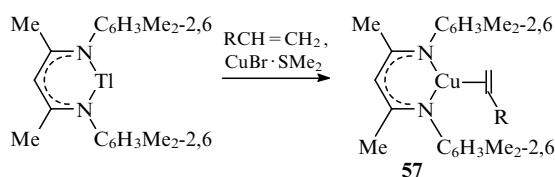


The metal-exchange method was also used for the preparation of copper complexes with β -aminovinylimines.^{109, 111, 115} Noteworthy are the syntheses using lithium salts **55a,b** and the $\text{CuCl}_2 \cdot 0.8 \text{ THF}$ complex,¹¹¹ *i.e.*, procedures combining the metal- and ligand-exchange reactions.²⁴ These reactions afforded mononuclear chelate compounds **56a,b** containing the labile chlorine atom, which can be replaced by the OAr or CNAr groups.¹¹¹

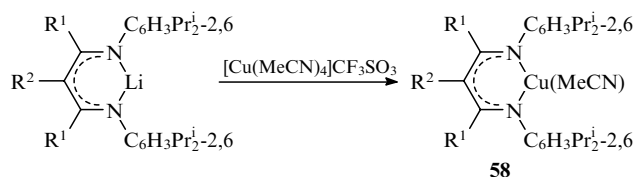


R = H (**a**), Me (**b**).

Monovalent copper chelates **57** and **58** were synthesised analogously.^{109, 115}

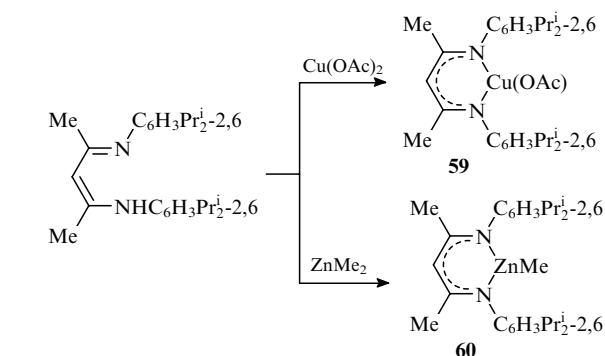


R = H, Ph.

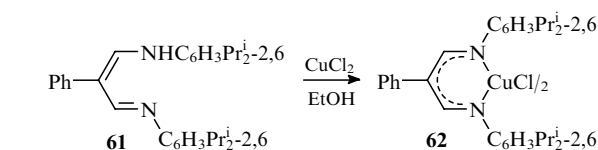


R¹ = H, Me, Bu^t; R² = H, Ph.

Copper chelate **59**¹¹⁴ and zinc chelate **60**¹¹² were synthesised from the corresponding ligands and $\text{Cu}(\text{OAc})_2$ or ZnMe_2 , respectively. The structures of virtually all chelate compounds described above were established by X-ray diffraction analysis.

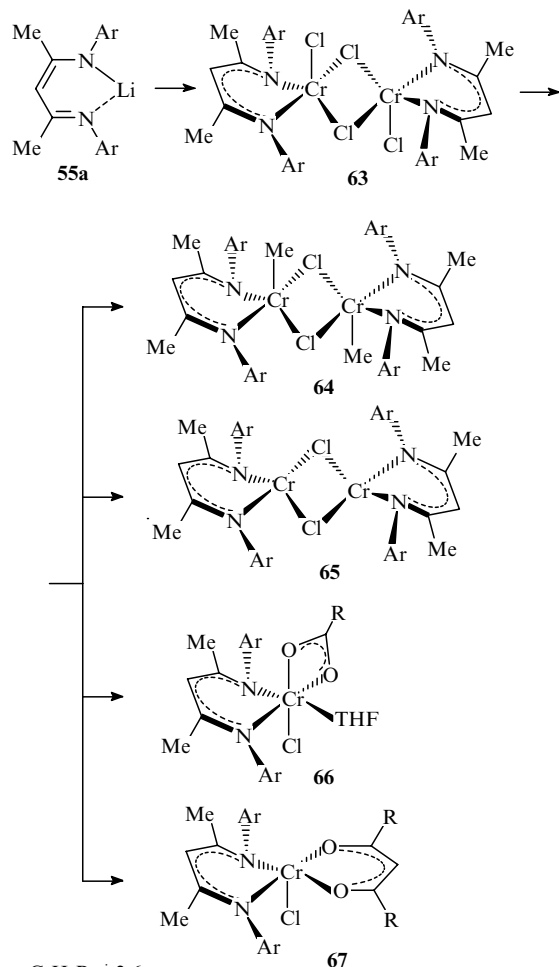


Binuclear complexes **49** were prepared primarily according to analogous methods, *viz.*, by the metal- or ligand-exchange reactions or with the use of a combined procedure. Thus, the reaction of aminovinylimine **61** with copper(II) chloride in alcohol gave rise to copper complex **62**, which was isolated and structurally characterised.¹¹⁷



Lithium complex **55a** was used for the preparation of bridged binuclear zinc chelates **49** ($M = \text{Zn}$; $A = \mu\text{-Cl}$, $\mu\text{-Br}$, $\mu\text{-OAc}$).¹⁰⁸

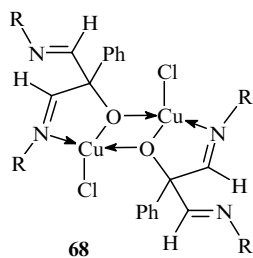
Binuclear complex **63**, which served as the starting compound for the preparation of chromium-containing chelates **64–67**, was prepared by the ligand-exchange reaction of lithium salt **55a** with the $\text{CrCl}_3 \cdot (\text{THF})_3$ complex in THF.¹³⁴



Ar = $\text{C}_6\text{H}_3\text{Pr}_2^{i-2,6}$.

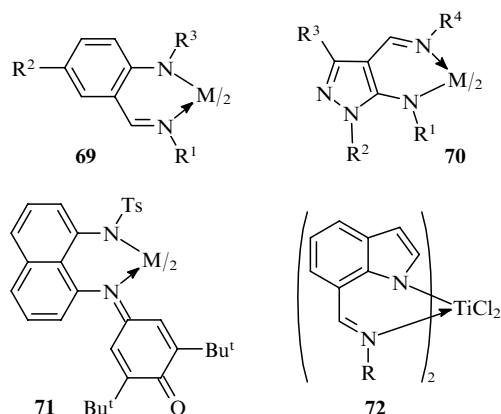
In some cases, binuclear complexes **49** were synthesised with the employment of specific techniques. For example, structures **49** ($\text{R}^1 = \text{Me}$, $\text{R}^2 = \text{H}$, $\text{R}^3 = \text{Ar}$, $\text{M} = \text{Zn}$; $\text{A} = \text{H}$, F , OAc , OH , OMe) were prepared from mononuclear zinc complexes **48** [$\text{R}^1 = \text{Me}$, $\text{R}^2 = \text{H}$, $\text{R}^3 = \text{Ar}$, $\text{M} = \text{Zn}$; $\text{R}^4 = \text{Me}$, Et , $\text{N}(\text{SiMe}_3)_2$] and reagents, which were used for the formation of bridging fragments.^{108, 112, 137, 138}

Recently,¹³⁹ it has been demonstrated that the reactions of β -aminovinylimines with CuCl_2 in alcohols can give rise to dimeric complexes **68** in which the aminoimine ligand is monodentately coordinated to the metal centre.

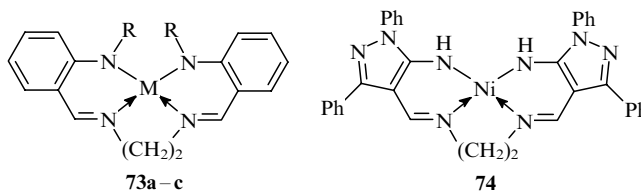


Chelates **69**,^{17, 20, 22, 24, 39, 99, 140–145} **70**,¹⁴⁶ **71**^{45, 147} and **72**¹⁴⁸ take an important place among chelate compounds containing the

six-membered MN_4 coordination unit, which were prepared on the basis of N,N-donor bidentate azomethine ligand systems.



These complexes were synthesised predominantly by the direct reactions of the corresponding ligands with salts (predominantly, acetates) of 3d metals. In some cases, chelates **69** were prepared by template^{140–142} or electrochemical^{39, 143, 144} synthesis methods. It should be noted that azomethines based on N-unsubstituted 2-aminobenzaldehyde and aliphatic (aromatic) monoamines are unstable. Because of this, most of the syntheses were carried out with the use of 2-monotosylaminobenzaldehyde imines as precursors.^{140–145} Complexes **72** ($\text{R} = \text{Ph}$, $\text{C}_6\text{H}_3\text{F}_2$ -2,6, $\text{C}_6\text{H}_3\text{F}_3$ -2,4,6) were prepared by the reactions of the lithium salt of 7-(N-aryliminomethyl)indole with titanium tetrachloride.¹⁴⁸ The Schiff base derived from 2-aminobenzaldehyde and ethylenediamine is quite stable. Hence, this Schiff base and sources of complex-forming metal were used for the preparation of chelate compounds **73a**¹⁴⁹ with tetradentate ligands.

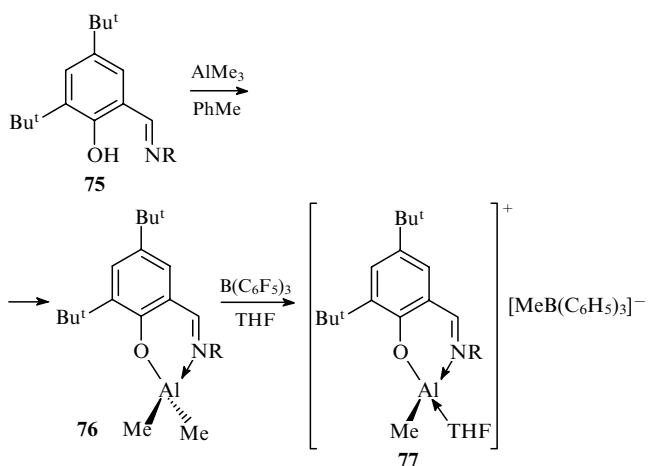


$\text{R} = \text{H}$, Me ; $\text{M} = \text{Ni}$ (a), Cu (b), $\text{FeCl}(\text{Br})$ (c).

Tricyclic chelates **73a**¹⁴⁹ were prepared by the reactions of the corresponding ligands with nickel acetate in methanol. Complexes **73b** were synthesised by the reaction of a suspension of $\text{Cu}(\text{OMe})_2$ in methanol with the ligand. Chelates **73c** were prepared by the reactions of $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$ or FeBr_3 with the corresponding ligands in acetone.¹⁵⁰ The synthesis of nickel complex **74** was described in the study.¹⁵¹

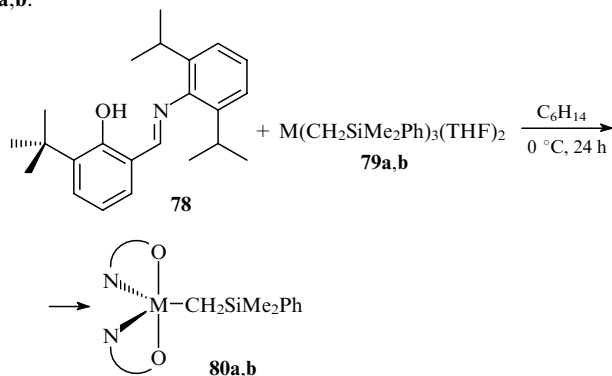
b. Chelate compounds with N,O-donor atoms

Metal chelates of bidentate hydroxyazomethines **1** ($\text{X} = \text{O}$) belong to the best-studied class of chelate compounds containing the six-membered MN_2O_2 coordination unit.^{2, 4, 7, 9–16, 18–25} These compounds still attract interest today. Considerable attention is given to the synthesis and properties of chelate compounds with poorly studied metals, viz., aluminium,¹⁵² scandium and yttrium,¹⁵³ titanium,^{154–156} rhenium¹⁵⁷ and molybdenum.¹⁵⁸ Aluminium(III) chelate compounds were synthesised from azomethine **75** and Me_3Al . These reactions can afford not only neutral chelates **76** but also cationic complexes **77**. The structure of coordination compound **77** was established by X-ray diffraction analysis.¹⁵²



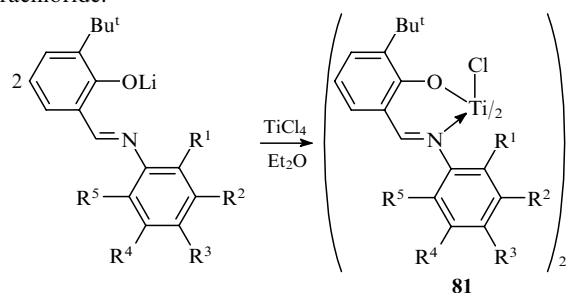
$\text{R} = \text{C}_6\text{H}_3\text{Me}_2\text{-2,6}, \text{C}_6\text{H}_3\text{Pr}_2\text{-2,6}, \text{C}_6\text{H}_3(\text{CF}_3)_2\text{-3,5 etc.}$

The reactions of Schiff bases **78** with organometallic derivatives **79a,b** gave rise to scandium and yttrium chelate compounds **80a,b**.¹⁵³



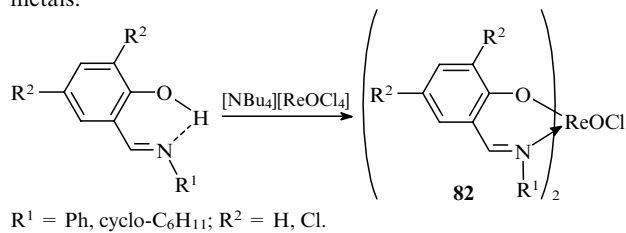
$\text{M} = \text{Sc (a)}, \text{Y (b)}$.

Titanium chelate complexes **81** were synthesised by the metal-exchange method from lithium salts of the ligands and titanium tetrachloride.^{154–156}

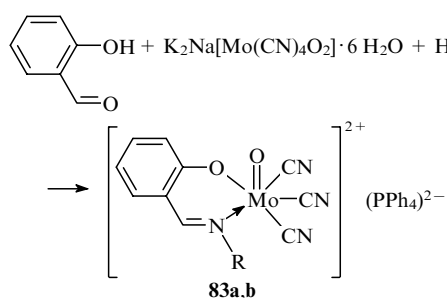


$\text{R}^1\text{--}\text{R}^5 = \text{H, F}$.

Chelates of Re(V) **82**¹⁵⁷ and Mo(VI) **83a,b**¹⁵⁸ were prepared with the employment of unusual sources of complex-forming metals.



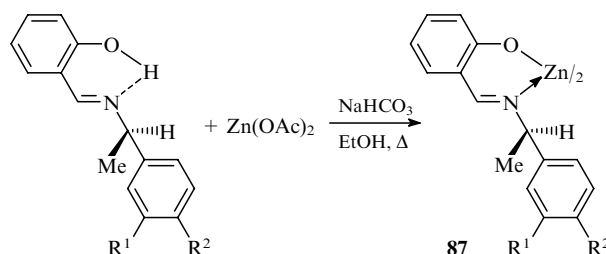
$\text{R}^1 = \text{Ph, cyclo-C}_6\text{H}_{11}; \text{R}^2 = \text{H, Cl}$.



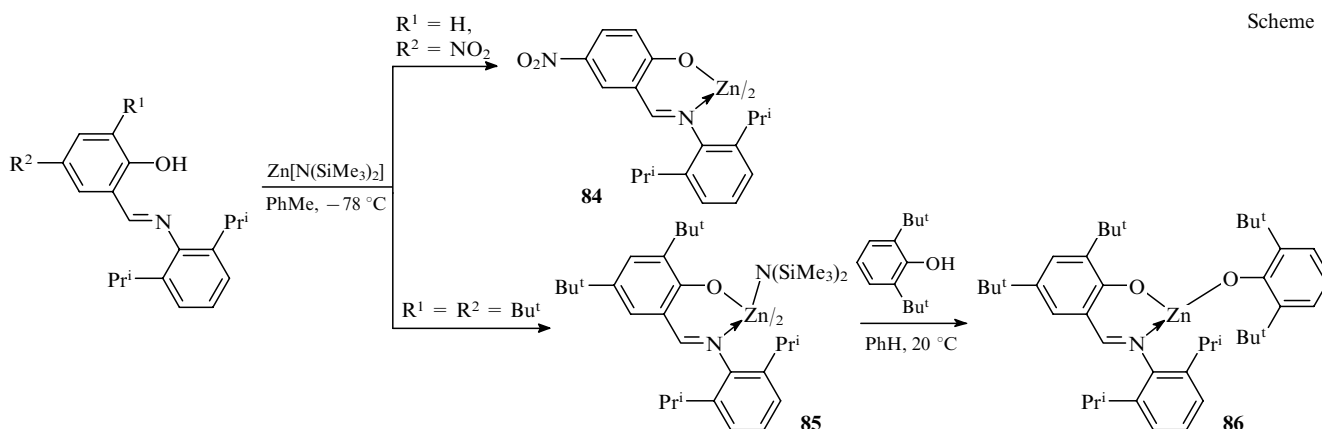
$\text{R} = \text{Me (a)}, (\text{CH}_2)_n\text{NH}_2; n = 2, 3 \text{ (b)}$.

An important line of investigation in the chemistry of complexes with hydroxyazomethine ligands deals with the synthesis and studies of chelate compounds **2** ($\text{X} = \text{O}$) containing various substituents $\text{R}^1\text{--}\text{R}^3$, including fragments annelated to the metalocycle. As an example we refer to the synthesis of zinc complexes **84–86** (Scheme 1).¹⁵⁹

The reactions of azomethines, which were prepared from salicylaldehyde and chiral α -phenylethylamines, with zinc acetate afforded optically active zinc complexes **87**.¹⁶⁰

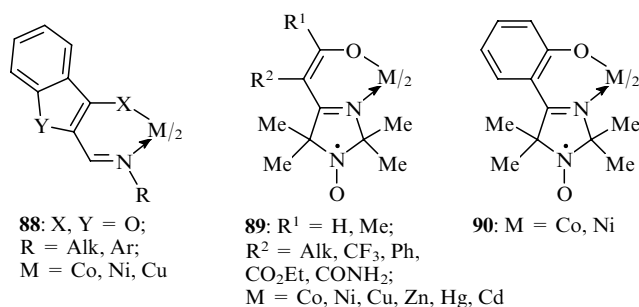


Metal chelates in which heterocyclic fragments are annelated to metalocycles were examined in the studies.^{20,22} For example, benzofuran derivatives of chelate compounds **88** were prepared.^{161,162} Chelates **89** and **90** were synthesised on the basis of β -aminovinyl ketones^{163–168} or *o*-hydroxybenzaldimines^{169,170} and the nitroxyl imidazoline radicals and their magnetic properties were studied. Complexes **89** and **90** were prepared



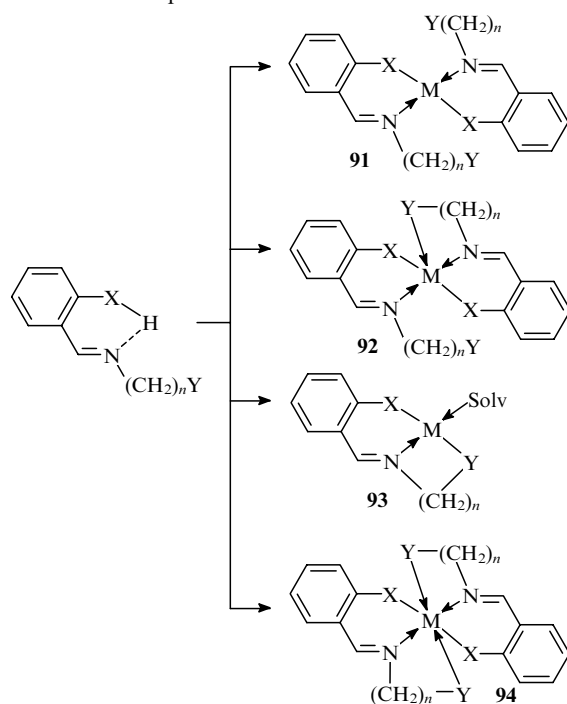
Scheme 1

predominantly from the corresponding ligands and metal acetates in aqueous ethanol.



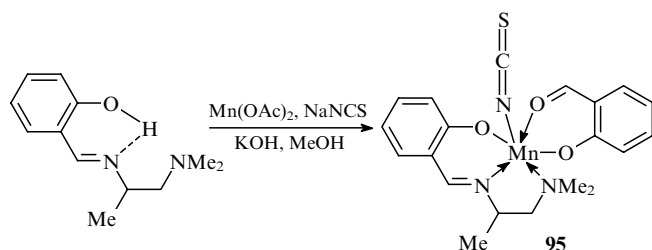
In some cases, *o*-hydroxyazomethine chelates were synthesised by the electrochemical method.^{24, 43, 60, 171, 172}

An increase in denticity of the hydroxyazomethine ligands can be achieved by the introduction of the substituents R containing centres which can be involved in additional coordination, in particular, the alkylamino, hydroxy, alkoxy or alkylthioalkyl fragments as well as their aryl analogues. Such ligand systems are involved in complexes **91–94**.^{12, 24}

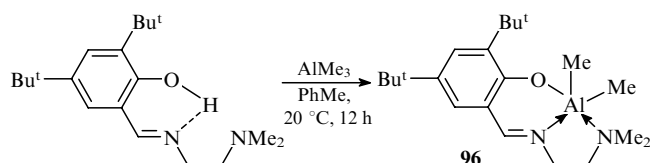


X = O; Y = NR₂, OR, SR; R = H, Alk, Ar; n = 2–4.

Salicylaldehyde-based azomethine complexes have been studied for many years.^{12, 173} In these complexes, additional coordination can occur through the dimethylaminoalkyl substituents. For example, a ligand of this type is present in the structurally characterised manganese chelate **95**.¹⁷⁴

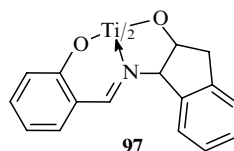


This type of metal binding was observed in complex **96**.¹⁷⁵

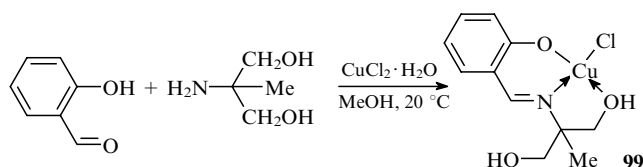
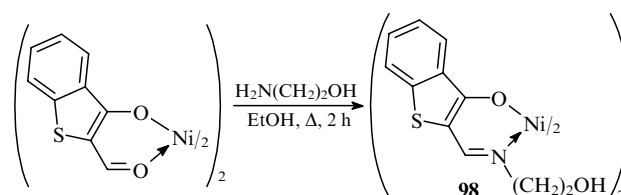


By contrast, X-ray diffraction analysis demonstrated that the nitrogen atom of the aminoalkyl substituent is not involved in additional coordination in molybdenum complexes **83b** synthesised by the template method.¹⁵⁸

Among chelate compounds **91–94**, complexes of salicylide-amino alcohols have received the most study. Early investigations devoted to their synthesis, structures and properties have been surveyed in reviews.^{176–178} Recently, chelate compounds of titanium(IV),¹⁷⁹ vanadium(V),^{180, 181} dioxomolybdenum(VI),^{180, 182, 183} cobalt(III),¹⁸⁴ nickel(II)^{185–187} and copper(II)¹⁸⁶ were prepared and characterised. Titanium complexes of type **93** containing the deprotonated OH groups were synthesised from the ligands and Ti(OPrⁱ)₄.¹⁷⁹ Complexes **93** with vanadium^{180, 181} and molybdenyl^{182, 183} were prepared by the ligand-exchange reactions with the use of acetylacetonates of these metals. As an example we refer to compound **97**.



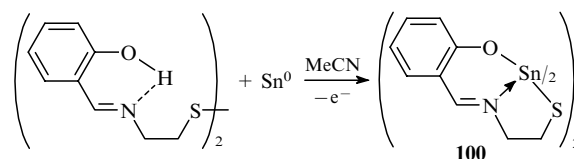
The structures in which the OH groups are retained are typical of nickel (**98**)¹⁸⁶ and copper (**99**)¹⁸⁷ complexes synthesised by the template method.



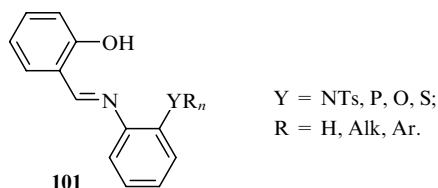
In the fluorine-containing barium β-ketoiminate complexes Ba[CF₃COCH=C(NR)CF₃]₂ [R = CH₂(CH₂CH₂O)₂, (CH₂)₂, (CH₂CH₂O)₂ or CH₂CH(CH₂CH₂O)₃], which were prepared from the corresponding ligands and BaH₂ in a mixture of heptane and THF,¹⁸⁸ the metal atom is coordinated by the oxygen atoms of the alkoxy groups.

Most of the complexes prepared on the basis of mercapto-alkylimines are bi-^{189, 190} or trinuclear.¹⁹⁰ However, Zelentsov and Suvorova¹⁹¹ expected that the mononuclear nickel complex could be isolated.

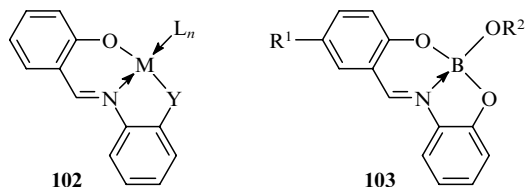
Iminothiol complexes **100** were prepared by the electrochemical cleavage of the disulfide bond.¹⁹²



Salicylideneanilines **101** containing various proton- and electron-donating groups YR in the *ortho* position of the *N*-aryl fragment are very widespread azomethine tridentate ligands.



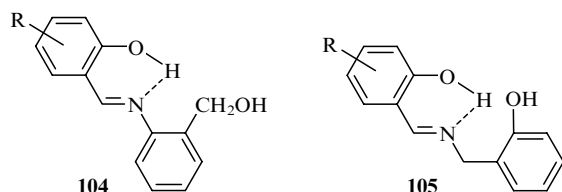
Although most of the complexes prepared on the basis of ligands **101** have binuclear structures (see Section IV), mononuclear chelates (predominantly of type **102**) were prepared with the employment of some complex-forming agents. Thus, mononuclear complexes of boron,¹⁹³ aluminium,¹⁷⁵ tin,^{194,195} rhenium,^{196–198} molybdenum,¹⁹⁹ tungsten,¹⁹⁹ cobalt,^{200–204} nickel,^{201–208} copper^{201,203,207,208} and cadmium^{202,209} are known. A series of chelate compounds under consideration were synthesised by the direct reactions of compounds **101** with different sources of metals, *viz.*, AlMe₃ (in PhMe), tin, nickel, zinc, copper and cadmium salts (in alcohols). Analogously, boron complexes **103** were synthesised by the reactions with B(OR)₃, where R² = Me, Et, Pr or Buⁿ, in a mixture of toluene and THF.¹⁹³



102: Y = NTs, P, O, S; L = Py, bipy, , etc.; n = 1, 2;

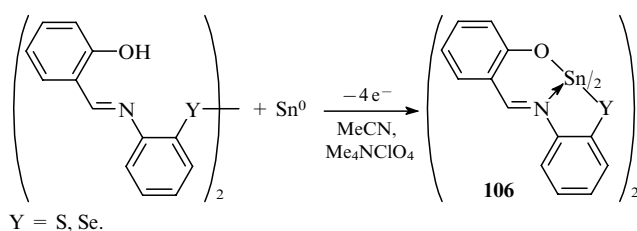
103: R¹ = H, Cl, Br; R² = Me, Et, Prⁿ, Buⁿ.

Oxorhenium chelates **102** (M = ReO) were prepared by the ligand-exchange reactions of [ReOCl₃(PPh₃)₂], compounds **101** and ligands L. In particular, 2-(2-hydroxyphenyl)benzoxazole,^{197,198} 2,3-dihydro-2-(2-hydroxyphenyl)benzothiazole¹⁹⁷ and triphenylphosphines containing the proton-donating group (OH or CO₂H) in the *ortho* position of one of the benzene rings¹⁹⁸ were used as the ligands L. Dioxomolybdenum and dioxotungsten complexes were prepared¹⁹⁹ from Schiff bases **104** and **105** and acetylacetonates of MoO₂ and WO₂, respectively (in MeOH).



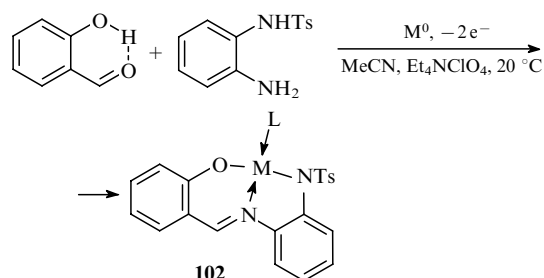
R = H, 5,6-C₄H₄-cyclo.

The electrochemical method is widely employed for the preparation of chelate compounds **102**.^{200–204,207} This method proved to be particularly useful in the case of chalcogen-containing tridentate azomethines. Thus, chelates **106** were synthesised from the corresponding disulfides and diselenides.^{194,210}



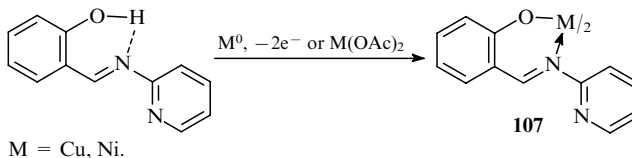
An important advantage of this method is that it allows one to use various N-donor ligands,^{200–208} including ambidentate 1-alkyl-2-aminobenzimidazoles.^{201–204}

Chelates **102**, like other complexes, can be prepared by the template electrochemical method.²⁰²

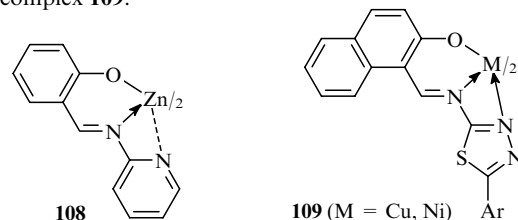


M = Ni, Zn; L = H₂O, MeCN.

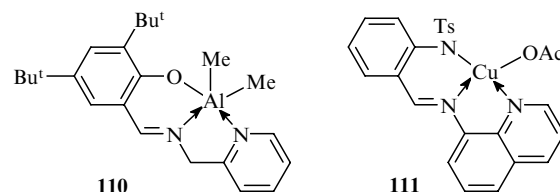
It should be noted that the donor centres Y in azomethines **101**, like those in other compounds containing N-donor fragments at the nitrogen atom,²⁴ are not necessarily involved in coordination to the metal atom. Thus, X-ray diffraction analysis demonstrated that the nitrogen atom of the pyridyl fragment in chelates **107**, which were obtained from the potentially tridentate pyridine-substituted azomethine by the reactions with metal salts or under the conditions of the electrochemical synthesis, is not bound to the metal atom.^{211,212}



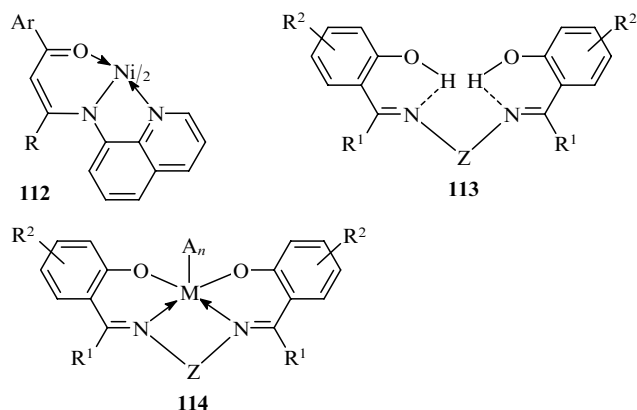
By contrast, X-ray diffraction analysis revealed the Zn–N_{py} interaction (the distance is ~ 2.8 Å) in the analogous zinc chelate **108**.²¹³ It was suggested that additional coordination also occurs in complex **109**.²¹⁴



The difference in the behaviour of the coordinatively active pyridyl substituent in complexes **107** and **108** was attributed to the instability of four-membered metallocycles.²¹⁵ Actually, stable bicyclic chelate compounds with tridentate ligands were obtained under conditions favourable for the formation of five-membered coordination units due to the insertion of the methylene group (complex **110**)¹⁷⁵ or the quinoline substituent (complexes **111**²¹⁶ and **112**²¹⁷).



Bissalicylidene derivatives of aliphatic, aromatic and heterocyclic diamines **113**^{2,9,12,20–22,24,218} serve as tetradentate N,O-donor azomethine ligands, which gave rise predominantly to tricyclic chelates **114**.



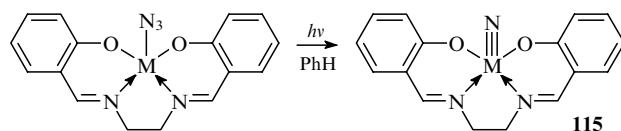
$R^1 = \text{H, Alk}; R^2 = \text{H, Alk, Ar, Hal, NO}_2, \text{OAlk}; A = \text{Alk, Hal};$

$Z = (\text{CR}^3\text{R}^4)_m, \text{Ar, HetAr}; R^3, R^4 = \text{H, Alk, Ar}; n = 0, 1, 2.$

In recent years, chelate compounds **114** with aluminium,^{218–221} gallium,^{218, 222} indium,^{218, 222–225} tin,²²⁶ titanium,²²⁷ manganese,^{228–237} vanadium,^{238, 239} chromium,^{230, 240} molybdenum,²⁴¹ cobalt,^{236, 241} iron,^{231, 236, 241} nickel,^{231, 236, 241, 242} ruthenium,^{243–245} palladium,²⁴⁶ osmium,²⁴⁷ copper^{231, 236, 246, 248–250} and zinc^{251, 252} have been prepared. Aluminium, gallium and indium complexes were synthesised by the reactions of ligands **113** with alkyl and other derivatives of these metals.²¹⁸

Chelate compounds of Group III metals were prepared with the use of a mixture of acetonitrile and THF²²¹ or cyclohexane²²² as the solvent. Tin complexes of the general formula R_2SnL ($\text{R} = \text{Me, Bu}^n, \text{Ph}$) were synthesised in benzene with the addition of triethylamine under an atmosphere of nitrogen starting from the corresponding tin(IV) dichloride and tetradentate Schiff bases derived from salicylaldehyde, 3-methoxysalicylaldehyde, 4-benzoyl-3-methyl-1-phenylpyrazol-5-one, *o*-phenylenediamine and 1,3-propylenediamine.²²⁶

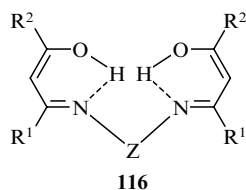
Complexes **114** ($\text{M} = \text{Mn}$: A is either absent²³⁶ or is ClO_4 ,^{228, 233} Cl ,^{229, 231, 237} H_2O ,²²⁹ $\text{M} = \text{Cr}$: A = Cl ²⁴⁰) were prepared from ligands **113** and the corresponding manganese or chromium salts in alcohol. Adducts of bis(salicylidene)ethylenediamine chelates of manganese and chromium with atomic nitrogen (**115**) were synthesised from azido complexes.^{230, 253}



$\text{M} = \text{Mn, Cr}.$

Osmium nitride complexes **114** [$\text{M} = \text{Os}$: $R^1 = \text{H}, R^2 = \text{H, Cl, Me, OMe}; A = \text{N, MeOH}; Z = (\text{CH}_2)_2$] were prepared by the reactions of the corresponding ligand **113** with $[\text{NBu}_4][\text{Os}(\text{N})\text{Cl}_4]$ in MeCN or MeOH.²⁴⁷

The direct reactions of the reagents were used in the synthesis of chelates **114** containing nickel ($\text{M} = \text{Ni}$; A is absent),²⁴² ruthenium ($\text{M} = \text{Ru}$; A = Cl),²⁴⁴ copper [$\text{M} = \text{Cu}$; A is absent; $R^2 = 5-(\text{N}=\text{NPh})$,²⁴⁹ OMe ²⁵⁰] or zinc [$\text{M} = \text{Zn}$; A = THF, Py; $R^2 = 3,5\text{-Bu}^t$, $3\text{-Bu}^t\text{-5-(4-Py)}$; L = Py or absent].^{251, 252} Ruthenium chelate compounds were also prepared by ligand exchange in the $\text{RuCl}_2(\text{PPh}_3)_3$ complex.²⁴⁵ The same synthetic approach

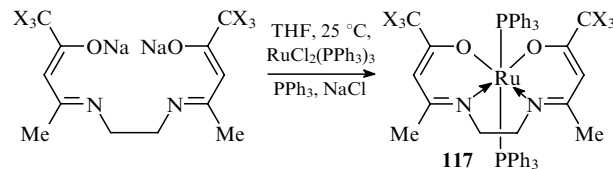


$R^1 = \text{Me, CF}_3; R^2 = \text{H, Me, CMe}_3; Z = (\text{CH}_2)_2, (\text{CH}_2)_3,$

$\text{MeCHCH}_2, \text{CH}(\text{CH}_2)_4\text{CH}.$

was applied in the preparation of chelates of Ru(II) ²⁵⁴ and Ru(III) ²⁵⁵ from bis- β -aminovinyl ketones **116**.

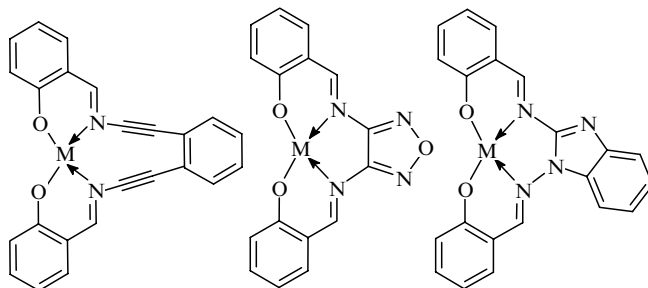
Ruthenium chelate compounds **117** were synthesised by combining the ligand- and metal-exchange reactions²⁵⁴ with the use of the triphenylphosphine complex $\text{RuCl}_2(\text{PPh}_3)_3$ and its arsine analogues $\text{RuY}_2(\text{AsPh}_3)_3$ ($\text{Y} = \text{Cl, Br}$) as the source of metal.²⁵⁵



$\text{X} = \text{H, F}.$

Copper and nickel chelate compounds with ligand **116** [$R^1 = \text{H}; R^2 = \text{C}_6\text{H}_4\text{OMe-4}; Z = (\text{CH}_2)_3, 1,2\text{-C}_6\text{H}_{10}\text{-cyclo}$] were synthesised in methanol with the use of acetates of the corresponding metals.²⁵⁶

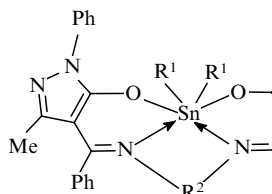
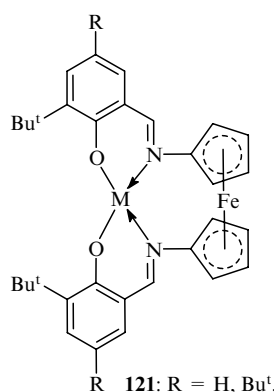
A series of studies were devoted to modifications of ligand systems of type **113** by varying the Z bridge (for example, complexes **118**,²⁵⁷ **119**,²⁵⁸ **120**,²⁵⁹ **121**²⁶⁰ and **122**²⁶⁰) and aldehyde fragment (complexes **123**²²⁶ and **124**²⁶¹).



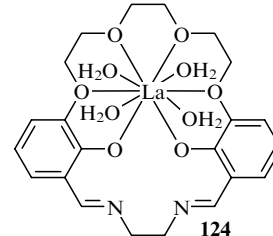
118: $\text{M} = \text{Ni, Cu}.$

119: $\text{M} = \text{Ni, Cu, Co, Zn, Cd}.$

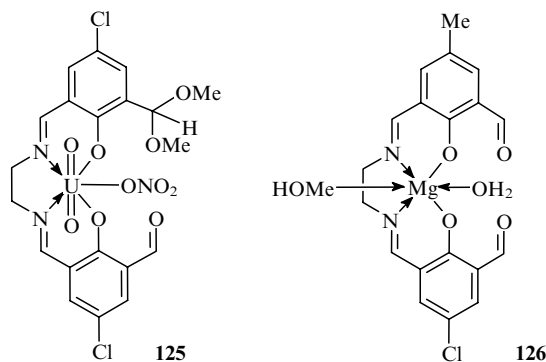
120: $\text{M} = \text{Ni, Cu, Co, Zn, Cd}.$



123: $R^1 = \text{Bu}^n, \text{Ph}; R^2 = (\text{CH}_2)_3, \text{C}_6\text{H}_4\text{-}o.$



It was demonstrated^{262–264} that potentially penta- or hexadentate N,O-donor azomethine systems containing the bis(salicylidene)ethylenediamine fragment, like the above-considered compounds **118–123**, form chelates with tetracoordinated ligands, such as complexes **125**²⁶² and **126**.²⁶⁴ Chelates **117** and **120–125** were synthesised from the corresponding ligands and various metal sources. Complex **118** was prepared by the template method.

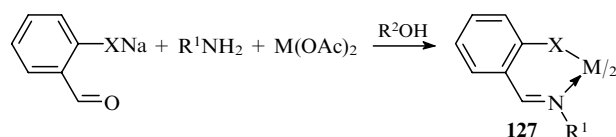


According to the X-ray diffraction data,²⁶¹ the ligand in complex **124** is coordinated through the crown fragment rather than through the azomethine group. It should be emphasised that ligands in complexes **124**–**126** can be considered as ambidentate ligand systems.²⁷ Taking into account that the lanthanum cation is the hardest acid of all the cations involved in these complexes,²⁴ the structure assigned to complex **124** seems to be justified.

c. Chelate compounds with N,S(Se)-donor atoms

In 1968, the template synthesis (method *a*) of metal chelates **127** of sulfur-containing bidentate Schiff bases generated from the sodium derivative of *o*-mercaptobenzaldehyde was carried out by two independent research groups.^{265,266} These compounds were the first representatives of azomethine chelates containing the MN_2S_2 coordination unit.

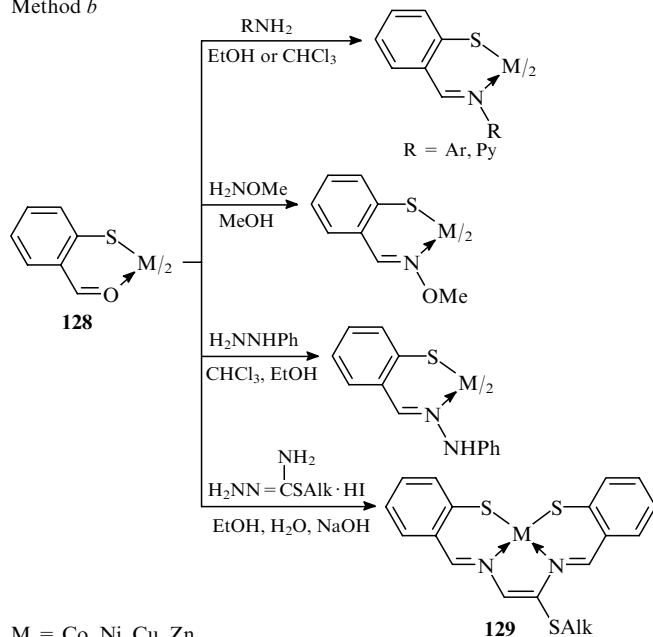
Method *a*



X = S, Se; R¹ = Alk, Ar, AlkO *etc.*; R² = Me, Buⁿ;
M = Co, Ni, Cu, Zn *etc.*

Complexes **127** are also often prepared by the reactions of stable mercaptosalicylaldehyde chelates with amines and their derivatives (method *b*).^{20,24}

Method *b*

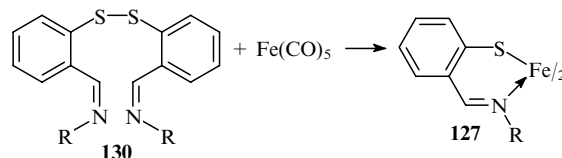


M = Co, Ni, Cu, Zn.

The use of chelates **128** enables one to construct coordination compounds **127** containing various substituents at the nitrogen atom, *viz.*, aryl,^{267,268} pyridyl,²⁶⁹ methoxy²⁷⁰ and phenylamino groups,²⁷¹ as well as alkylthiovinyl-bridged complexes **129**.²⁷²

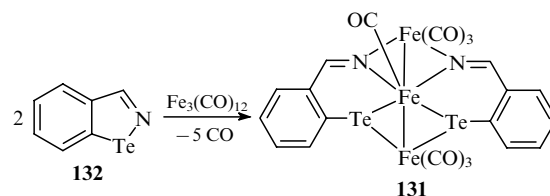
The method *a* is more universal than the method *b* because it allows one to prepare not only chelate compounds **127** containing the MN_2S_2 coordination unit but also complexes of Schiff bases with the MN_2Se_2 chelate unit.²⁷³

Chelates **127** can also be prepared starting from bisazomethine disulfide **130** and iron pentacarbonyl.²⁷⁴

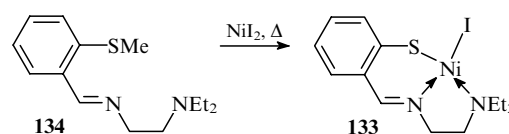


R = C₆H₄OMe-4.

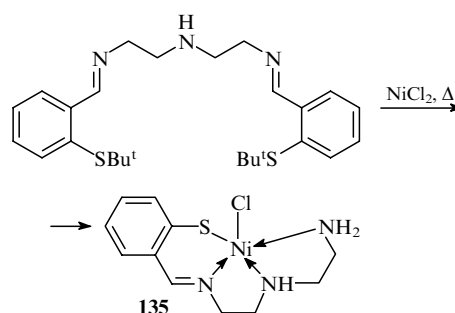
Complex compounds **131** synthesised from benzotellurazole **132** can be considered as tellurium-containing analogues of chelates **127**.²⁷⁵



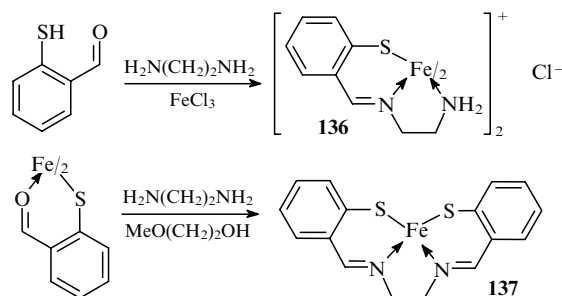
Tridentate sulfur-containing azomethine complexes **133** were first prepared according to an original procedure employing the reactions of nickel iodide with Schiff base **134**.²⁰

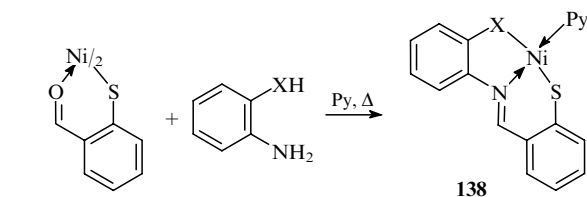


Tetracoordinated nickel complexes **135** were synthesised analogously.²⁷⁶



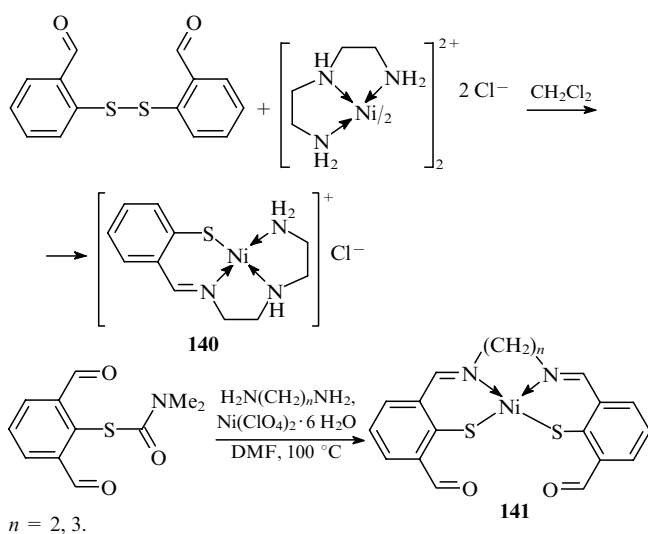
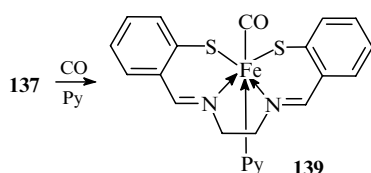
Complexes **136**,²⁷⁷ **137**²⁷⁴ and **138**²⁷⁸ were constructed by the template method.



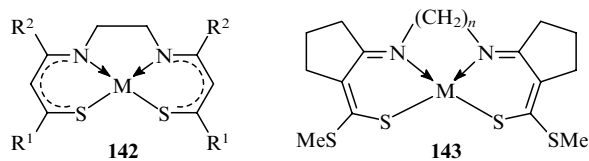


X = NTs, O, S.

The template synthesis²⁷⁹ was used for the preparation of chelates of tetradentate N,S-donor azomethine ligands **139**,²⁷⁴ **140**²⁸⁰ and **141**.^{281, 282}

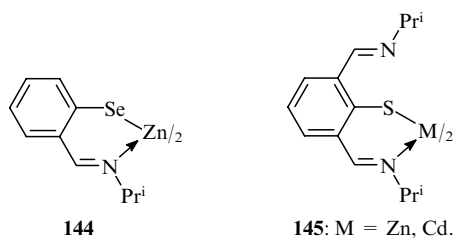


The synthesis and structures of the structural analogues of these chelate compounds, *viz.*, chelates **142** and **143**, were described in the studies cited in review²⁰ and monograph.²⁴

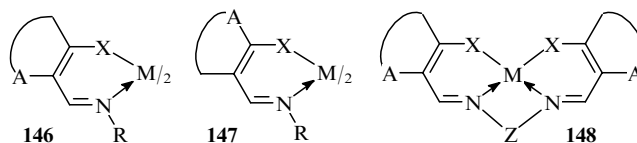


M = Co, Ni, Zn;
R¹ = Alk, Ar; R² = H, Alk.

Let us emphasise that the rational design of chelate compounds of azomethine N,S(Se)-donors is of fundamental importance in the synthesis of complexes with selenium-containing ligands (for example, **144**²⁸³) or complexes **145**²⁰ containing alterdentate ligands, which are difficult to prepare.^{284–286} The latter complexes play an important role in studies of the stereo-dynamics of tetracoordinated azomethine structures.²⁸⁶



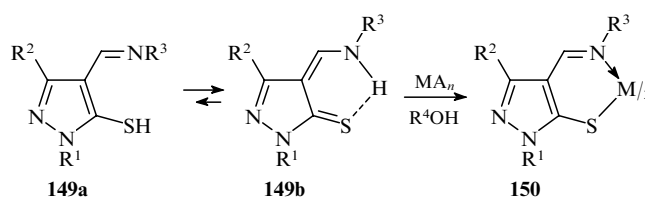
Investigations of the synthesis, structures and properties of chelate compounds of heteroaromatic Schiff bases containing N,S(Se)-donor centres **146–150** were started in the late 1960s–early 1970s.^{8, 161, 287–290}



A = O, S; X = S, Se; M = Co, Ni, Cu, Zn.

These complexes have still attracted attention in subsequent years.^{20, 22, 24, 267, 269, 291–307}

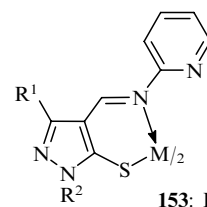
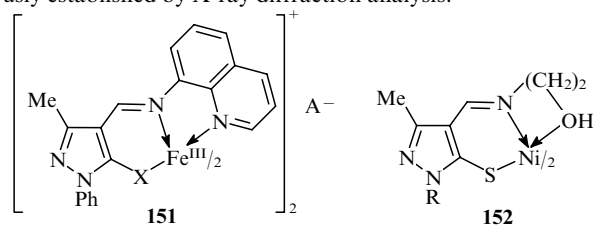
Azomethines derived from thio-substituted heterocyclic aldehydes (for example, compound **149a**), which exist in the thione-amine form **149b**,⁷⁷ are more stable than their aromatic analogues. Because of this, chelate compounds **150** are synthesised primarily by direct reactions of the corresponding ligands with metal salts.²⁴



In some cases, chelates of type **88** (X = S, Y = O) were prepared by template synthesis.¹⁶¹

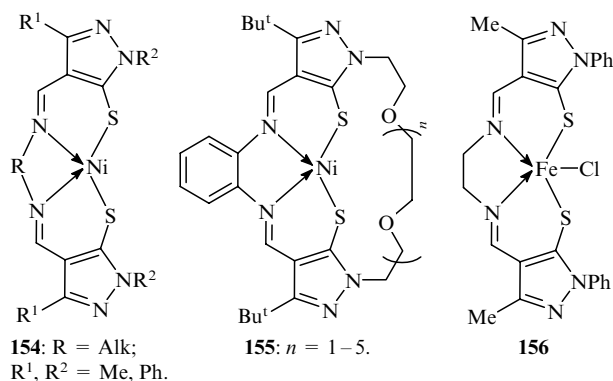
Of the chelate compounds under consideration, complexes **150** containing the pyrazole fragment annelated to the metallo-cycle deserve most attention.^{20, 288–307} In these complexes, *d* metals (Co, Ni, Pd, Cu, Zn, Cd, Hg) act as complex-forming agents.²⁰ The synthesis of copper complexes of this type has presented substantial difficulties for many years. The first representative of these complexes (**150**, M = Cu; R¹ = Prⁱ; R² = Me, R³ = 2-Py) was prepared as late as 1992.²⁶⁹ Later on, these chelates became readily available.^{299–301, 303–307}

Some chelate compounds with tridentate ligands **149** [R³ = (CH₂)₂OH,^{185, 308} 2-pyridyl,^{269, 294, 309} 8-quinolyl^{298–300}] were synthesised. The structure of compound **151** was unambiguously established by X-ray diffraction analysis.²⁹⁸

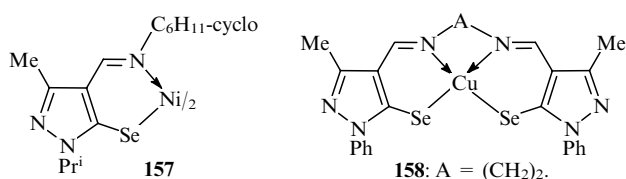


The coordination of the oxygen atom of the hydroxy group to the metal atom is observed in complex **152**.¹⁸⁵ By contrast, the potentially tridentate pyridine-containing ligand in compound **153** is in fact (according to the X-ray diffraction data) bidentate.^{269, 292, 294}

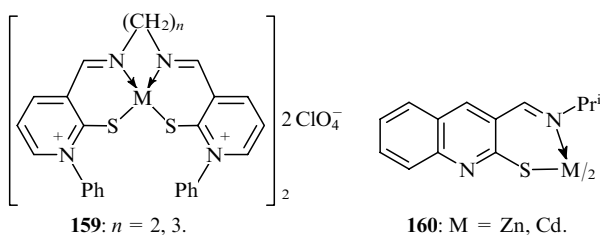
Nickel complexes of **154**²⁹⁶ and **155**²⁹¹ and iron complex **156**²⁹⁸ can be cited as examples of chelates with tetradentate N,S-donor ligands. These chelates were synthesised by the reactions of the corresponding ligands with metal salts [Ni(OAc)₂, MeOH; FeCl₃, EtOH].



Examples of heteroaromatic azomethine chelates containing the six-membered MN₂Se₂ coordination unit are known, among which are complexes of nickel **157**³⁰⁹ and copper **158**.³⁰⁴



In conclusion, it should be noted that in searching for azomethine ligands on the basis of heterocyclic aldehydes, researchers were oriented primarily to five-membered heterocycles, *viz.*, furan, thiophene, their benzo analogues and azole systems. However, chelate compounds, such as complexes **159**³¹⁰ and **160**,³¹¹ can also be synthesised.



These complexes contain Schiff bases as chelating ligands, which were prepared from six-membered azine heteroaromatic aldehydes.

Chelates **160** are of importance in the investigation of the problem of the stereochemical non-rigidity of azomethine metal complexes.^{285, 286}

3. Structures of azomethine metal chelates

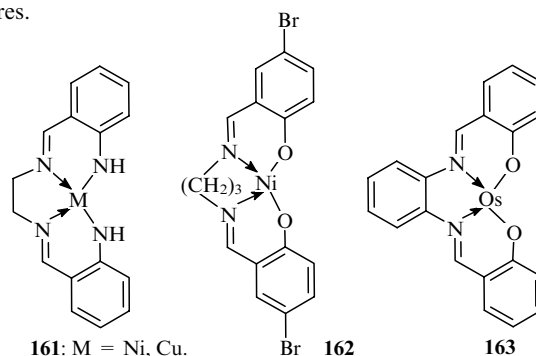
The structures of most of the above-considered chelates were unambiguously established by X-ray diffraction analysis. The detailed discussion of X-ray diffraction data is beyond the scope of the present review. Let us only briefly consider the structural aspects of the directed construction of azomethine metal chelates of a desired stereochemistry by varying the fine structure of ligand systems and electronic configuration of complex-forming metals.

Although data from X-ray diffraction analysis are available only for a limited number of five-membered metal chelates formed by bidentate Schiff bases, they provide evidence that chelate compounds containing the MN₄ or MN₂O₂ coordination units are tetrahedral.^{20, 22, 24, 65} Metal chelates containing the MN₂S₂ coordination units (M = Ni, Pd) have planar structures with a *cis* arrangement of the ligands.^{79–86, 312}

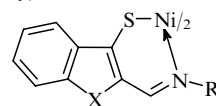
The structures of azomethine chelate complexes containing six-membered metallocycles and the same set of donor centres were studied in more detail.^{2, 4, 12, 14, 20–22, 313–319} It was demonstrated that tetrahedral or distorted tetrahedral polyhedra are typical of chelate compounds containing the MN₄ coordination unit (M = Co, Ni, Cu).^{17, 20, 24}

Most of complexes with the MN₂O₂ coordination unit (M = Ni, Cu) have planar structures with a *trans* arrangement of the ligands.^{12, 20, 21, 24, 313–315} Palladium complexes are characterised exclusively by the square-planar coordination.²¹ The tetrahedral coordination is observed in all beryllium complexes³¹⁷ and in most cobalt,³¹⁶ zinc, cadmium and mercury complexes.^{285, 286} Chelate compounds of *d*⁸ elements containing the MN₂S₂ coordination unit have *cis*-planar structures.^{20, 22, 24, 25} These structural features of chelate azomethine complexes have been discussed in the literature many times, including from the viewpoints of the mutual effect of metals and ligands²¹ and stereochemistry of metal chelates of the ML₂ type.³²⁰

Most alkylene- or arylene-bridged chelate compounds with tetradentate bisazomethine ligands have planar tricyclic structures. In addition to the above-discussed bis(salicylidene)ethylenediamine chelates characterised by X-ray diffraction analysis, complexes **161**,¹⁵⁰ **162**³¹⁸ and **163**³¹⁹ also have analogous structures.



The coordination units in chelates of the MN₄, MN₂O₂ and MN₂S₂ types adopt a tetrahedral configuration as a result of annelation of heteroaromatic fragments to metallocycles.^{20–22, 24} For example, these structures are typical of benzofuran- and pyrazole-based azomethine chelates (**164a** and **150**, respectively).²⁰



164a,b: X = O (**a**), S (**b**); R = Buⁿ, Ph.

A substantial flattening of the structure is observed on going from azomethines of the benzofuran series **164a** to azomethines of the benzothiophene series **164b**.²⁰

When examining the dependence of the stereochemistry of azomethine chelate compounds of type **2** on the nature of the substituent R⁴, the effects associated with the volume of this substituent or with the presence of additional donor centres are generally considered. The former effect causes primarily steric distortions of the polyhedra.^{12, 21} The latter effect leads to an increase in the coordination number of complex-forming metal from 4 to 5 or 6.^{22, 24, 25} Relying on these notions, the directed synthesis of complexes with the desired geometry of the coordination unit can be carried out.

Since the steric effects of the substituents at the nitrogen atom (R⁴) have been discussed in sufficient detail,^{12, 20, 21, 24} we will consider only some examples of these effects on the structures of azomethine chelates **2**.

In the crystalline state, nickel chelates **2** (M = Ni; R⁴ = H, Alk, Ar) have square-planar or distorted tetrahedral configurations depending on the volume of the R⁴ substituent,^{21, 313} whereas the complex configurational equilibria including planar, tetrahedral and octahedral (intermolecularly associated) structures, were observed in solutions of these chelate compounds.²¹ Distortions of the tetrahedral structures in copper chelates of type **2**, which are caused by substituents at the nitrogen atom exhibiting different steric effects, were unambiguously established by X-ray diffraction analysis. However, there is no consensus of opinion on the

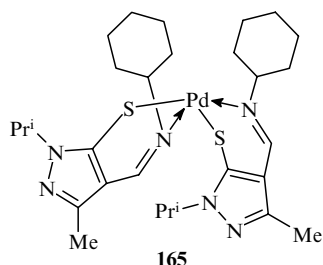
structures of these complexes in solution (*cf.* Ref. 21). It is believed that square-pyramidal or distorted tetrahedral configurations as well as square–tetrahedron equilibria can occur in solution.

The influence of the nature of the substituents at the nitrogen atom, which are able to form additional coordination bonds, on the structures of complexes **2** has been the subject of investigation over the past 40 years. The presence of these substituents leads primarily to an increase in the coordination number of the central atom in chelates **2**, *i.e.*, the coordination is changed from square-planar or tetrahedral to penta- or hexacoordinated. This fact allows one to perform the directed synthesis of chelate compounds of the azomethine series with pyramidal or octahedral structures.

In recent years,^{101, 105–115} considerable attention has been given to the investigation of the structures of β -aminovinylimine chelates **48** containing the bulky diisopropylphenyl substituents R^3 at the nitrogen atom. In chelates with composition MLR^3 , the access to complex-forming metals is sterically hindered.

Ligands containing the same substituents can form chelates of different stereochemical types.^{22, 24, 215} In complexes of pyridine-containing azomethines, the nitrogen atom of the heterocycle can either form a bond with the metal atom (compound **108**²¹³) or not (compound **107**²¹²). The quinoline nitrogen atom is generally coordinated to the metal atom (compounds **111**^{215, 216} and **112**²¹⁷).

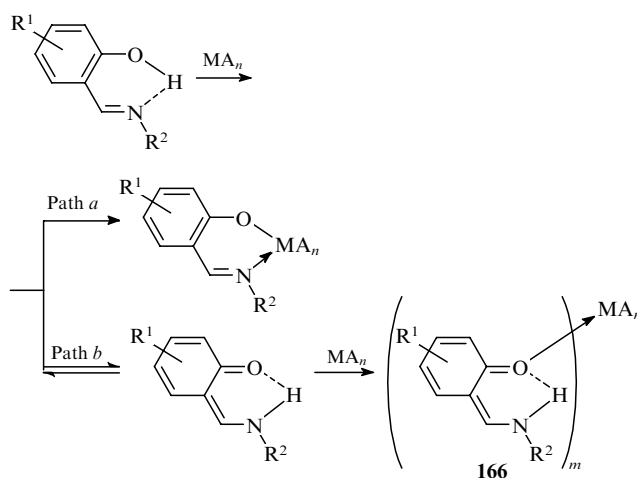
The dependence of the stereochemistry of chelate compounds on the nature of the metal atoms was partially considered at the beginning of this section. Noteworthy also is structure **165** characterised by the *trans* arrangement of the donor atoms and the 'umbrella' conformation of the coordination unit untypical of azomethine chelates of d^8 metals with the N,S-ligand environment.^{292, 293} The formation of this structure is associated with several factors. In palladium complexes, the ligands generally exhibit the square-planar coordination mode. However, the pyrazole fragment and bulky cyclohexyl substituents at the nitrogen atoms induce structural distortions.



The structural analysis of nickel chelates with Schiff bases of aromatic and heterocyclic *o*-hydroxy(thio)aldehydes clearly showed the influence of the fine structure of ligand systems on the structures of azomethine metal chelates. Three coordination modes, *viz.*, planar with a *cis* or *trans* arrangement of the ligands and tetrahedral, were found in the known complexes. The coordination mode is changed if the nature of the heteroatom in the chelate ring is changed, bulky substituents are inserted at the azomethine nitrogen atom, or on going from derivatives of aliphatic or aromatic aldehydes to heterocyclic analogues (Fig. 1).

III. Molecular complexes with azomethine ligands

o-Hydroxyazomethines serve as classical chelating ligands (Section II.2.b). However, as was first demonstrated in 1964,³²¹ these compounds can also be used for the preparation of molecular complexes **166**.^{20, 22, 24, 28, 29, 322–325}



$R = \text{Alk, Ar}; M = \text{Cu, Zn, B, Al, Sn, Ti, Th}; A = \text{Hal, NO}_3, \text{NCS}; m = 1, 2; n = 2–4.$

The reaction path depends on the nature of the solvent.³²³ Thus, metal chelates (Section II.2.b) are formed predominantly in media with high dielectric permeability (alcohols; path *a*), whereas molecular complexes **166** are generated primarily in aprotic non-polar media with low basicity (hydrocarbons, their halogen derivatives, ethers or mixtures of these solvents; path *b*).

Some reactions proceed in mixtures of benzene and alcohols. Thus, the direct reaction of the ligands with $ZnCl_2$ afforded complex **167**.³²⁶

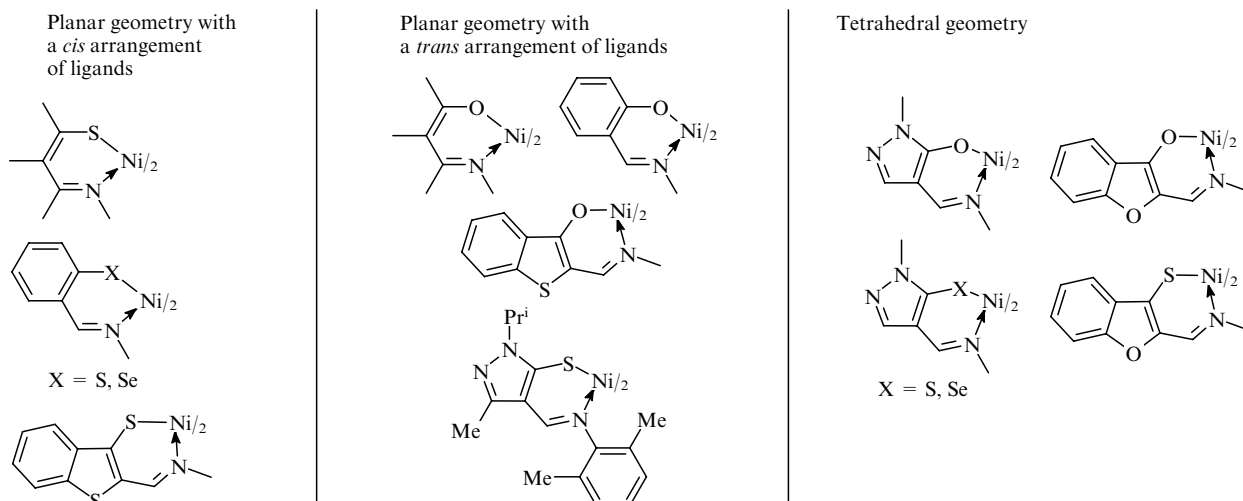
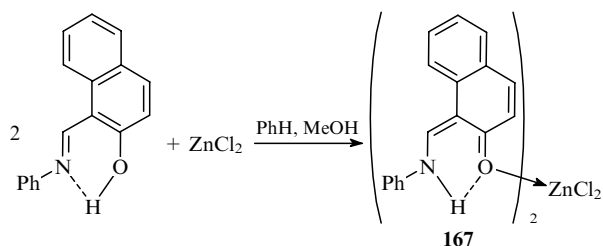
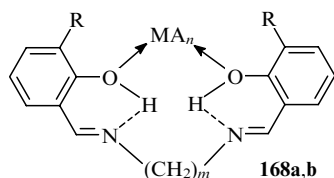


Figure 1. Coordination modes in nickel complexes.



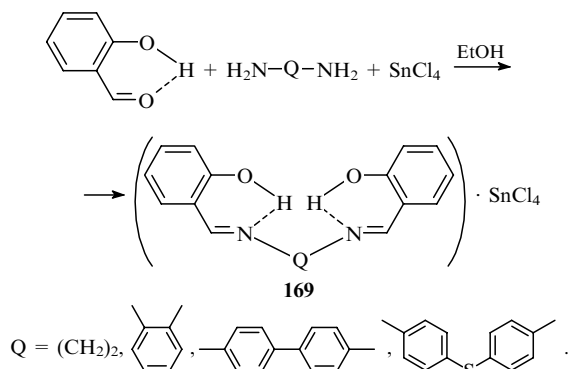
Bis(salicylidene)alkylenediamine molecular complexes **168a**³²⁷ and **168b**³²⁸ were synthesised analogously.



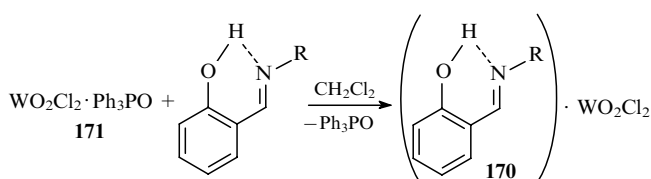
168a: R = H, M = Ca, A = NO₃, *m* = 3, *n* = 2;

168b: R = H, Me, OMe; M = Ti, Zr; A = F, Cl; *m* = 2, *n* = 4.

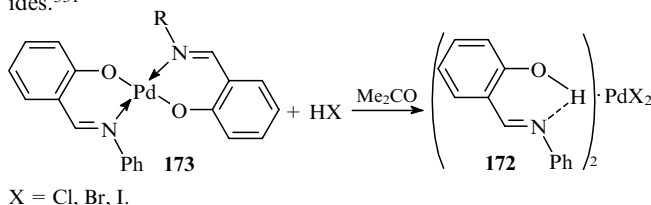
The template synthesis methods are employed more rarely. However, this approach was used for the preparation of adducts **169**.³²⁹



Molecular complex **170** was synthesised by ligand exchange in tungsten complex **171**.³³⁰

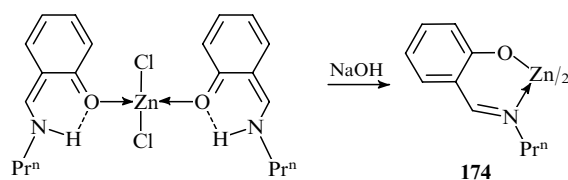


It was demonstrated that molecular complexes **172** could be prepared from chelates **173** under the action of hydrogen halides.³³¹



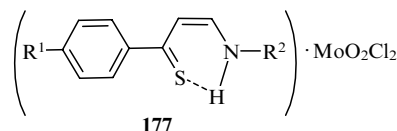
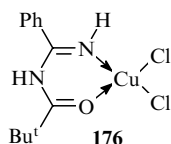
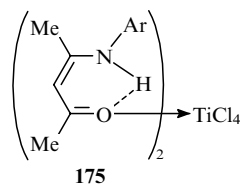
X = Cl, Br, I.

Recently,³³² metal chelates **174** were synthesised starting from a molecular complex analogous to complex **167**.



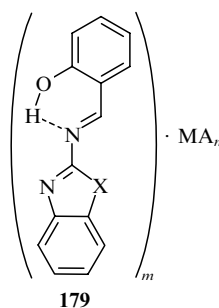
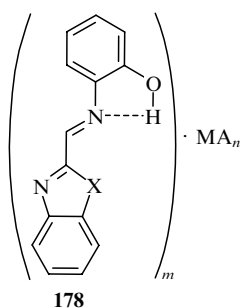
Taking into account the data on the synthesis of molecular complex **172**,³³¹ the possibility of the interconversion of chelates **2** and molecular complexes **3** may be considered as proved.

Among recent studies, let us mention the investigations of adducts of metal halides with β -aminovinyl ketones **175**^{101, 333} and their analogues **176**³³⁴ and **177**.³³⁵



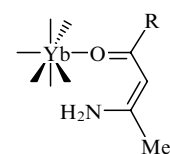
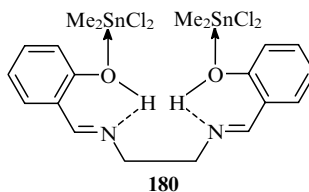
R¹ = H, Br; R² = C₇H₁₅, Bz, C₆H₄Me-4, C₆H₄OMe-4, C₆H₄Br-4.

Molecular complexes **178** and **179** of metal halides with hydroxyazomethines containing five- or six-membered chelating fragments^{336–338} were prepared by the reactions of the corresponding ligands with metal chlorides in anhydrous benzene (M = Sn, Ti) or methanol (M = Cu, Zn, Cd). Palladium complexes **178** and **179** were synthesised by the ligand-exchange reactions of Schiff bases with PdCl₂(PhCN)₂.



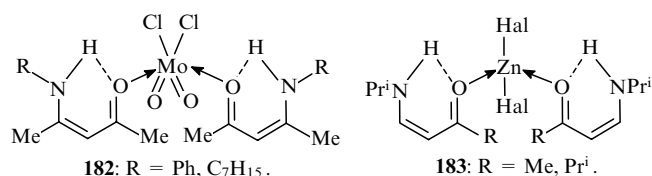
X = NR, O, S; M = Sn, Ti, Pd, Cu, Zn, Cd; *m* = 1, 2; *n* = 2, 4.

Several structural types were proposed for the molecular complexes under consideration.^{20, 27, 29, 322–324} X-Ray diffraction studies demonstrated that hydroxyazomethines and β -aminovinyl ketones in molecular complexes **180** and **181a,b** act as monodentate ligands containing the O-donor centre. For the first time, this coordination mode was unambiguously established by X-ray diffraction analysis of complexes with bis(salicylidene)ethylenediamine **180**³³⁹ and tris(acetylacetonato)(4-aminopent-3-en-2-one)ytterbium **181a**.^{15, 340}



181: R = Me (a), Ph (b).

It is believed³³⁹ that complexes **180**, like compound **168a**,³²⁷ contain the ligand in the hydroxyimine form. However, X-ray diffraction analysis of complex **167**, which made it possible to locate the positions of protons in the structure, showed that the ligand occurs as the quinone-imine tautomer.³²⁶ According to the results of X-ray diffraction analysis, the ligands in complexes **182**^{341, 342} and **183**³⁴³ also occur in the form of β -aminovinyl ketones.



It should be emphasised that IR spectroscopy cannot be employed for revealing the mode of location of the coordination bond and establishing the tautomeric form of the hydroxyazomethine or β -aminovinyl ketone ligands because the absorption bands corresponding to both types of coordination (at the nitrogen atom of the C=N bond or at the oxygen atom of the carbonyl group) have similar frequencies. The ¹H NMR spectra also do not provide conclusive information for the solution of these problems.³⁴⁴

The data surveyed in this section provide the basis for the directed stereochemical²⁴ and regioselective^{24,345} syntheses of azomethine metal chelates.

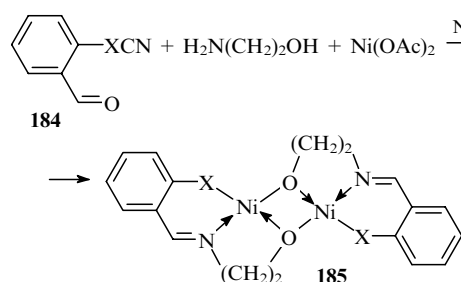
IV. Bi- and polynuclear azomethine complexes

Bi- and polynuclear complexes containing azomethine ligand systems are formed by the reactions of bi- and polydentate Schiff bases or their complexes as well as of polymeric azomethines with metal sources or upon polymerisation of monomeric metal complexes.

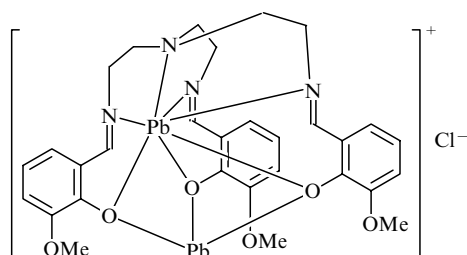
1. Bi- and polynuclear complexes of polydentate Schiff bases and their analogues

A series of chelating azomethines form not only mononuclear complexes but also bi- and polynuclear structures. Such structures were constructed and characterised for chelates prepared on the basis of bidentate Schiff bases of *o*-aminophenol **17**^{64,346} and its thio analogue **31**,³⁴⁷ tridentate imino alcohols **83** (Y = OR) and iminothio alcohols **83** (Y = SR).^{24,177}

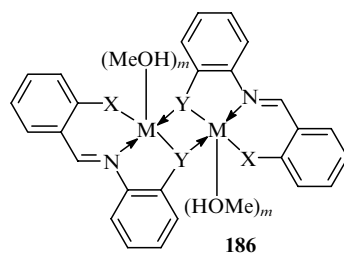
Reactions of substituted benzaldehydes **184** with aminoethanol and nickel acetate afforded binuclear chelates **185**.³⁴⁸



The lead complex with composition [Pb₂L]Cl was prepared by the reaction of the tripodal N(CH₂CH₂N=CH-C₆H₃OMe-3-OH-2)₃(H₃L) ligand with PbCl₂ in methanol in the presence of a base.³⁴⁹

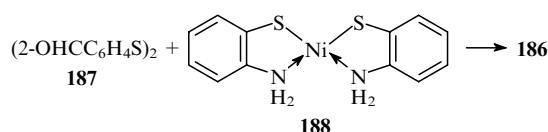


Binuclear complexes **186** with tridentate azomethine ligands **2**, **24**, **280**, **350**–**353** were synthesised primarily from the ligands and the corresponding metal acetates.^{350–353}

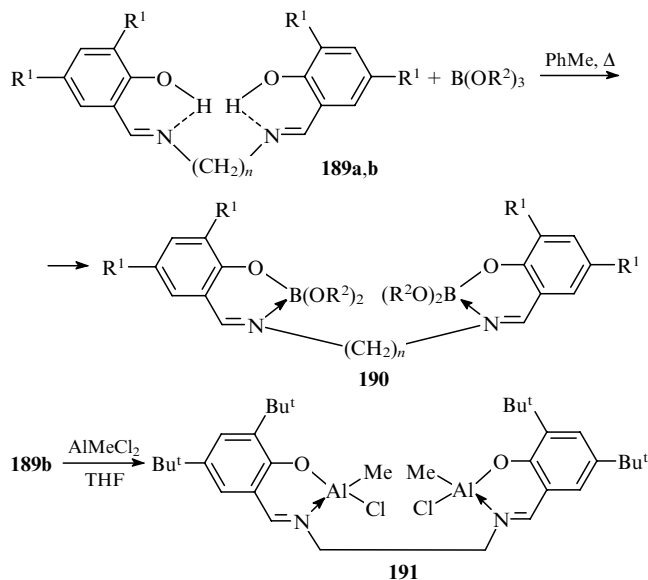


M = Co, Ni; X, Y = NTs, O, S; m = 0, 1, 2.

Binuclear nickel complex **186** (X = Y = S, M = Ni, m = 0) was prepared by the template method from disulfide **187** and complex **188**.²⁸⁰



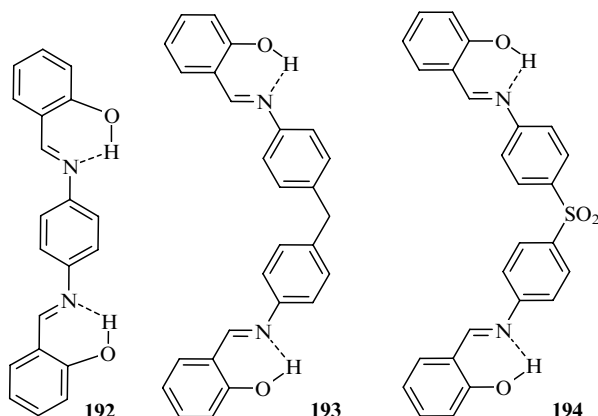
Tetradentate azomethine ligand systems of the bis(salicylidene)ethylenediamine series^{34,218} form not only mono- but also binuclear chelates.^{225,251,354–363} Such chelates were prepared for boron,^{218,357} aluminium,^{218,354,359} gallium,²¹⁸ indium,²¹⁸ titanium,³⁵⁸ europium and yttrium,^{225,357} cobalt,^{355,363} chromium and molybdenum,³⁴ iron,³⁵⁶ nickel and copper,³⁶¹ and zinc.^{251,360} Complexes containing the bridging bis(salicylidene)alkylidene-amino ligands **189a,b**, such as **190**³⁵⁷ and **191**,³⁵⁴ are the most widespread binuclear chelate compounds.



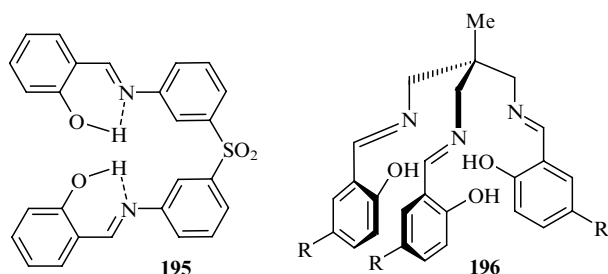
R¹ = H (**a**), Bu^t (**b**); R² = Me, Et; n = 2–6.

Conceivably, these binuclear structures are generated through the formation of intermolecular dimers due to coordination of the metal atoms by the oxygen atoms of the adjacent complex molecules.³⁴

Bisbidentate Schiff bases **192**,³⁶⁴ **193**,³⁶⁵ **194**³⁶⁵ and **195**³⁶⁶ show promise for the construction of bi- and polynuclear azomethine complexes.

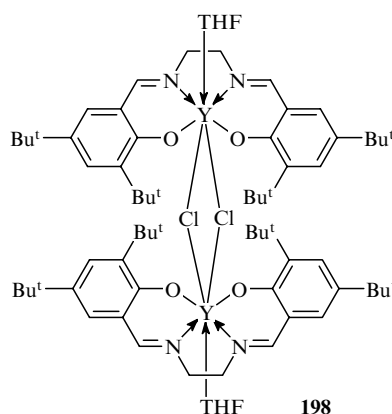
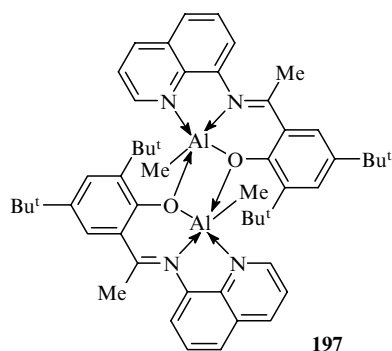


Binuclear structures were prepared on the basis of compounds **192**–**194**. Tetranuclear complexes were derived from ligand **195**. Tripodal hexadentate ligands **196** gave rise to bi- and trinuclear nickel complexes.³⁶⁷



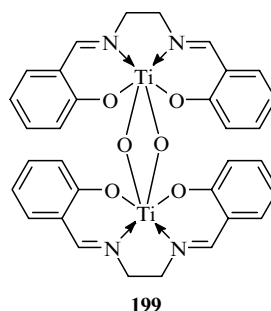
R = H, OMe.

Various bridging atoms, such as oxygen (for example, compound **197**¹⁷⁵) or chlorine (compound **198**³⁶⁸), play an important role in the formation of binuclear structures.

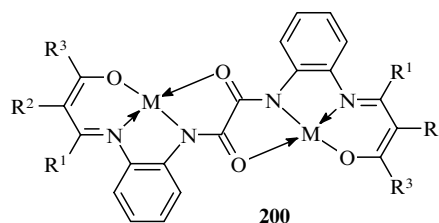


In some cases, atomic oxygen serves as an intermolecular bridge to form, for example, oxotitanium dimeric,^{369–372} trimeric

and tetrameric^{370,373} complexes of tetradentate Schiff bases. Structure **199** provides an example of dimeric complexes.³⁷²



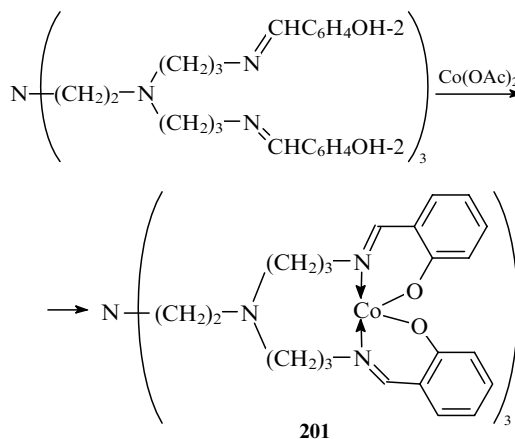
There are data on oxygen-bridged complexes derived from bidentate Schiff bases. For example, complexes of di- μ -oxodimanganese(IV) with *N*-alkyl-substituted salicylideneamines were synthesised.³⁷⁴ Binuclear chelates **200**³⁷⁵ formed by the complex polydentate ligand containing two β -ketoiminate fragments also belong to this type of complexes.



R¹ = H, Me; R² = H, COMe;

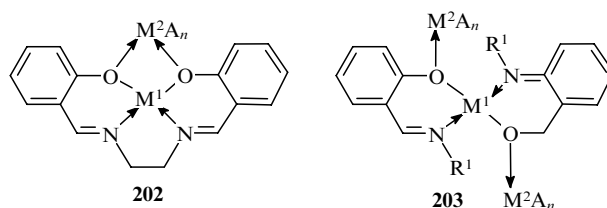
R³ = Me, Ph, C₆H₄NO₂-4; M = Ni, Cu.

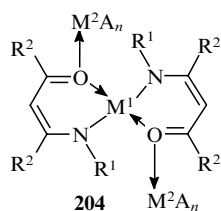
Trinuclear oxygen-bridged complexes **201**^{376,377} were prepared based on dendrimers with salicylideneamine groups.



2. Bi- and polynuclear complexes with metal-containing azomethine ligands

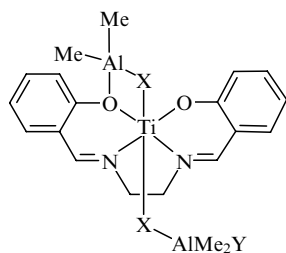
In the 1960s, it was demonstrated^{378–381} that the reactions of chelate compounds containing the azomethine ligands M¹L_m with metal salts M²A_n can give rise to bi- (**202**^{380,381}) and trinuclear (**203**³⁷⁸ and **204**³⁷⁹) structures.



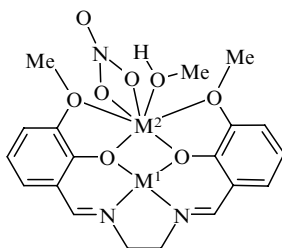


$R^1 = \text{Alk, Ar}; M^1 = \text{Ni, Cu}; M^2 = \text{Co, Ni, Cu, B, Al, Ti, Sn};$
 $A = \text{Hal, NO}_3.$

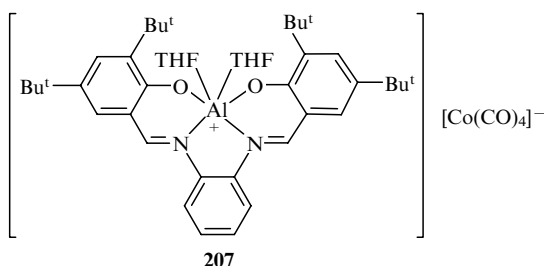
The direct reactions of ligands with sources of complex-forming metals were used for the preparation of complexes **205**,³⁵⁸ **206**³⁸² and **207**.³⁸³



205: $X = \text{Cl, Br}; Y = \text{Me, Cl}.$



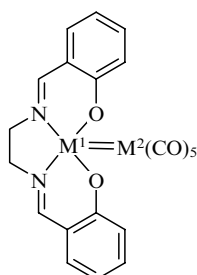
206: $M^1 = \text{Co, Ni, Cu, Zn};$
 $M^2 = \text{Na, K, Cs}.$



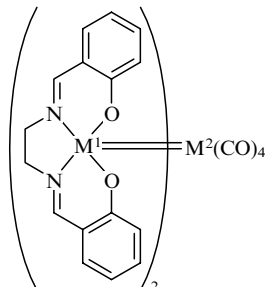
207

It should be noted that alkali salts in the heteronuclear structures under consideration can act as Lewis acids (M^2A_n). In particular, this is evidenced³⁸² by the formation of adducts **206** in the reactions of salicylaldehyde complexes of divalent metals (Co, Ni, Cu, Zn) with sodium, potassium and cesium salts. β -Amino-vinyliminate-based complexes **206** were described in the study.³⁸⁴

Unlike the above-considered binuclear halide complexes **202**, which were prepared by the reactions of the corresponding ligands with metal halides, coordination compounds of metal carbonyls were synthesised by ligand-exchange reactions.³⁸⁵ These reactions afforded two types of complex compounds with the M^1-M^2 and $M^1-M^2-M^1$ bonds, *viz.*, $M^1LM^2(\text{CO})_5$ (**208**) and $(M^1L)_2M^2(\text{CO})_4$ (**209**), respectively.



208



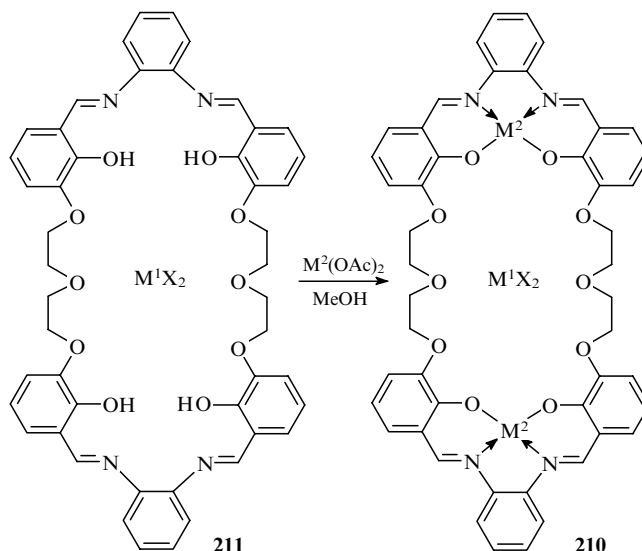
209

$M^1 = \text{Ge, Sn, Pb}; M^2 = \text{Cr, W}.$

Binuclear complexes can be prepared by the reactions of metal chelates, for example, of bis(salicylidene)ethylenediamines or bis(tris)- β -diketonates, in chloroform.³⁸⁶⁻³⁹¹ In azomethine chelate compounds, Ni(II)³⁸⁷⁻³⁹¹ and Cu(II)^{386, 389, 391} serve as the

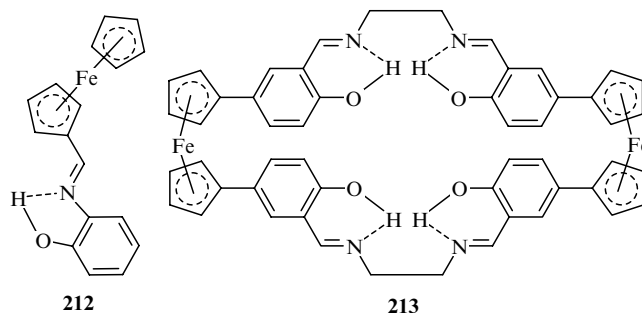
M^1 metal and hexafluoroacetylacetonates of Ba and Mg,³⁹⁰ Y(III),^{386-389, 391} La(III)^{389, 391} and Gd(III)^{386, 389, 391} act as metal salts (M^2A_n). The structures of these complexes were established by X-ray diffraction analysis. Like in complexes **202**, the coordinatively unsaturated oxygen atoms of the bis(salicylidene)ethylenediamine anion are involved in coordination to lanthanides.

Bi- and trinuclear complexes were synthesised starting from coordination compounds of crown ethers containing the chelating hydroxyazomethine fragments.³⁹²⁻³⁹⁴ As an example of these compounds, we refer to heterotrinuclear complex **210** generated from heterobinuclear complex **211**.³⁹²



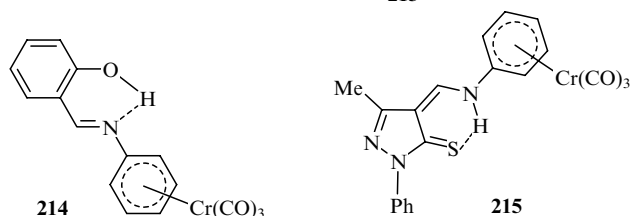
$M^1 = \text{Ba}(\text{CF}_3\text{SO}_3)_2; M^2 = \text{Cu, Ni}.$

It should also be noted that Schiff bases containing organo-metallic fragments can be used as azomethine ligands. Ferrocene derivatives **212**^{395, 396} and **213**³⁹⁷ as well as derivatives of benzene chromium tricarbonyls **214**³⁹⁸ and **215**³⁹⁹ are examples of these Schiff bases.



212

213

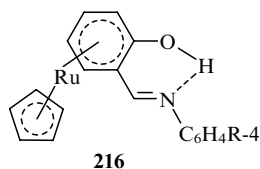


214

215

Ligands **212**, **213** and **214** give rise only to metal chelates, whereas azomethine **215** produces molecular complexes.

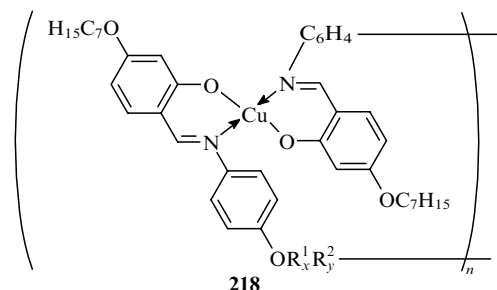
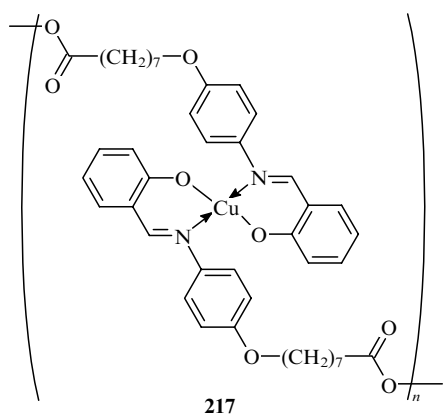
Ruthenium complex **216** shows promise as a ligand for the preparation of tri- and oligonuclear coordination compounds.⁴⁰⁰ The former complexes can be synthesised by the reactions of ligand **216** with divalent metal acetates and the latter complexes can be prepared on the basis of metal salts in oxidation states 3 and higher.



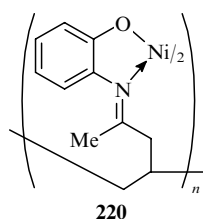
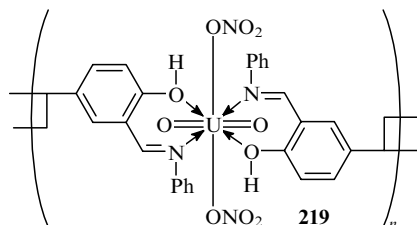
3. Azomethine metal polymers

Main methods for the preparation of polymers containing chelates of Schiff bases and their analogues involve the reactions with chelating macroligands and polymerisation of metal monomers.^{31–33, 401–405}

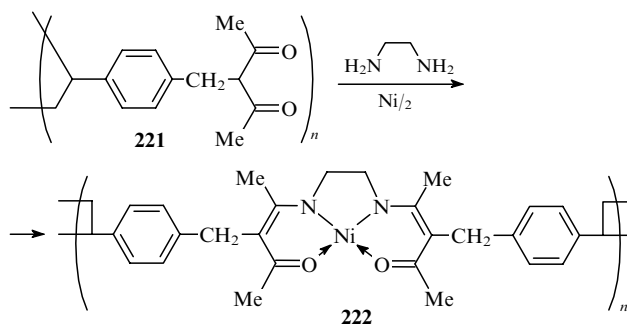
Chelating polymeric azomethine ligands are used in synthetic reactions similar to those involving monomeric Schiff bases and their analogues (see Sections II and III). Thus, the reactions of the ligands with metal salts afforded polymers containing chelates (for example, **217**,⁴⁰⁶ **218**⁴⁰⁷) and molecular complexes (**219**⁴⁰⁵). The metal exchange gave rise to metal polymers **220**.³²



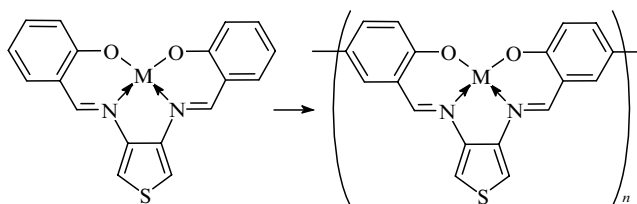
$R^1 = (CH_2)_{12}O$; $R^2 = (CH_2CH_2O)_3$; $x = 0-100$; $y = 100-x$.



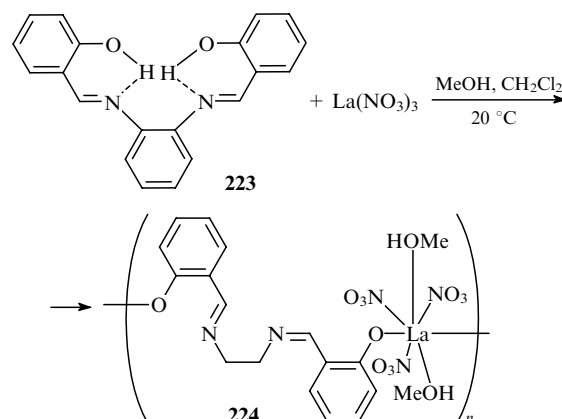
Polymer **222** was prepared from ligand **221** with the use of the template method.³² This approach is particularly efficient when metal polymers cannot be prepared by the reactions of ligands with metal salts or through metal exchange.



The oxidative polymerisation of monomeric chelates was used for the preparation of polymers with bis-salicylidene derivatives of aromatic^{408, 409} or heterocyclic^{410, 411} amines.



In some cases, polymeric azomethine complexes can be prepared in the course of usual syntheses. In particular, the reaction of ligand **223** with La(III) nitrate afforded polymeric structure **224** containing fragments of molecular complexes with the bis(salicylidene)ethylenediamine ligand coordinated through the oxygen atom.⁴¹²



Polymeric complexes of Schiff bases can also involve bridging fragments, for example, oxygen⁴¹³ or metal chelates.⁴¹⁴

V. Conclusion

The available data on metal complex compounds with azomethine ligands make it clear that the employment of the techniques of rational design in the search for ligand systems and synthesis procedures can be a help in performing the directed synthesis of complexes in which the mode of coordination and geometry of metalocycles are prespecified.

In addition to synthetic and structural problems arising in research on metal coordination compounds with azomethine ligands, theoretical and applied aspects are also of great importance, including competitive coordination,^{24, 27} standard and non-standard binding of metals to chelating ligands,^{28, 29} stabilisation through the complex formation of tautomeric forms untypical of free ligand systems⁷⁷ and isomerism of coordination units within chelates.^{24, 27}

Complexes of Schiff bases and their structural analogues are of practical importance because they allow one to perform the directed design of new types of azomethine coordination com-

pounds exhibiting catalytic, magnetically anomalous and liquid-crystalline properties. In this connection, it should be emphasised that metal chelates of Schiff bases in which the complex-forming metal atom is shielded by bulky substituents (compounds of type **48**: $R^1 = C_6H_3Pr_2^1$), belong to new-generation catalysts for polymerisation, copolymerisation, enantioselective synthesis and oxidation of alkenes (predominantly, epoxidation). In addition to the studies cited in the present review^{101, 105–136} these problems have also been considered in the studies devoted to the same subject.^{415–417}

Bi- and trinuclear complexes of type **204** ($A = Hal$; see also Ref. 418) serve as efficient catalysts for oligo- and polymerisation as well as for hydrogenation. These complexes, like binuclear chelates **202** (MA_n are lanthanide tris-hexafluoroacetylacetonates),^{386, 419} and azomethine coordination compounds with azole free radicals **89** and **90** (molecular ferromagnetics)⁴²⁰ exhibit magnetically anomalous properties.

Data on azomethine metal complexes possessing liquid-crystalline properties have been surveyed in the review⁴²¹ and more recent publications.^{422, 423}

Taking into account considerable advances that have been made in the construction of biomimetic models of active sites of non-haeme metalloproteins on the basis of azomethine metal chelates,^{267, 295, 299, 307, 424, 425} this line of studies shows considerable promise.

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Basic achievements in the coordination chemistry of modified monosaccharides

Yu A Zhdanov, Yu E Alekseev

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Abstract. The published data on the complexation of chemically modified carbohydrates (acetalated and acetylated monosaccharides, carbohydrate podands and coronands as well as nitrogen-, phosphorus-, sulfur- and selenium-containing monosaccharide derivatives) are generalised and systematised. The structural diversity of the metal complexes formed is demonstrated and the effect of the ligand chirality on the chiralities of the corresponding coordination points is discussed. The bibliography includes 155 references.

I. Introduction

Various aspects of the coordination chemistry of natural carbohydrates have been detailed in a number of reviews.^{1–8} The coordination chemistry of chemically modified carbohydrates has been studied in far less detail; the data available^{8–11} discuss only some aspects of this field of research. The interest in this topic is connected with further improvement of methods of synthetic chemistry of carbohydrates.

Chemical modification of monosaccharides aimed at the preparation of ligands consists predominantly in the coupling of natural monosaccharides, which are continuously reproduced upon photosynthesis, to *a priori* complex-forming (in the extreme case, chelatogenic) fragments. This approach allows a considerable increase in the structural diversity of carbohydrate complexes, which are chiral by nature. Such complexes and their metal complexes are necessary for the preparation of chirally pure pharmaceuticals.

This review is an attempt to get a better insight into this branch of chemistry. The material presented herein is arranged according to the principle used in our previous review.⁶ The ligands are classified into oxygen, nitrogen-, phosphorus-, sulfur- and selenium-containing monosaccharide derivatives according to the type of donor heteroatoms. Metal cations for each ligand class are cited in the order of complexity of their electronic configurations and in conformity with their positions in the Periodic Table, *i.e.*, *s*-, *p*-, *d*- and *f*-metals.

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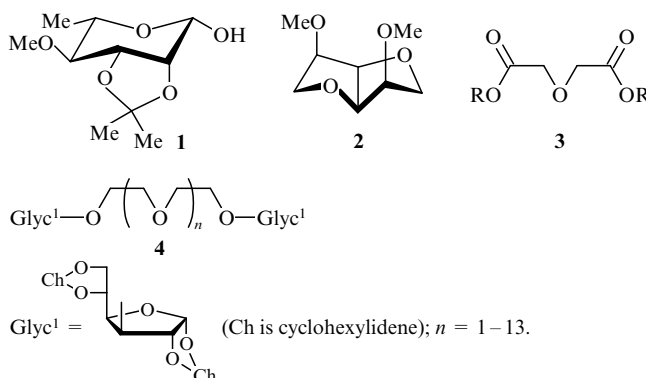
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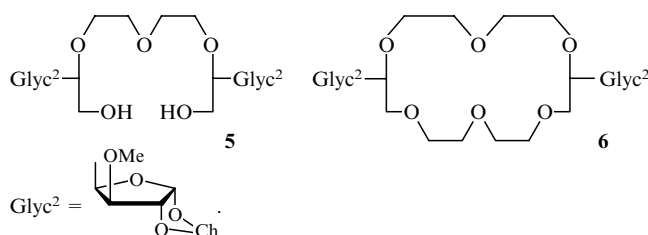
II. Metal complexes of monosaccharide *O*-derivatives

1. Complexes with *s*-metal cations

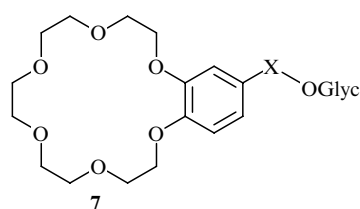
Free water-soluble monosaccharides represent^{2,3,6} weak complexones of *s*-metal cations owing to strong competition of water molecules for the coordination of these cations. *O*-Alkylation (acylation) or acetalation of monosaccharides increases their hydrophobicities as a result of which the corresponding derivatives become soluble in organic solvents where they play the role of moderate *s*-metal complexones due to the lack of water. This can be exemplified by the acetalated monosaccharide **1** (see Ref. 12) and the di-*O*-methyl derivative **2**.¹³ Thus substitution of the O(CH₂)₂OH and O(CH₂)₂O(CH₂)₂OEt fragments for the methoxy groups in compounds **1** and **2** yields^{12,13} carbohydrate podands (acyclic analogues of crown esters);² their affinities for *s*-metal cations markedly exceed those of the starting monosaccharides. This is especially typical of podands **3** (R is a per-*O*-acetylated monosaccharide residue)¹⁴ and **4**.¹⁵



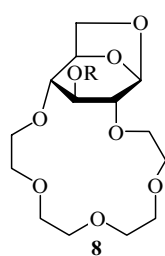
As can be judged from qualitative reactions, regioisomeric mixtures of podands and coronands (*e.g.*, compounds **5** and **6**)^{15–19} readily bind alkali metal cations.



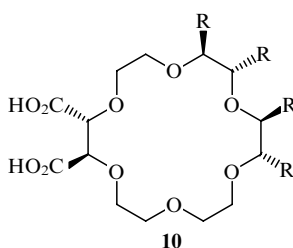
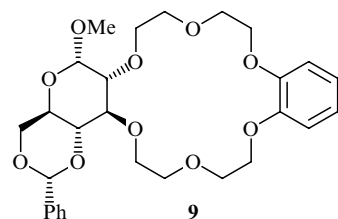
The coordination of coronands **7**,²⁰ **8**²¹ and **9** (see Ref. 22) involves carbohydrate fragments. Ethers **10** (see Ref. 23) and a coronand **11** coordinate *s*-metals in a similar way, *i.e.*, with the involvement of carboxy groups.²⁴ This imparts additional stability to complexes of the above-mentioned ligands.



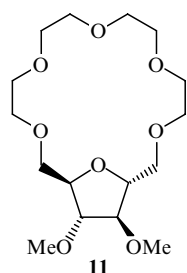
X = CH₂COCH₂, CH₂;
Glyc is an acetalated or acetylated
monosaccharide residue.



R = H, Ac.



R = H, CO₂H.

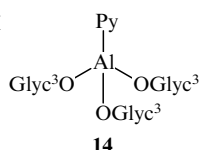
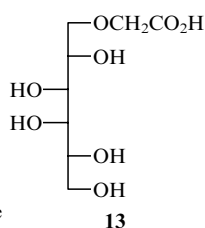
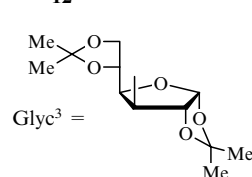


2. Complexes with *p*-metal cations

This type of complex, like complexes with *s*-metal cations, are relatively scarce. They include a series of borates of acetalated sugars (*e.g.*, compound **12** and its derivatives).²⁵ The *O*-carboxymethyl derivative **13** binds Al(III) and some *d*-metal cations.²⁶ In a homoleptic complex **14**, the aluminium atom and three carbohydrate ligands form a trigonal pyramid.²⁷

Glyc³ – OBEt₂

12



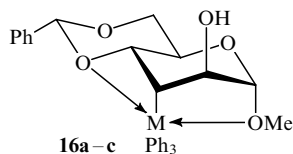
Py is pyridine.

The Sn(IV) complexes of the general formula **15** are the most extensively documented in the literature.^{28–30} Organotin compounds with organometal fragments directly bound to the carbohydrate core^{31,32} are characterised by intramolecular coordination of the type **16a**.³¹

GlycO – (CH₂)_nSnR₃

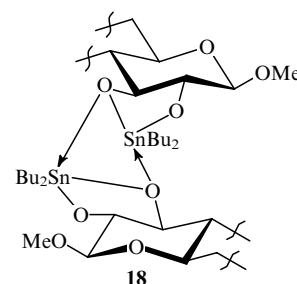
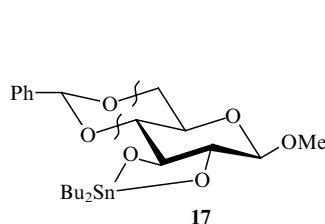
15

R = Me, Bu, Ph;
Glyc is an acetalated monosaccharide
residue;
n = 0–2.

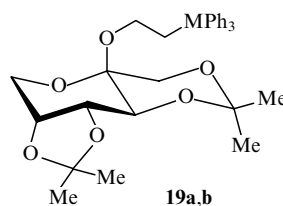


M = Sn (a), Si (b), Pd (c).

The stannylene carbohydrate acetals **17** form dimers **18**.^{33,34} Some analogous derivatives form trimers and even pentamers.³⁴



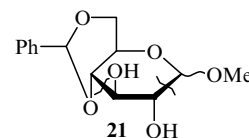
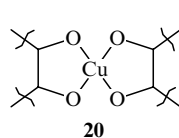
For other *p*-metals, only complexes of the type **16b,c** and **19a,b** have been described.³⁰



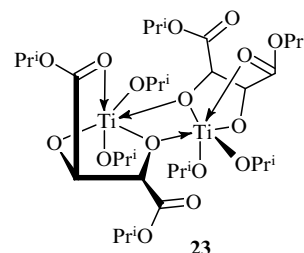
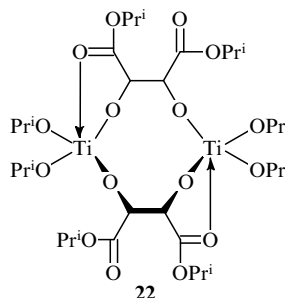
M = Si (a), Pb (b).

3. Complexes with *d*-metal cations

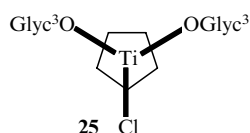
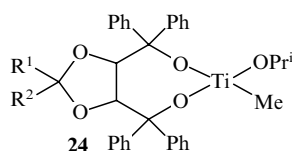
d-Metal complexes are especially fully and diversely represented in the coordination chemistry as a whole and in the coordination chemistry of modified monosaccharides, in particular, which to some extent is characteristic of complexes of monosaccharide *O*-derivatives. Thus the above-mentioned *O*-carboxymethyl derivative **13** is coordinated²⁶ not only with the *p*-cation of Al³⁺, but also with *d*-cations Cu²⁺, Fe³⁺, Co²⁺, Ni²⁺ and Mn²⁺. The formation of copper bischelates **20** in the selective *O*-alkylation (acylation) of the acetalated glycoside **21** in organic solvents in the presence of copper(II) has been described.³⁵



We failed to retrieve any literature data on complexes of monosaccharide *O*-derivatives with *d*-metal cations of subgroups IB and IIIB. *d*-Metal complexes of subgroup IVB were studied in some papers devoted to the use of monosaccharide Ti(IV) complexes in modern organic synthesis.^{36–41} Ti(IV) complexes containing D- and L-tartaric acid derivatives, which are employed in the highly efficient enantioselective Sharpless epoxidation of allyl alcohols (optical yields 80%–100%) have been studied in most detail.^{36–38} (Sharpless was awarded a Nobel prize in 2001.⁴²) The Sharpless catalysts form very diverse structures in solution^{43,44} with cyclic (**22**)^{36–38,45} and bridge-type (**23**) dimers predominating.^{38,45,46}

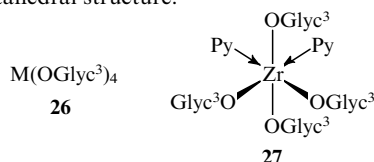


Titanium complexes **24** serve as nucleophilic reagents in some enantioselective transformations.^{39–41} The chlorine atom in complex **25**,⁴⁷ which is a structural analogue of the complex **14**, is readily exchanged for alkyl and other groups, *e.g.*, the allyl group.⁴⁸ Like organometallic compounds, the substitution product adds enantioselectively to the carbonyl group.⁴⁸



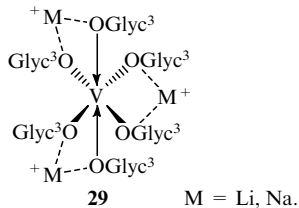
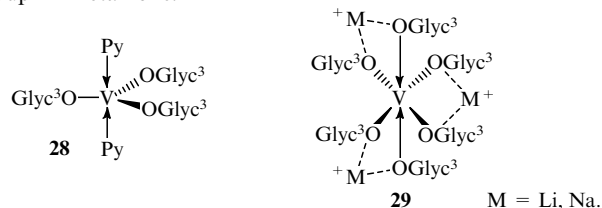
$R^1 = \text{H, Me}; R^2 = \text{H, Ph, Bu}^t$.

The chiral ligands in the homoleptic complexes **26** based on diacetone glucose²⁷ and the oxygen-rich periphery form cavities which favour further coordination. X-Ray diffraction analysis data suggest that two pyridine and two carbohydrate ligands in the complex **27** are localised in the equatorial plane of the pseudo-octahedral structure.²⁷



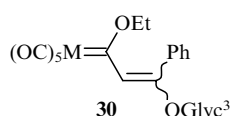
$M = \text{Ti, Zr, Hf}$.

In the case of *d*-metals of subgroup VB, the vanadium-di-*O*-isopropylidene-D-glucose complex **28** is the only complex described so far.⁴⁹ According to X-ray diffraction analysis data, the ligands in this complex form a propeller-shaped structure having a Λ -configuration. Reaction of the complex **28** with lithium and sodium alcoholates of di-*O*-isopropylidene-D-glucose yields complexes $[\text{V}(\text{OGlyc}^3)_6\text{M}_3]$ ($M = \text{Li, Na}$) where the carbohydrate ligands form an environment for M^+ which resembles that of the solvate complex (structure **29**).⁵⁰ Thus, metal complexes of modified sugars can in principle be used as ligands for group IA metal ions:

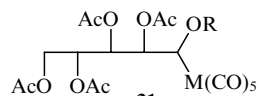


$M = \text{Li, Na}$.

Carbohydrate-containing *d*-metal complexes of subgroup VIB are represented in the literature by carbene complexes of two types. The first of them includes complexes **30**⁵¹ where the acetalated carbohydrate moiety is in the β -position relative to the carbene carbon atom. In the second type of complex (**31**),⁵² the acetylated carbohydrate fragment is linked directly to the carbene carbon atom.

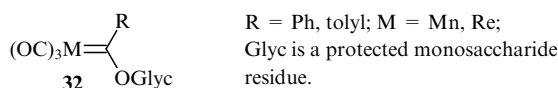


$M = \text{Cr, W}$.



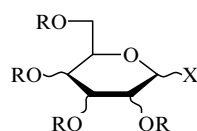
$R = \text{Me, Et}; M = \text{Cr, Mo, W}$.

Carbene complexes of the second type (e.g., **32**) have been known for *d*-metals of subgroup VIIB.⁵³

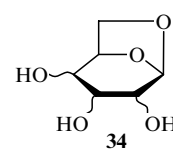


$R = \text{Ph, tolyl}; M = \text{Mn, Re};$
Glyc is a protected monosaccharide residue.

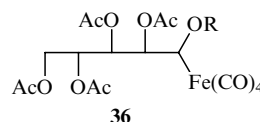
Complexes **33** were prepared⁵⁴ from acetylated glycosyl bromides by exchange reaction with $\text{NaMn}(\text{CO})_5$. Interactions of 1,6-anhydrohexopyranoses **34** with Mn^{2+} , Mn^{3+} and Mn^{4+} follow the Angyal rule;^{3,6} the ligand complexes with the axial-equatorial-axial orientation of the three vicinal hydroxy groups are the most stable.⁵⁵



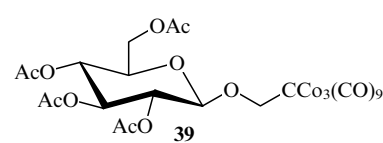
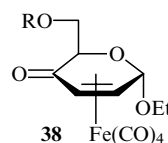
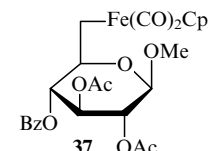
33: $R = \text{Ac}; X = \text{Mn}(\text{CO})_5$;
35: $R = \text{Me}; X = \text{Fe}(\text{CO})_2\text{Cp}$
(Cp is cyclopentadienyl).



The structurally unique iron carbonyl complexes **35**,⁵⁶ **36**⁵² and **37**⁵⁷ and the π -complex **38**⁵⁸ are of interest among carbohydrate compounds of group VIII metals. μ^3 -Carbide clusters, e.g., compound **39**, have been prepared.⁵⁹

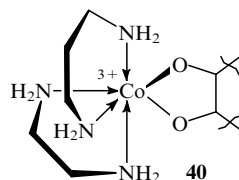


$R = \text{Me, Et}$.

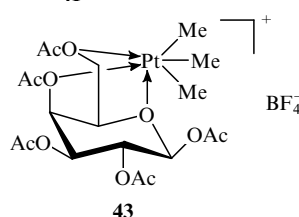
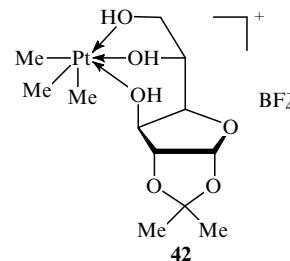
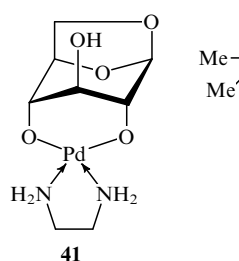


$R = \text{H, Ts}$.

In strongly alkaline aqueous media, vicinal diol groups of partially protected monosaccharides undergo deprotonation; the deprotonated forms of these compounds coordinate the metal complex *trans*- $[(\text{en})_2\text{CoCl}_2]\text{Cl}$ (en is ethylenediamine) to yield complexes **40** with a predominant Λ - or Δ -configuration depending on the stereochemistry of the monosaccharide.⁶⁰



Complex $[\text{Pd}(\text{OH})_2(\text{en})]$ reacts with 1,6-anhydro- β -D-glucose (levoglucosan) in strongly alkaline aqueous solutions⁷ to afford complex **41** (by analogy with the complex **40**). The complex $[\text{PtMe}_3(\text{Me}_2\text{CO})_3]^+\text{BF}_4^-$ is coordinated with acetalated aldoses (e.g., di-*O*-isopropylidene-D-glucose Glyc^3OH) to give the complex **42** with elimination of the terminal isopropylidene protective group. Per-*O*-acetylated aldoses form complexes similar to **43**.^{7, 61}



III. Metal complexes of nitrogen-containing monosaccharide derivatives

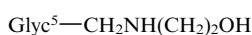
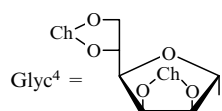
The predominance of nitrogen-containing ligands in coordination chemistry on the whole⁶² is also characteristic of the coordination chemistry of carbohydrates. Nitrogen-containing monosaccharide derivatives coordinate virtually all known metals.

1. Complexes with *s*-metal cations

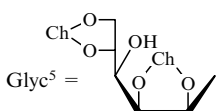
The majority of *s*-metal complexones in the series of nitrogen-containing monosaccharides, *e.g.*, the amino derivatives **44**, **45**,⁶³ **46–48**,⁶⁴ **49** and ^{65, 66} **50**,^{67, 68} and the amido derivatives **51–59**, have simple structures.⁶⁹ Typical *s*-metal complexones, such as the azapodands **60** (see Ref. 70) and **61** have also been prepared.⁶⁹ The ability of these compounds to form complexes with *s*-metals was estimated by qualitative reactions.⁶⁴



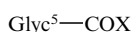
44



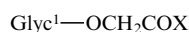
45



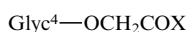
46–50



51–54

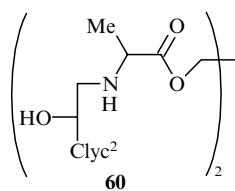


55, 56

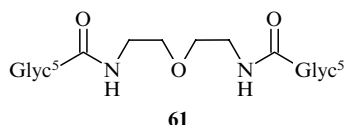


57–59

Compound	X
46	NH ₂
47, 51, 55, 57	NH(CH ₂) ₂ OH
48, 52, 56, 58	N(CH ₂ CH ₂ OH) ₂
49	NHC(CH ₂ OH) ₃
50	NHCHRCO ₂ [−] Na ⁺ (R = H, Me, CH ₂ Me, CH ₂ OH, CH ₂ C ₆ H ₄ OH-4)
53, 59	NHCH ₂ CO ₂ [−] Na ⁺
54	NHCHMeCO ₂ [−] Na ⁺

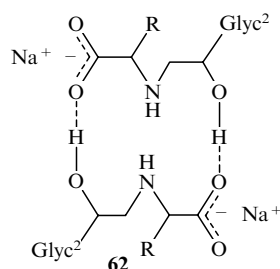


60



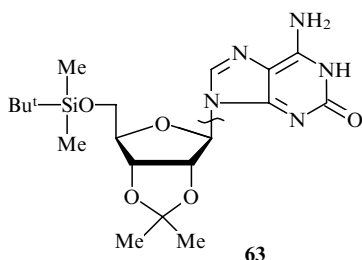
61

The podand activity of *N*-glycosylaminocarboxylates is probably due to their ability^{70, 71} to form the dimers **62** in non-polar media. The formation of the tetramer **64** from the acetalated *N*-glycoside, *viz.*, guanosine **63**, which also occurs in non-polar media, is yet another example of aggregation of cavity-free compounds into those with cavities.^{72–74} The tetramer **64** forms stable L₂M complexes (L = **64**) with K⁺ and Cs⁺ where the coordination apparently involves the carbonyl oxygen atoms. An

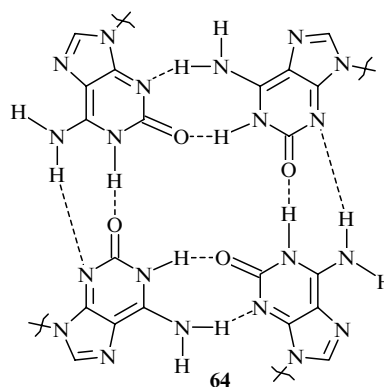


62

R = H, Et.



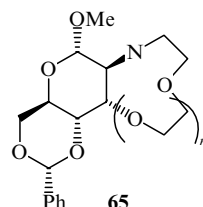
63



64

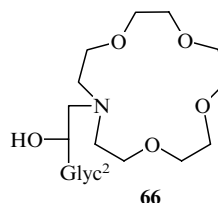
important role is played by the structure of the carbohydrate fragment; thus substitution of *O*-acetyl groups for the isopropylidene protective group in compound **63** prevents aggregation.⁷⁴

A series of carbohydrate azacrown ethers **65** form stable complexes with Na⁺ and K⁺ ions [logK_{st} = 4–6 (in CDCl₃)].⁷⁵ The azacoronands **66** and **67** (see Ref. 64) catalyse the enantioselective reduction of a prochiral ketone acetophenone under phase-transfer conditions with optical yields of 48% and 20%, respectively.⁷⁶

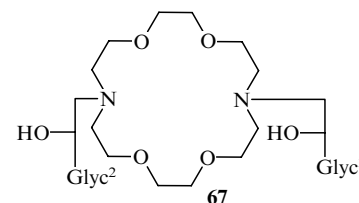


65

n = 3, 4.



66



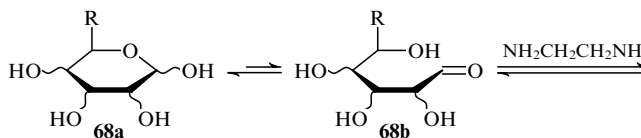
67

2. Complexes with *d*-metal cations

In contrast to the poorly investigated coordination of nitrogen-containing monosaccharide derivatives with *p*-metal cations, there is a considerable body of data on analogous complexes with *d*-metal cations.

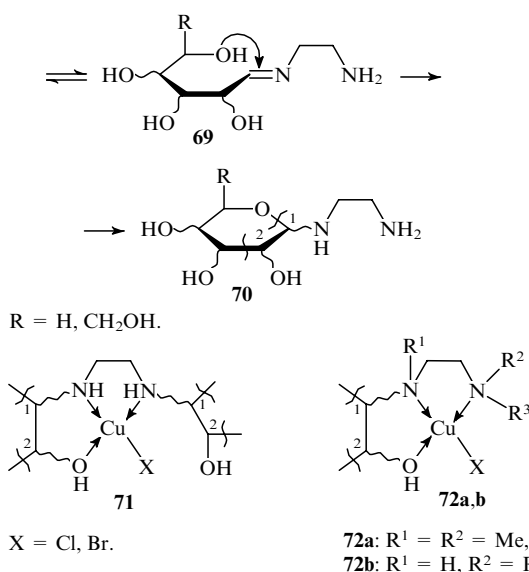
a. Complexes of *N*-glycosides and related compounds

N-Glycosides containing chelate-forming fragments as aglycons are unstable; therefore, their complexes with metals are prepared using different approaches, *e.g.*, reactions of aldoses with ethylenediamine with subsequent addition of copper(II) halides to the reaction mixtures.⁷⁷ At first, aldose **68a** as the aldehyde (form **68b**) reacts with ethylenediamine to produce the Schiff base **69**, which is immediately cyclised into *N*-glycoside **70**. In turn, the free amino group in compound **70** reacts with the aldose resulting in bis-*N*-glycoside, which yields complex **71** upon addition of copper(II) salts.⁷⁷ In the case of *N,N'*- and *N,N*-dimethylethylenediamine, only one amino group is involved in the formation of *N*-glycosides; the resulting complexes have the structures **72a** and **72b**, respectively.

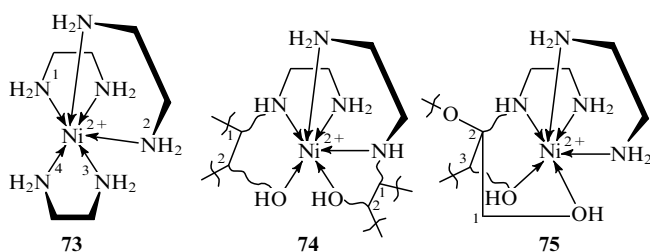


68a

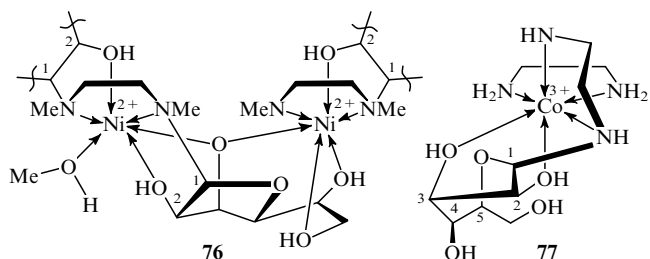
68b



The reactions of aldoses with $[\text{Ni}(\text{en})_3]^{2+}$ (**73**) afford the biscarbohydrate complexes **74**.^{9, 78} Apparently, the aldehyde form **68b** first reacts with the amino groups N(1) and N(2) of the complex **73** as is shown in the previous scheme, **68b** $\rightarrow$ **69** $\rightarrow$ **70**, the reacting ligands being localised in the coordination sphere of the complex. Further, the hydroxy groups at C(2) of the carbohydrate residues incorporated into the metal complex displace the ligand with the amino groups at N(3) and N(4) from the coordination sphere (as in the case of formation of the complex **40**) and are coordinated with the central metal atom (the formation of metal complexes by ligand exchange⁶²). The reactions with ketoses yield monocarbohydrate complexes **75**;^{9, 78, 79} noteworthy, the coordination involves the primary hydroxy group at C(1) in addition to the secondary hydroxy group at C(1).



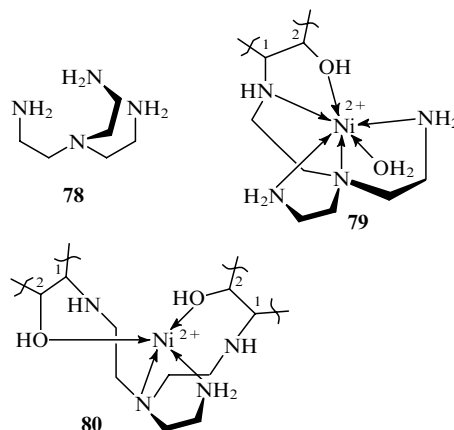
Reaction of D-mannose with the Ni(II)–*N,N'*-dimethylethylenediamine complex yields compound **76** having unusual bridging structure;^{9, 80} one of the carbohydrate ligands in this complex assumes a furanose form seldom occurring in carbohydrate metal complexes. The $[\text{Ni}(\text{tn})_3]^{2+}$ complex (tn is trimethylenediamine) reacts with aldoses like $[\text{Ni}(\text{en})_3]^{2+}$ to yield products analogous to the complex **74**.^{9, 81} A similar result was obtained in the case of the Ni(II) β -alanine complex.^{9, 82}



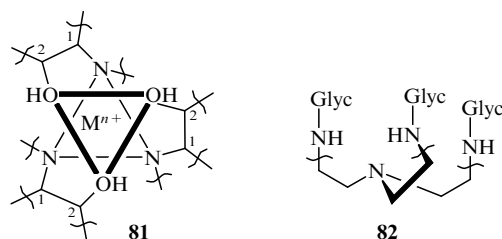
Substitution of Co^{3+} for Ni^{2+} significantly changes the mode of coordination of the carbohydrate ligand: the conformation of the six-membered ring of the single carbohydrate ligand in

complex **77** is considerably distorted, which facilitates involvement of the hydroxy group at C(3) in the coordination.^{9, 83, 84}

The main principles of the geometry of the metal complexes under discussion are retained in the case of a structurally more complex amino component, viz., *N,N*-bis(2-aminoethyl)ethylenediamine (tren) **78**. Thus the reaction with nickel(II) yielded mono- (**79**) (in the case of D-glucose) and biscarbohydrate (**80**) complexes (in the case of D-mannose).⁸⁵

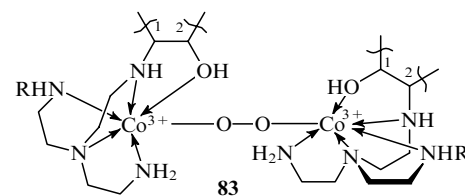


Triscarbohydrate complexes **81** with Ni^{2+} (see Refs 9, 85 and 86) and Co^{3+} (see Refs 9, 85 and 87) using *N*-glycosides **82** as ligands could also be synthesised.



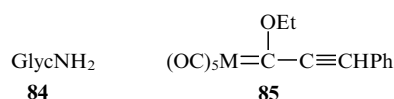
$M = \text{Ni}^{2+}, \text{Co}^{3+}.$

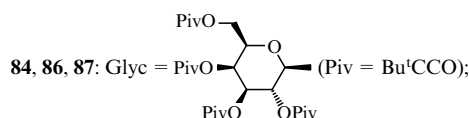
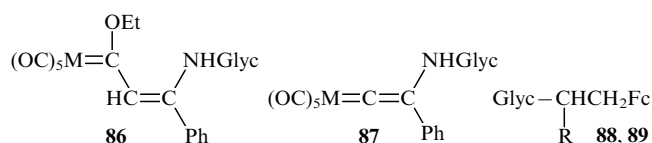
All the metal complexes synthesised are characterised by a specific anomeric configuration (α or β) of the glycosidic imino group, λ - or δ -conformation of the five-membered metallocycles and helical Λ - or Δ -configuration⁸⁸ of the chelate point owing to the transfer of chirality from the carbohydrate ligands to the metal centre. Reversible chiral inversion of the Λ -diastereomer into the Δ -diastereomer in complex **81** ($M = \text{Co}^{3+}$) after substitution of the sulfate ion as the counterion for the halide ion has been described for the first time.⁸⁷ The synthesis of a bridging double-charged complex **83** based on D-glucose is another step forward.⁸⁹



R is D-glucose residue.

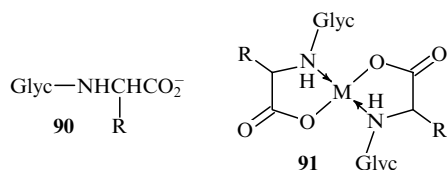
In a similar scheme (viz., by the reaction of a carbohydrate ligand with a metal-containing derivative), starting from *N*-glycoside **84** and alkynylcarbene complexes **85**, a mixture of complexes **86** and **87** (3 : 2) was obtained.⁹⁰ Ferrocenyl derivatives **88** and **89** were synthesised analogously.⁹¹



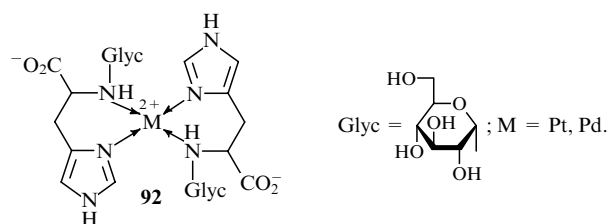


85–87: M = Cr, W; **88, 89:** Glyc is a protected or free monosaccharide; Fc is ferrocenyl; R = H (**88**), CH₂Fc (**89**).

The N,O-coordination of amino acid *N*-glycosides **90** (as salts) is a characteristic of complexes **91** with salts M₂[M²Cl₄] (M¹ = Na, K; M² = Pt, Pd). *N,N*-Coordination (structure **92**) is observed only in the case of histidine.^{7,92}

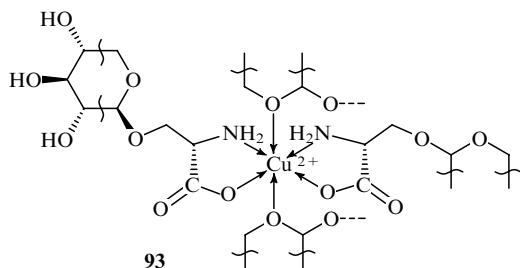


R = H, Me, CH₂OH, CH(OH)Me, CH₂CONH₂, (CH₂)₂CO₂Na.

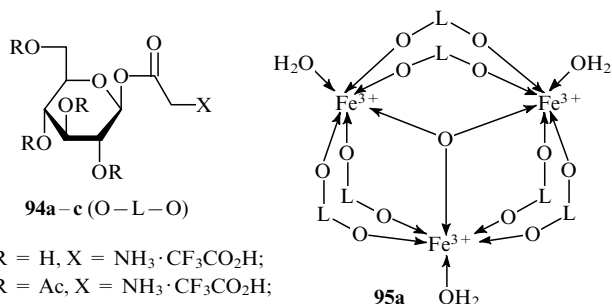


b. Complexes of *O*- and *C*-substituted monosaccharides with nitrogen-containing fragments

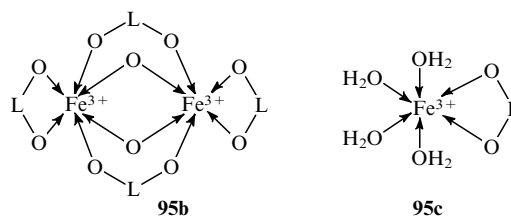
The central metal atom in the copper complex **93** of *O*-(β-D-xylopyranosyl)-L-serine is surrounded⁹³ by four carbohydrate ligands with a distorted octahedral configuration.



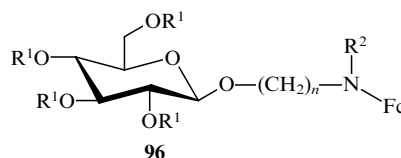
The D-glucopyranosyl ester of glycine **94a** and its partially (**94b**) and fully substituted (**94c**) derivatives coordinate Fe(III) exclusively through the oxygen atoms of the carboxy groups to yield complexes **95a–c**,⁹⁴ their structures are simpler the larger the number of protective groups.



a: R = H, X = NH₃·CF₃CO₂H;
b: R = Ac, X = NH₃·CF₃CO₂H;
c: R = Ac, X = NHCO₂Bu^t.

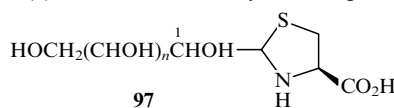


O-Glycoside analogues **96** of the ferrocenyl derivatives **88** and **89** have been prepared.⁹⁵



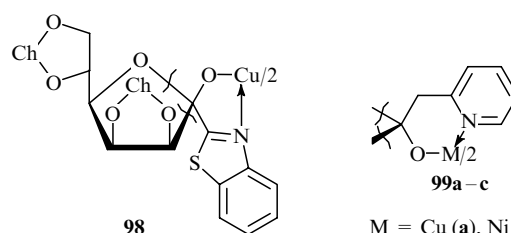
R¹ = H, CH₂Ph; R² = Me, CH₂Fc; n = 2, 3, 5.

The type of coordination in 2-[poly(hydroxyalkyl)]thiazolidine-4-carboxylic acids **97** depends on the nature of the metal ion.^{96–98} The Cr²⁺ cation in complexes ML₂ (L = **97**), as in α-amino acid metal complexes, is coordinated through the imino group and the carboxy group of the heterocyclic fragment.⁹⁶ Similar structures are formed with Zn²⁺, the latter being coordinated at the hydroxy group through the C(2) atom of the carbohydrate residue.⁹⁷ The Pd²⁺ cation is coordinated through the nitrogen and sulfur atoms of the heterocyclic fragment⁹⁸ (the so-called competitive coordination⁶²). It is interesting to note that the stability constants of zinc complexes depend on the chirality of the C(1) atom of the carbohydrate fragment.⁹⁷

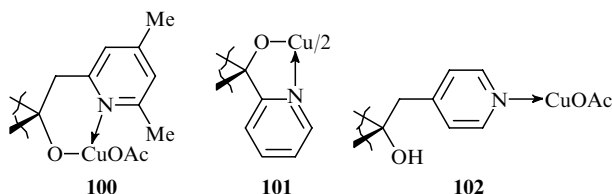


n = 2, 3

Metal complexes **98–102** were prepared in high yields using the electrochemical method.^{99,100} The copper chelates **98, 99a** and **101** possess a distorted planar configuration of the chelate point, and other complexes have octahedral structures.^{99,100}

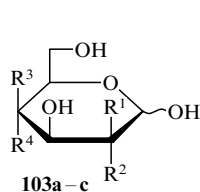


M = Cu (**a**), Ni (**b**), Co (**c**).

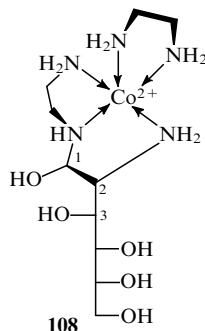
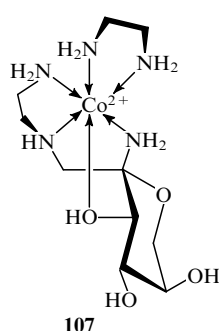
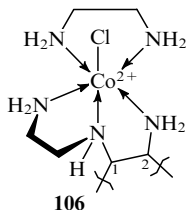
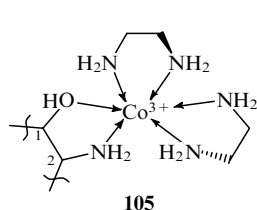
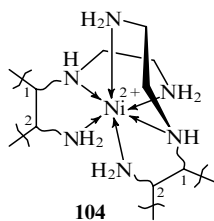


c. Complexes of amino sugars and their derivatives

D-Glucosamine (**103a**), D-mannosamine (**103b**) and D-galactosamine (**103c**) react with [Ni(en)₃]²⁺ to yield complexes **104**^{9,101} similar to complexes **74** containing an amino group at C(2) instead of a hydroxy group. Reactions of D-glucosamine **103a** with [Co(NH₃)₃]³⁺, [Co(en)₃]³⁺ and [Co(phen)₂]³⁺ (phen is phenanthroline) yield complexes **105** by a ligand exchange mechanism.^{9,102} The use of an alternative workup of the D-glucosamine (**103a**)–[Co(en)₃]³⁺ mixture (see Ref. 103) gave eight monosaccharide metal complexes.

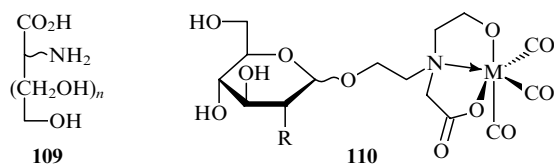


- a: $R^1 = R^3 = \text{H}$, $R^2 = \text{NH}_2$, $R^4 = \text{OH}$;
 b: $R^1 = \text{NH}_2$, $R^2 = R^3 = \text{H}$, $R^4 = \text{OH}$;
 c: $R^1 = R^4 = \text{H}$, $R^2 = \text{NH}_2$, $R^3 = \text{OH}$.

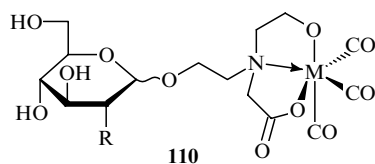


Among the complexes isolated,¹⁰³ only compound **106** with a pyranose form of the carbohydrate ligand is a normal product. In the other complexes, D-glucosamine **103a** is transformed into both D-mannosamine **103b** by the Lobry de Bruyn–van Ekenstein rearrangement,^{104,105} and D-fructosylamine by the Amadori rearrangement¹⁰⁵ (complex **107**). Complex **108** where D-glucosamine exists in an unusual open aminal form is of most interest. The complexes formed are diastereomerically pure and have a Δ - or Λ -configuration at the chelate point. The study¹⁰³ is undoubtedly one of the key studies in the coordination chemistry of carbohydrates, since it demonstrates extreme flexibility of unprotected monosaccharides in complexation with metals.

The oxidation products of the glycosidic hydroxy group of 2-amino sugars, *i.e.*, the carbohydrate α -amino acids **109**, coordinate *d*-metal ions only through the carboxy and amino groups.^{106–108} Complexes **110** provide yet another illustrative example of the non-involvement of the carbohydrate fragment in the coordination.¹⁰⁹

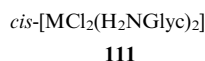


$n = 3, 4$.

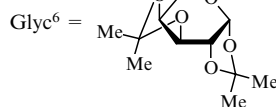
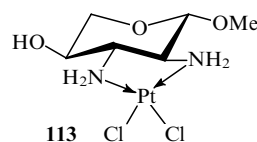
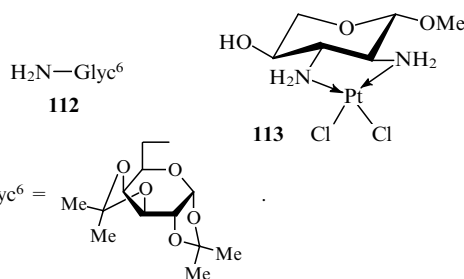


$R = \text{H, OH}$; $M = \text{Re, Tc}$.

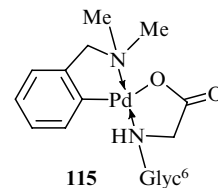
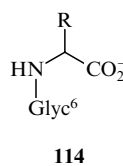
Monoamino sugars of the type **103a–c** form complexes **111** with platinum metals.^{9,110} The protected amino sugar **112** yields complexes of analogous structures.^{9,110} In the case of synthetic vicinal diamino sugars, coordination (*e.g.*, with the formation of the complex **113**) follows the same scheme.⁹



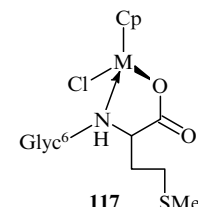
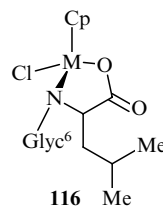
$M = \text{Pd, Pt}$; Glyc is a protected or free monosaccharide.



The reaction of protected *N*-glycosylaminocarboxylates **114** with platinum metal complexes gives complexes **115–117**.^{9,111}

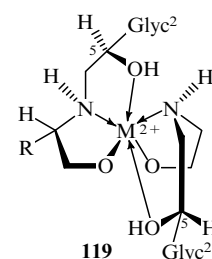
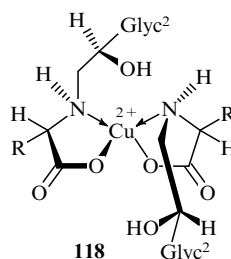


$R = \text{H, CH}_2\text{CHMe}_2, \text{CH}_2\text{Ph, (CH}_2)_2\text{SMe}$.



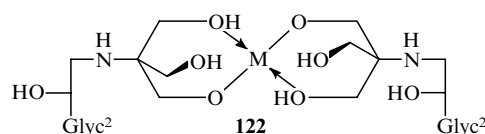
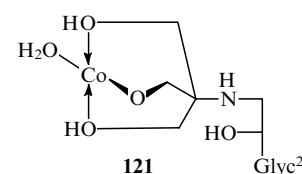
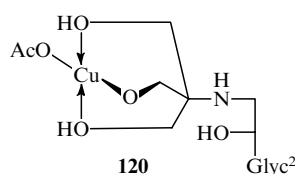
$M = \text{Rh, Ir}$.

Complexes of *N*-glycosylaminocarboxylate **50** with Cu^{2+} (**118**) have a square-planar structure, whereas with Co^{2+} and Ni^{2+} ions, octahedron **119** is formed involving the hydroxy groups at the C(5) atom of the carbohydrate fragment.^{19,112–115}



$M = \text{Ni(II), Co(II)}$.

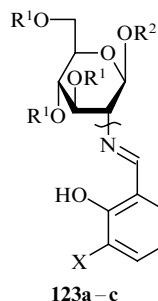
The structures of complexes of a carbohydrate amino derivative **49** with *d*-metal cations depend on the basicity of the medium. In alkaline media, reactions with the corresponding metal acetates yield monosaccharide complexes **120** and **121**, while in neutral media, bisaccharide complexes **122** are formed.⁶⁶



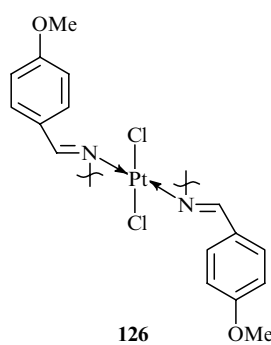
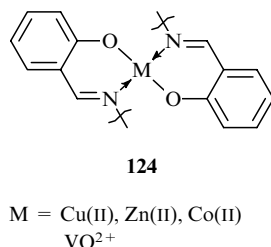
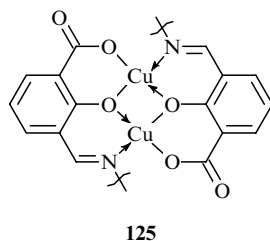
$M = \text{Cu(II), Ni(II)}$.

Some papers describe metal complexes of the Schiff bases prepared from natural and synthetic amino sugars. Thus the

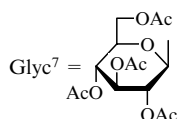
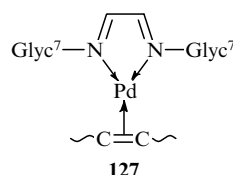
Schiff bases **123a,b** of both unprotected and protected D-glucosamine form ordinary bischelates **124**,^{116–118} while the carboxylic derivative **123c** reacts with Cu(II) to give the binuclear bridging complex **125**.¹¹⁷ In the case of Pt(II), the coordination involves the nitrogen atoms to yield complex **126**⁷ due to the absence of a donor substituent in the *ortho*-position of the aromatic ring (all the hydroxy groups in the carbohydrate fragment are acetylated).



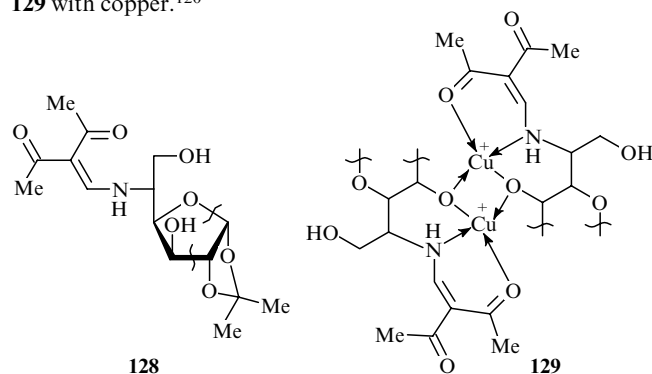
- a: R¹ = Ac, R² = Me, X = H;
 b: R¹ = R² = X = H;
 c: R¹ = Ac, R² = Me, X = CO₂H.



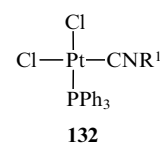
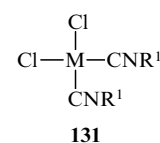
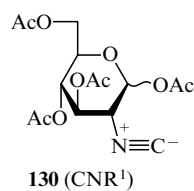
Mixed zero-valent palladium complexes **127** in which the double Schiff base is used as a carbohydrate ligand and dimethyl fumarate, fumarodinitrile and maleic anhydride are used as alkene components, have been synthesised.¹¹⁹



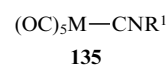
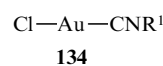
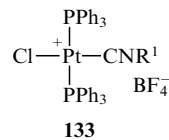
The coordination capabilities of amino sugars can be significantly enlarged owing to the introduction of coordinating fragments into the amino group as can be exemplified by the β-oxoamino derivatives **128**, which form binuclear complexes **129** with copper.¹²⁰



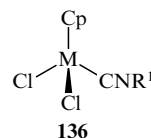
The ability of isocyanides, *e.g.*, compound **130** obtained from D-glucosamine, to enter into ligand exchange reactions was successfully employed¹²¹ in the preparation of complexes **131–136** with different structures. Complexes **132** and **134** can add other isocyanides as well as amines and alcohols, *e.g.*, with the formation of complexes **137**.¹²²



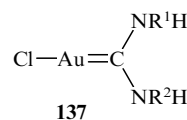
M = Pd, Pt.



M = Cr, W.

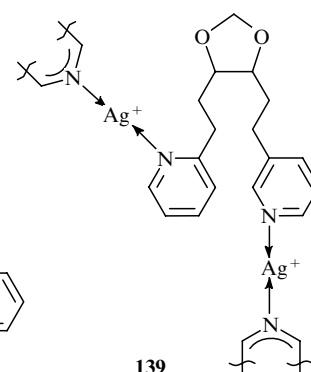
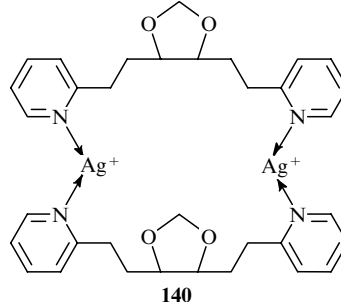
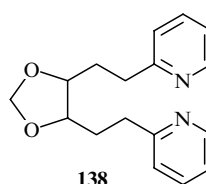


M = Rh, Ir.



R² = Bu^t, Ph.

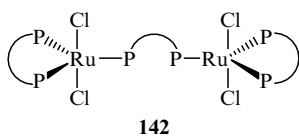
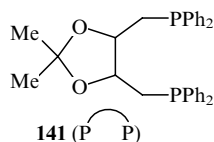
Special mention should be made of a yet another interesting peculiarity of the complexation of the compounds under discussion. The feasibility of a transfer of chirality from a carbohydrate ligand to a metal centre in metal complexes of chemically modified carbohydrates was demonstrated above. A most illustrative example of this phenomenon is the reaction of the diol derivatives **138** (obtained from tartaric acid) with silver triflate,¹²² which yields either the polymeric complex **139** in the form of a right- or left-handed helix (supramolecular polymeric complexes, helicates¹²³), or, in the case of the *meso*-diol, the cyclic dimer **140**, depending on the chirality of the starting diol.



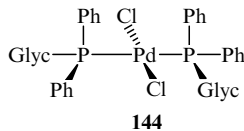
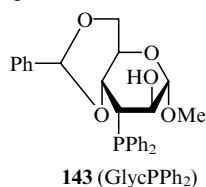
IV. Metal complexes of phosphorus-, sulfur- and selenium-containing monosaccharide derivatives

The discovery by Wilkinson of the ability of chlorotris(triphenylphosphine)rhodium(I) to efficiently catalyse homogeneous hydrogenation of alkenes at room temperature¹²⁴ gave a strong impetus to the appearance of a vast number of publications devoted to the molecular design and applications of this type of catalyst including enantioselective ones. This, in turn, generated the need for the synthesis of some organophosphorus carbohydrate derivatives, such as phosphines, phosphinites, phosphites and hydrogen phosphonates and phosphates.

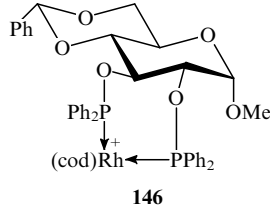
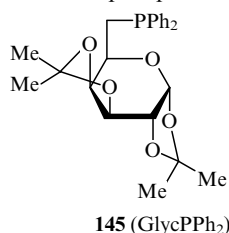
Chiral phosphines **DIOP** (**141**) are the most popular phosphine ligands used in catalysis; the ruthenium complex **DIOP–Ru₂Cl₄[(-)-DIOP]₃** has a hypothetical structure **142**.^{125, 126}



The monophosphine ligand **143** reacts with Pd(II) to give complex **144**.¹²⁷

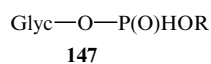


A series of [Rh(cod)(PPh₂Glyc)₂]ClO₄⁻ complexes (cod is cyclooctadiene) have been synthesised from acetalated monosaccharide monophosphine derivatives, *e.g.*, compound **145**.⁷

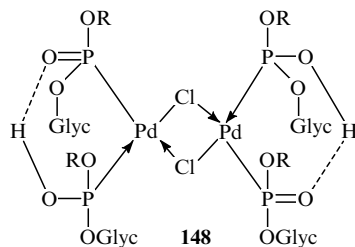


Synthetically more accessible phosphinites react with Rh(III) to yield complexes **146**^{3, 128–132} similar to monophosphine complexes of the acetalated ligands **145**.

Many studies by Russian investigators have been devoted to the complexation of carbohydrate phosphites (see, *e.g.*, a review¹³³). Thus hydrogen phosphonates derived from acetalated monosaccharides **147** yield palladium complexes **148**.^{134–137}

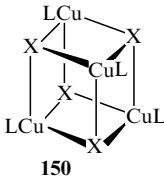
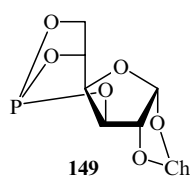


R = Et, Pr, Prⁱ;
Glyc is an acetalated monosaccharide residue.

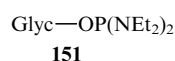


Treatment of the readily available phosphite (Glyc³O)₃P with Cu(CO)Cl gives the tetramer {CuCl[P(OGlyc³)₃]}₄ having a cubic structure.¹³⁸

The bicyclopophosphite complexes LCuX (L = **149**; X = Br, I),^{139–142} with a cubic structure (**150**) in the solid state, have been prepared.¹⁴³

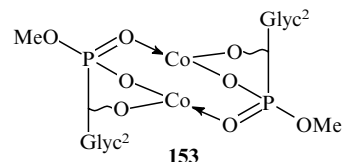
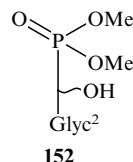


Phosphorodiamidites **151** form complexes (η³-C₃H₅)Pd(L)Cl and L₂Rh(CO)Cl¹⁴⁴ as well as *trans*-[PtCl₂L₂] (L = **151**).¹⁴⁵ Their structures and the coordination sites of metal ions have not been established.^{144, 145}

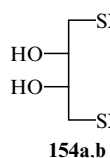


Glyc is an acetalated monosaccharide residue.

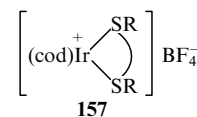
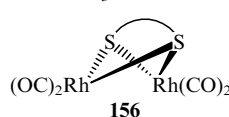
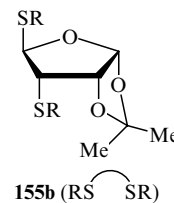
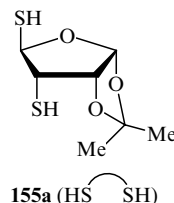
Carbohydrate phosphates have been investigated in less detail. The preparation of a cobalt complex with the phosphonate **152**¹⁴⁶ having a hypothetical dimeric structure **153** has been reported.



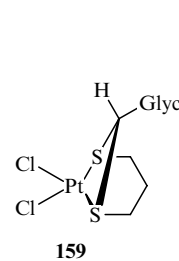
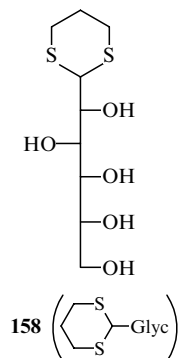
Some papers are devoted to sulfur- and selenium-containing monosaccharides, particularly thiolates and selenolates. These compounds are, in principle, soft bases, therefore the complexes of the corresponding carbohydrate derivatives with soft cations, such as Au⁺, and platinum metal cations (the principle of hard and soft acids and bases¹⁴⁷), have been studied first. Thus dithiol **154a** forms a mixed complex **154b** with gold(I).¹⁴⁸ The HS–SH group in the dithiol–rhodium complex **155a** forms a part of the chelate centre (structure **156**).⁷ The iridium cation in complex **157** prepared from the thioethers **155b** (R = Me, Prⁱ, Ph) is coordinated in a similar way.⁷



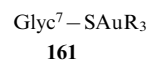
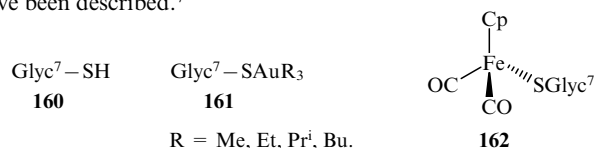
a: X = H
b: X = AuPEt₃.



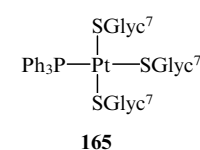
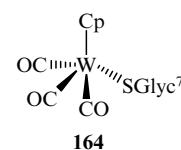
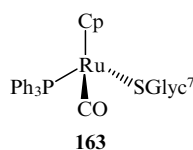
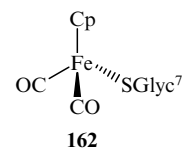
The readily available carbohydrate dithianes react smoothly with K₂[PtCl₄]; thus compound **158** yields the complex **159**.⁷



A fairly large number of papers are devoted to complexes of acetylated β-D-thioglucose **160**. Gold complexes **161** are used in medicine^{149, 150} along with analogous gold complexes containing a deacetylated carbohydrate fragment. Iron, ruthenium, tungsten and platinum complexes **162–165** with acetylated thioglucose have been described.⁷

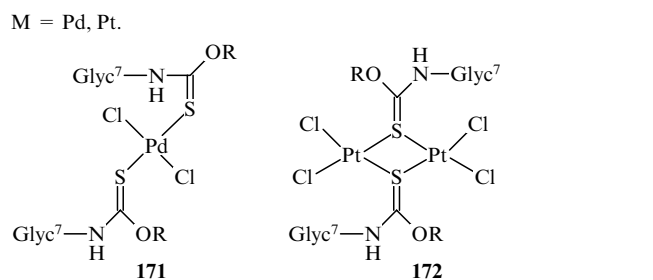
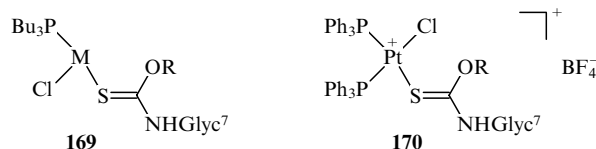
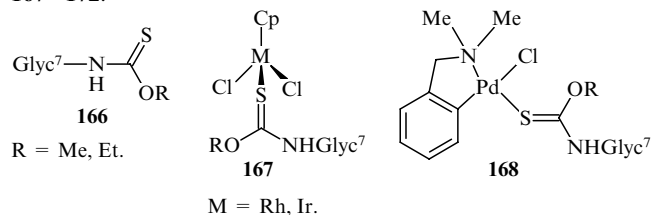


R = Me, Et, Prⁱ, Bu.

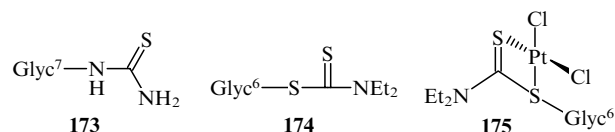


Some complexes of sulfur- and nitrogen-containing carbohydrate ligands have been investigated. Thiocarbamates **166** react

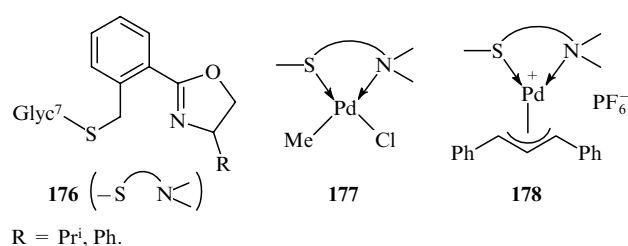
with bridge binuclear platinum complexes to yield complexes **167–172**.⁷



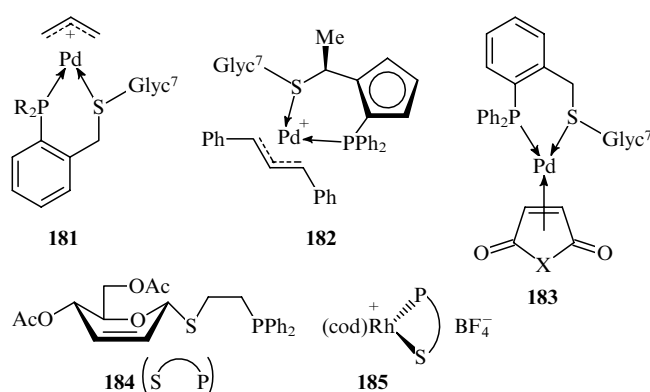
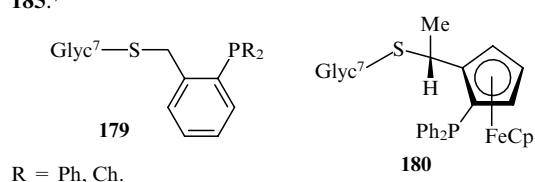
The metal atom in complexes with the thiourea ligand **173** (L) [M(η⁵-Cp)Cl₂L] (M = Rh, Ir), [Pd(*o*-C₆H₄CH₂NMe₂)ClL] and [MCl₂L₂] (M = Pd, Pt) is coordinated through the nitrogen atoms.⁷ The ligand **174** containing an *N,N*-dithiocarbamoyl fragment forms the complex **175** with bidentate *S,S*-coordination.⁷



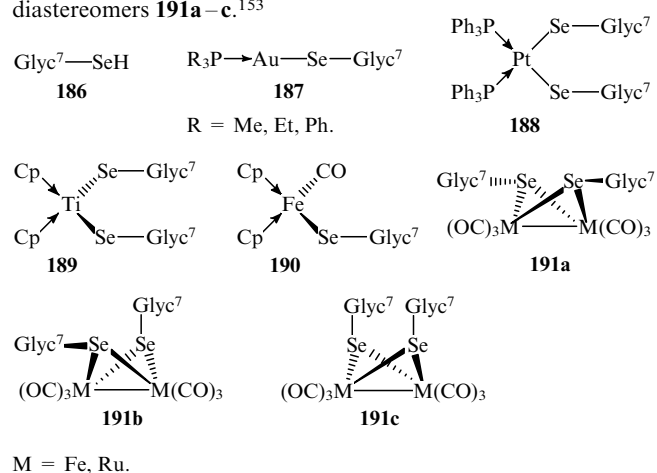
The dihydrooxazole thioglucose derivatives **176** form complexes **177** and **178** with palladium.⁷ By virtue of its allylic structure, the latter complex is represented by two diastereomers differing in the position of the central allylic proton relative to the dihydrooxazole substituent R.



π-Allylic complexes are also typical of ligands **179** and **180** containing both sulfur and phosphorus. Thus the aryl ligand **179** forms complexes **181**,^{7, 151} whereas the ferrocenyl ligand **180** yields the complex **182**.^{7, 152} Zero-valent palladium complexes **183** have also been prepared. An analogous derivative of the unsaturated thio sugar **184** coordinates the Rh(II) cation to yield the structure **185**.⁷



Selenium-containing monosaccharides described in the literature are represented only by the selenoglucose derivative **186**, which was used as a source of complexes **187–191** having different structures.^{7, 153} The latter complex represents a mixture of three diastereomers **191a–c**.¹⁵³



V. Conclusion

The progress in the coordination chemistry of carbohydrates is favoured by three main factors, *viz.*, inexhaustibility of this class of compound due to continuous photosynthetic reproduction, the diastereomeric purity of carbohydrates and the chirality of metal complexes formed from them, which is associated with chirality transfer from the ligands to the metal centres.

Chemical modification of monosaccharides enables one to enhance considerably their coordination capabilities, particularly owing to the diversity of their oxygen donor centres. Moreover, hydrophobisation of starting monosaccharides makes possible the preparation and further utilisation of their metal complexes in non-aqueous media.

Localisation of coordination points of monosaccharide metal complexes localised in close proximity to the ligands often changes their conformation, anomeric configuration and even the nature as a result of molecular rearrangements (see, *e.g.*, Ref. 6 and this review). Mention should be made in this connection of the conversion of oximes of the aldehydo-forms of monosaccharides into the corresponding amides in the presence of Cu²⁺ (Beckman rearrangement).¹⁵⁴ Although such rearrangements are still very rare, their number will inevitably increase and, as a consequence, novel methods for the modification of carbohydrates by complexation with metals will be developed. At present, the chemistry of carbohydrates is still imperfect due to the use of accessory reagents, formation of side products, *etc.*¹⁵⁵ In our opinion, progress in this area will be achieved through further development of the coordination chemistry of modified carbohydrates.

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Metal-oxide based nanoobjects: reactivity, building blocks for polymeric structures and structural variety †

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Abstract. From the unique ‘library’ of molybdenum-oxide based building blocks/fragments under reducing conditions in aqueous solution a huge variety of nanoobjects, allowing specific reactions at well-defined positions, can be generated. This enables us to perform a new type of nanochemistry. Examples include the well-known molecular big-wheel of the type {Mo₁₇₆} and big-ball of the type {Mo₁₃₂} including their derivatives which are considered here. In addition, the by far largest structurally well-characterised cluster having 368 molybdenum atoms with the shape of a lemon is outlined and discussed. The bibliography includes 71 references.

I. Introduction

The deliberate synthesis of multifunctional compounds and materials from well-known building blocks which can be easily generated or are available from a ‘virtual’ library is one of the most challenging problems in contemporary chemistry. Pertinent targets include the synthesis of materials, *e.g.*, based on cross-linked building blocks with desirable electronic properties. In solutions of oxoanions of the early transition elements an enormous variety of compounds can be formed by linking together metal–oxygen building blocks.^{1–9} The corresponding reactions are based on libraries with (virtual) building blocks, *i.e.* polyoxometallate (POM) fragments which, under appropriate conditions, lead to the generation of clusters ranging from those of mere aesthetic beauty to unusual materials. Examples include the spherical cluster anion {Mo₇₂^{VI}Mo₆₀^VO₃₇₂(CH₃COO)₃₀(H₂O)₇₂}^{42–} (also known as an inorganic superfullerene or keplerate[‡]), and the ring-shaped cluster anion {Mo₁₂₆^{VI}Mo₂₈^VO₄₆₂H₁₄(H₂O)₇₀}^{14–} (see Fig. 1 and reviews cited above). Additionally, interesting molecular magnets, novel-type supramolecular compounds, compounds with extended structures including those with mesoporous networks,^{3–7} and surfactant-encapsulated giant clusters soluble in organic solvents (with the option of generating monolayers and Langmuir–Blodgett films) can be obtained.^{10–14} In this context, we intend here to demonstrate perspectives for a new type of nanochemistry by highlighting:

- the possibility of performing reactions at well-defined positions of well-defined nanoobjects;
- the possibility of linking the nanoobjects;
- the possibility of obtaining numerous novel giant members of this ‘nanosociety’.

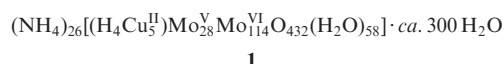
The results described here are not included in previous reviews.^{1–9}

II. Reactions at well-defined sites of well-defined nanoobjects: an example

1. Synthetic and structural aspects

The possibility of performing chemical reactions at well-defined sites of well-defined nanoobjects opens up interesting perspectives for the chemist, especially if novel functionalities emerge.^{1–17} For example, the high-yield facile synthesis of giant spherical {Mo₁₃₂} (Fig. 1 *a*)¹⁸ and ring-shaped {Mo₁₅₄} (Fig. 1 *b*)^{19,20} (first reported in Ref. 19 but not with optimal synthesis) molybdenum-oxide based clusters provides us with easily accessible nanostructured landscapes with nano-sized cavities and a variety of different functional groups. In particular, it proved possible to incorporate paramagnetic metal centres, *e.g.*, Cu²⁺ ions, inside the tetrahedral cavities of the {Mo₁₅₄}-type rings formed by four O atoms with appropriate size. It is significant that our approach paves the way to the deliberate synthesis of a broad range of compounds, which can be obtained by altering the boundary conditions, such as the pH, temperature, and/or the presence of different substrates, while on the other hand, it also opens up new perspectives for studies in the sense of a novel type of self-assembly (see also Ref. 21).

The synthesis of a cluster containing Cu²⁺ ions involves reduction of an acidified aqueous polymolybdate with copper powder. The ammonium salt of this cluster is obtained as the black crystalline compound **1**.¹⁵



Single crystal X-ray diffraction studies show the presence of the [{Mo₈^{V/VI}O₂₆(μ₃-O)₂X_i(H₂O)₃Mo^{V/VI}}]₁₄{Mo₂^{VI}O₅(H₂O)₂}₈]^{26–} cluster anion (ΣX_i = 4H + 5Cu) (**1a**), which can be considered as

† Dedicated to Prof. Ilya Moiseev.

‡ By definition, keplerates are compounds having one central point, the barycentre (either occupied by an atom or vacant), around which one or more spherical shells of atoms contained in the cluster are located. These atoms are vertices of Platonic or Archimedean solids.

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a derivative of the aforementioned prototypal tetradecameric ring-shaped cluster anion $\{\text{Mo}_{154}\}$, ($\{\text{Mo}_{154}\} \equiv \{\text{Mo}_8\}_{14}\{\text{Mo}_1\}_{14}\{\text{Mo}_2\}_{14}$) (**2a**).^{4–7} The cluster anion **1a** lacks six $\{\text{Mo}_2\}$ building blocks as compared to the parent $\{\text{Mo}_{154}\}$ anion. Moreover, it contains non-uniformly distributed Cu^{2+} centres — with a maximal occupation number of 0.73 — in the 14 tetrahedral cavities marked by four oxygen atoms. The Cu^{2+} cations replace five of the 14 protons of the parent cluster **2a**, which are bonded to one of the two $\mu_3\text{-O}$ atoms that are involved in the formation of the cavities (Fig. 2). In the case of high H^+ ion concentrations, the maximum degree of protonation is attained, *i.e.*, all fourteen cavities of the cluster **1a** are occupied by protons bonded to the $\mu_3\text{-O}$ bridging atom.⁵ In presence of the HCOONH_4 buffer, the degree of protonation of cluster **1a** is lower and consequently Cu^{2+} ions can be coordinated to the basic four O atoms of the corresponding tetrahedral cavity.

2. Electronic spectra and magnetic aspects

Although the resonance Raman ($\lambda_e = 1064$ nm) and IR spectra of **1a** are nearly identical to those of the parent cluster **2a**, the electronic spectrum of the former exhibits, as a result of the abundance of Cu^{2+} centres, an additional band at ~ 520 nm and a blue shift of the higher energy intervalence charge transfer (IVCT) transition localised in the $\{\text{Mo}_5^{\text{V/VI}}\text{O}_6\}$ -type compartments,⁵ each of them containing two delocalised $4d$ electrons. The change in the charge transfer is caused by the fact that the encapsulated Cu^{2+} ions are coordinated to the $\mu_3\text{-O}$ atoms which belong to the $\{\text{Mo}_5\text{O}_6\}$ compartments, thus resulting in an electron density redistribution in this compartment.

The room-temperature EPR powder spectrum of compound **1** is similar to the spectra of tetrahedral copper complexes containing $\{\text{CuX}_4\}$ groups, in particular, $\{\text{CuO}_4\}$ types, and therefore indicating the presence of Cu^{2+} (d^9) centres. The spectrum is characterised by $g_x = 2.07$, $g_y = 2.15$, and $g_z = 2.37$, as well as by the hyperfine splitting constant $A_z = 125$ G (related to the nuclear spin of $^{63/65}\text{Cu}$ with $I = 3/2$). The values indicate that the $\text{Cu}^{2+} \cdots \text{Cu}^{2+}$ magnetic interactions are practically negligible ($\text{Cu} \cdots \text{Cu} \approx 6.2$ Å). This observation is also supported by magnetic susceptibility measurements. At high temperatures, the $\chi_{\text{mol}}T$ curve was found to reach a plateau at ~ 2.86 emu K mol^{−1}, which corresponds to about six Cu^{2+} centres per formula unit for $g = 2.2$. As the calculated inter- and intra-molecular antiferromagnetic coupling constants are very small, $\chi_{\text{mol}}T$ decreases only at temperatures below ~ 20 K. The temperature variation of the magnetic susceptibility can be described using the Curie–Weiss equation

$$\chi = \frac{C}{T - \theta}$$

with a very low Weiss temperature ($\theta = -0.5$ K).¹⁵

3. General aspects

Modification of the parent $\{\text{Mo}_{154}\}$ ring-type cluster anion **2a** — by introduction of paramagnetic Cu^{2+} ions under certain self-assembly conditions — is possible because of the presence of O_4 -type cavities with dimensions in agreement with the characteristic $\text{Cu}—\text{O}$ distances (2.0 ± 0.1 Å). The assembly of this cluster starts from simple mononuclear $\{\text{Mo}_n\}$ -type units, followed by the construction of larger intermediate building blocks (abundant in a virtual ‘library’), which are finally transformed into a mesoscopic organised complex ring-shaped structure — with a variety of functional groups — *via* molecular recognition processes for Cu^{2+} centres which get integrated at the suitable sites of the cluster.

The highly symmetrical mesoscopic $\{\text{Mo}_{154}\}$ -type parent cluster (see Fig. 1), which is the primary target of the self-assembly process in this case based only on molybdate, can undergo a variety of modifications due to alteration of the boundary conditions, or in other words, due to environmental influences, as for example, the presence of Cu^{2+} ions.

In this context, it is important to remember that assembly processes based on simple building blocks lead preferably to highly symmetrical species,[§] such as rings.^{4,5} This is consistent with many observations in cluster chemistry (see, for example, Ref. 24). Important is in this context that mesoscopic systems can, in spite of a high overall symmetry, exhibit versatile reactivity owing to the presence of large numbers of substructures with different functional groups. This feature is especially noteworthy as the accepted view is that higher symmetry leads to a decrease in the number of structural details and therefore reactivities. This rule actually only holds for smaller discrete species and crystalline systems with macroscopic homogeneity and microscopic translational invariance but not for discrete mesoscopic molecular-type species. An example for relevant mesoscopic systems is the situation with spherical viruses, mentioned in most biochemistry books.

It follows from the foregoing discussion that the molybdenum-oxide based ring-shaped clusters can be considered as nanostructured landscapes having a variety of functional groups at well-defined positions.^{4–7,20} This permits various types of reactions, including catalytic ones, to be carried out at strictly defined positions. These reactions include coordination of activated ligands, but also amphiphilic and multiphilic ones (for example, diprotonated cysteine ligands[¶]), which may lead to the generation of unusual surfaces within the cavities,²⁵ and the incorporation of metal centres or small fragments into appropriate cavities.

Another conclusion related to this work is that the reactivity and the electron density distribution in nanoobjects can be varied both by defect generations and by incorporation of open-shell heterometal atoms. In this particular case, the influence of the Cu^{2+} metal centres on the distribution of delocalised electrons within the above-mentioned compartments is indicated by the shift of the IVCT band from ~ 750 nm for the parent $\{\text{Mo}_{154}\}$ anion⁵ to ~ 680 nm for anion **1a**.¹⁵ Thus, one can adjust (tune) the electron density distribution, and even the related catalytic activity of the present type of nanoobjects, which can act as selective oxidants.²⁶

III. Nanoobjects as building blocks for extended structures

1. Synthetic and structural aspects

The search for extended structures based on linked nano-sized stable (!) building blocks and possessing specified electronic and magnetic properties is an exceptionally worthy task because such compounds could provide new types of functionalised materials.²⁷ In this context we attempted the synthesis of the large well-defined metal-oxide based nanoparticles with unique host properties in order to use them as building blocks. Linking these blocks according to $\text{M}—\text{O}—\text{M}$ or $\text{M}—\text{O}—\text{M}'$ patterns can furnish, in principle, a broad range of compounds differing in architecture.

Our route to unique extended structures involved the use of spherical metal-oxide based keplerate-type clusters with icosahedral symmetry.^{4,5} (The internal cavity diameter in this type of structures is sufficiently large even for encapsulating Keggin-type clusters. The related composites could be prepared through a facile synthesis.²⁸) Linking such large spherical objects gives rise

§ The process can formally (!) be correlated with a general symmetry formalism or symmetry-evolution principle for a quasi-isolated system.²² One important aspect of the symmetry-evolution principle is that the highly symmetrical species are often also preferably formed as they are kinetically inert. However, this principle is inapplicable to macroscopic chemical reaction systems as structure-formation-based precipitation is equivalent to symmetry breaking.²³

¶ Multiphilic ligands like cysteine containing various functional groups ($-\text{NH}_3^+$, $-\text{CO}_2\text{H}$, $-\text{S}—\text{S}—$) can be coordinated to the inert wall of the cavity.

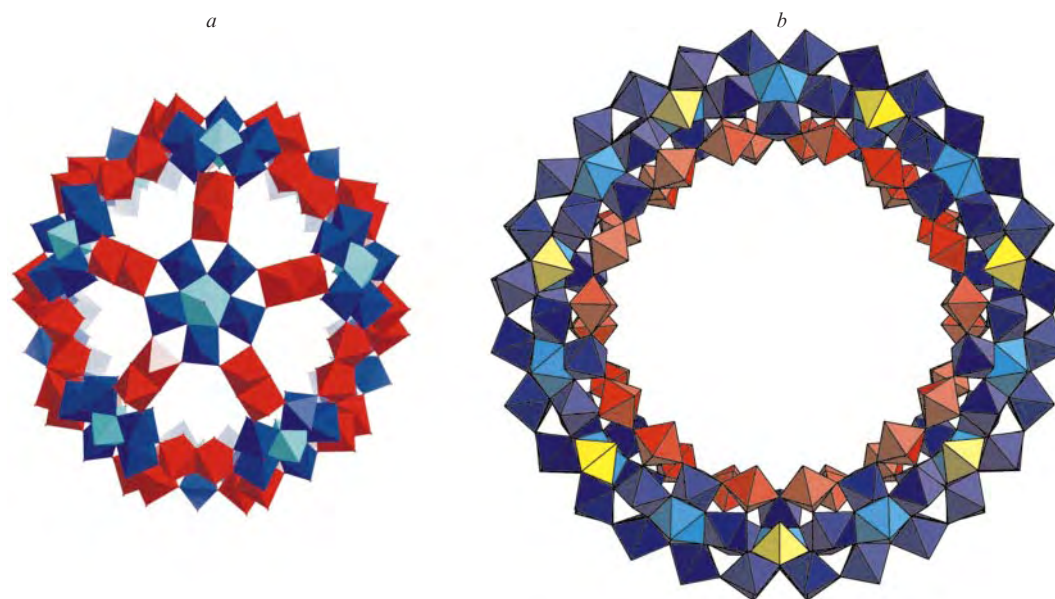


Figure 1. Spherical $\{\text{Mo}_{132}\}$ - (a) and ring-shaped $\{\text{Mo}_{154}\}$ -type (b) clusters (the $\{\text{Mo}_1\}$ unit cannot be seen in this view; see Fig. 2) shown in polyhedral representation. The spherical cluster shows the pentagonal units in blue and the linkers in red.

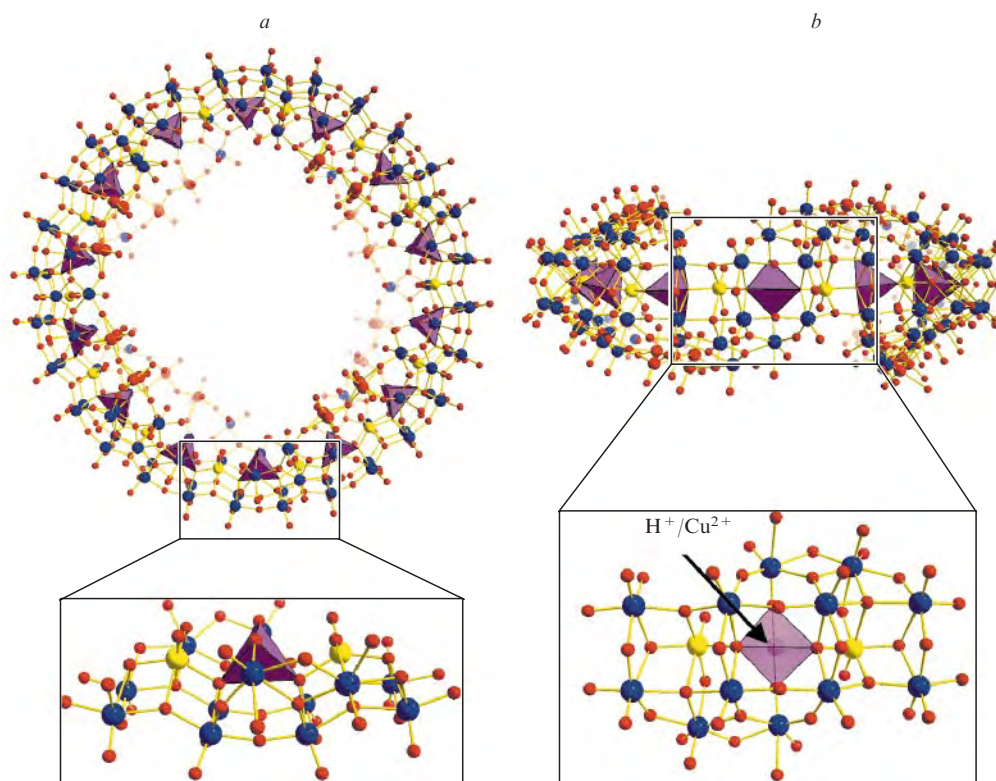
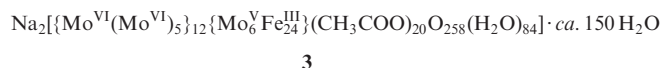


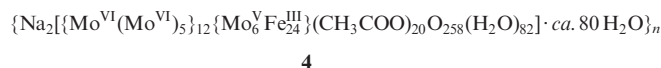
Figure 2. Molecular structure of the cluster anion **1a** [top (a) and side (b) views] in crystals of **1** in the atomic representation. The $\{\text{O}_4(\text{Cu})\}$ tetrahedra are given in polyhedral representation. Colour code: oxygen is red, molybdenum is blue, except those of the $\{\text{Mo}_1\}$ shown in yellow. This drawing was first published in Ref. 15.

for instance to chain-type structures. Analogous chain structures are also produced upon linking fullerenes.^{29–31}

As an example, we shall consider the synthesis and structure of an unusual mixed-valence compound **3**, containing the discrete $\{\text{Mo}^{\text{VI}}(\text{Mo}^{\text{VI}})_5\}_{12}\{\text{Mo}_6^{\text{V}}\text{Fe}_{24}^{\text{III}}\}$ -type keplerate cluster **3a**.¹⁶



The black compound **3** is formed upon the addition of iron(II) chloride to an aqueous solution of sodium molybdate acidified with acetic acid in presence of air. Upon drying, a novel type of room-temperature solid-state reaction takes place, yielding compound **4** with a chain structure.¹⁶



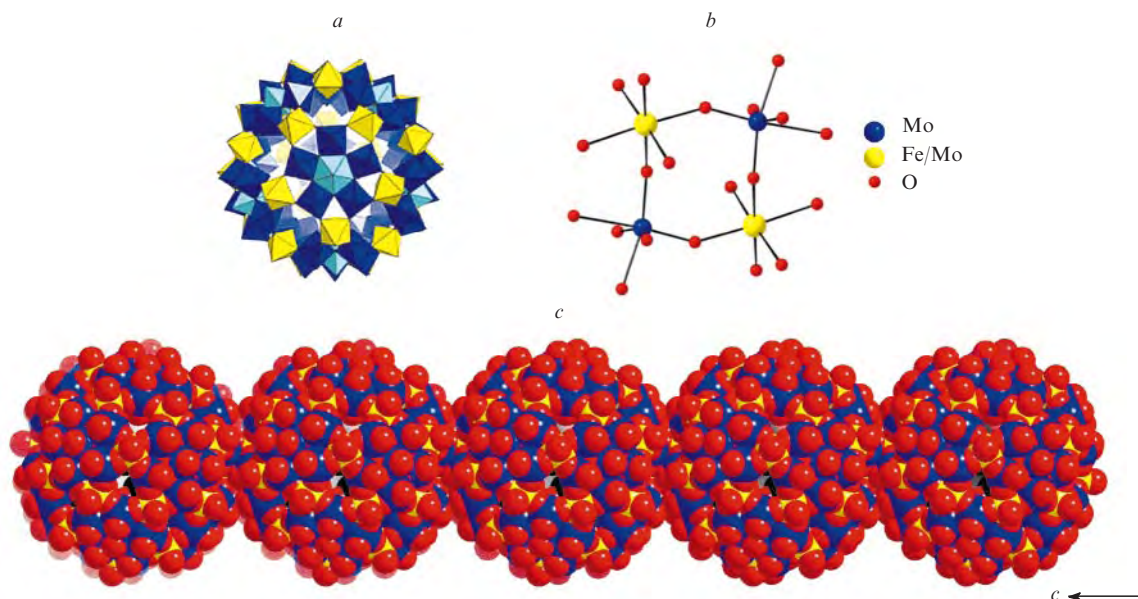


Figure 3. Structure of the discrete anion **3a** in crystals of **3** (*a*, polyhedral representation); structure of the chain **4a** in crystals of **4** (*c*, space-filling representation; the Mo positions can be identified), and the linking area of the chain **4a** [*b*, atomic representation; bond lengths (Å) and angles (deg) in the $\{\text{M}_4\text{O}_4\}$ rings ($\text{M} = \text{Mo}/\text{Fe}$): $\text{Mo}-\text{O}$: 1.72–1.78; $\text{Fe}-\text{O}$: 1.96–1.98; $\text{Mo}-\text{O}-\text{Fe}$: 147.0–149.9; $\text{O}-\text{Mo}-\text{O}$: 101.5; $\text{O}-\text{Fe}-\text{O}$: 93.2]. This drawing was first published in Ref. 16.

(In general, mixed-valence compounds of this type with extended structures possess remarkable electronic properties.³²)

During the formation of **3**, Fe^{II} ions are oxidised to Fe^{III} , only a minor portion of the Fe^{II} ions being used to reduce Mo^{VI} centres. Nevertheless, the presence of Fe^{II} ions is necessary, because beginning the synthesis with Fe^{III} as the starting material leads even in the presence of a reducing agent immediately to a non-crystalline precipitate.

Both the spherical cluster $[\{\text{Mo}^{\text{VI}}(\text{Mo}^{\text{VI}})_5\}_{12}\{\text{Mo}_6^{\text{V}}\text{Fe}_{24}^{\text{III}}\} \cdot (\text{CH}_3\text{COO})_{20}\text{O}_{258}(\text{H}_2\text{O})_{84}]^{2-}$ (**3a**) (note: there is an error limit in the charge) and the related chains comprise 12 pentagonal $\{\text{Mo}^{\text{VI}}(\text{Mo}_5^{\text{VI}}\text{O}_{21})\}$ -type building blocks, containing a central pentagonal $\{\text{MoO}_7\}$ bipyramid sharing edges with five $\{\text{MoO}_6\}$ octahedra. The pentagonal fragments are connected through 24 $\{\text{Fe}^{\text{III}}(\text{H}_2\text{O})_2\}^{3+}$ and 6 $\{\text{Mo}^{\text{VO}}(\text{H}_2\text{O})\}^{3+}$ linkers which are statistically distributed over the 30 vertices of an icosidodecahedron.[†] The six *4d* electrons of the Mo linkers are partially delocalised over positions of the pentagonal $\{\text{Mo}(\text{Mo}_5)\}$ building groups. The bidentate acetate ligands are located inside the sphere and are coordinated simultaneously to the two metal atoms Fe and Mo. Thus, they function as bridges between the Fe and Mo centres. In the crystals of **4**, the icosahedral spherical building blocks, *i.e.*, of the type $\{\text{Mo}(\text{Mo}_5)_5\}_{12}\{\text{Mo}_6\text{Fe}_{24}\}$ (Fig. 3*a*), are linked to form chains (Figs 3 and 4 as well as Scheme 1) through $\text{Mo}_\text{A}-\text{O}-\text{Fe}_\text{B}$ and a $\text{Fe}_\text{A}-\text{O}-\text{Mo}_\text{B}$ group (A and B stand for two neighbouring spheres). This results in a nearly square $\{\text{Fe}_2\text{Mo}_2\}$ fragment (Fig. 3*b*) the centre of which coincides with a crystallographic inversion centre. Interestingly, the geometric details of the $\text{Fe}_\text{A}-\text{O}-\text{Mo}_\text{A}$ - (inside a sphere), $\text{Fe}_\text{A}-\text{O}-\text{Mo}_\text{B}$ - and $\text{Fe}_\text{B}-\text{O}-\text{Mo}_\text{A}$ -type units do not differ significantly ($\text{Mo}\cdots\text{Fe} \sim 3.6$ Å). As shown below, this has important implications for the magnetic properties of compound **4**. The $\{\text{Fe}_2\text{Mo}_2\}$ square fragment in **4** is topologically equivalent to the cyclobutane fragment found in dumbbell-shaped $\{\text{C}_{60}\}_2$ dimers. The latter unit is also built up by two intra- and two inter-sphere C–C bonds.²⁹

[†] The presence of octahedral $\text{Fe}^{\text{III}}\text{O}_6$ groups could also be proved by Mössbauer spectroscopy. The presence of one $\{\text{Mo}^{\text{VI}}\text{O}\}^{4+}$ linker group, instead of $\{\text{Mo}^{\text{VO}}\}^{3+}$, and the related change of the number of Na atoms cannot be completely ruled out within the error limits of the invoked analytical techniques.

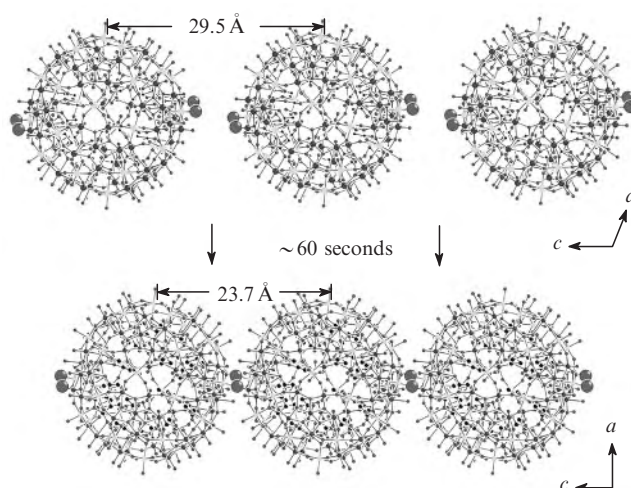
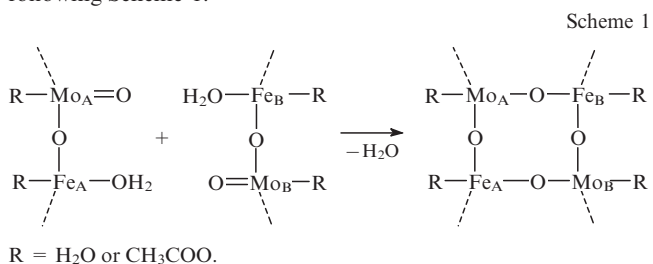
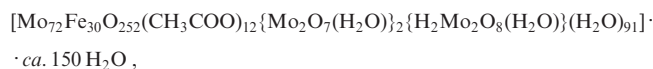


Figure 4. Schematic demonstration of the room-temperature solid-state reaction leading to the formation of the chain of **4** caused by linking the spheres **3a**. This drawing was first published in Ref. 16.

When compound **3** loses crystal water, the discrete spherical clusters **3a** approach one another, which is followed by their condensation to give infinite chains. The linking is caused by the fact that H_2O ligands in the $\{\text{Fe}^{\text{III}}(\text{H}_2\text{O})_2\}^{3+}$ fragments in sphere A are substituted by terminal $\text{Mo}=\text{O}$ groups of the $\{\text{Mo}(\text{Mo}_5)\}$ pentagons belonging to the neighbouring sphere B. Thus, the $\text{Mo}=\text{O}$ group formally acts as ligand in accordance with the following Scheme 1.



The reaction is driven by the gain in entropy caused by the release of water molecules. This solid-phase S_N -type reaction, which functions well for compound **3**, does not happen, however, for the yellow compound **5**



5

which contains the $\{\text{Mo}^{\text{VI}}(\text{Mo}_5^{\text{VI}})\}_{12}\{\text{Fe}_{30}^{\text{III}}\}$ -type discrete neutral clusters.^{33,34} The reason is that cluster **3** shows the S_N -type reaction initiated by the $\text{Mo}=\text{O}$ groups due to the increase in the electron density on the terminal oxygen atoms of these groups caused by the influence of six partially delocalised $4d$ electrons, which are not abundant in the non-reduced **5**.

Not only the crystallinity but also the space group ($P2_1/n$) is preserved throughout the solid-state reaction $\mathbf{3} \rightarrow \mathbf{4}$. Comparison of the packing of the spherical clusters **3a** in the crystal lattices of compounds **3** and **4** has shown that the distances between the spherical $\{\text{Mo}(\text{Mo})_5\}_{12}\{\text{Mo}_6\text{Fe}_{24}\}$ -type units in **4** are shortened drastically along the crystallographic c axis (see Fig. 4) compared to the corresponding distances in **3**; as a result, the crystal lattice parameter c in **4** is 5.7 Å shorter than that in **3**.

2. An interesting mesoscopic magnetism

A convenient way of explaining the magnetism of compound **4** is to compare it with the cluster of compound **5** (see Refs 33, 34), which is the largest molecular paramagnet known.³⁵ In both systems, the antiferromagnetic exchange interactions between the $\text{Fe}(\text{III})$ centres ($S = 5/2$) abundant in a nearly perfect octahedral environment are mediated by the $\text{O}-\text{Mo}-\text{O}$ groups.

In the case of **5**, the $\chi_{\text{mol}}T$ value increases with an increase in T from 20 to 300 K (Fig. 5), and at room temperature, it approaches the value expected for 30 uncorrelated centres with $S = 5/2$, namely, 131.25 emu K mol⁻¹ (the spin-only value for $g = 2.0$). The room-temperature value of $\chi_{\text{mol}}T$ found for compound **4** is equal to 104.0 emu K mol⁻¹, which is closely similar to the value (105.0 emu K mol⁻¹) expected for 24 uncorrelated $\text{Fe}(\text{III})$ centres with $S = 5/2$. Since the partially delocalised $\text{Mo } 4d$ electrons in **4**, as in the reduced $\{\text{Mo}_{102}\}$ -type keplerate,³⁶ are strongly coupled, they contribute only to a negligible extent to the overall magnetic moment. Thus, the high-temperature results indicate that six of the thirty positions of the icosidodecahedron occupied by $\text{Fe}(\text{III})$ magnetic centres in the cluster of **5** are occupied in **4** by effectively non-magnetic centres. The magnetic susceptibilities measured in the 20–300 K range are in very good agreement with the Curie–Weiss function down to very low temperatures; however, the Weiss temperatures calculated for **4** and **5** differ significantly: $\theta(\mathbf{4}) = -13 \text{ K}$, $\theta(\mathbf{5}) = -21.6 \text{ K}$.

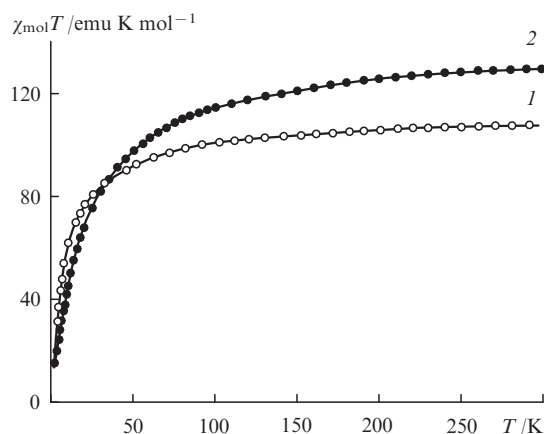


Figure 5. Comparison of the temperature dependences of $\chi_{\text{mol}}T$ for compounds **4** (curve 1) and **5** (curve 2).

These $\theta(\mathbf{4})$ and $\theta(\mathbf{5})$ values can be explained in terms of the following simple model. Since the geometric parameters of the corresponding $\text{Fe}-\text{O}-\text{Mo}-\text{O}-\text{Fe}$ groups, including the bridges between the spheres, are virtually identical in compounds **4** and **5**, the same single Heisenberg exchange constant J is assumed for the nearest-neighbour $\text{Fe}\cdots\text{Fe}$ interactions (see Ref. 37). Important is that θ is proportional to the absolute number of nearest-neighbour $\text{Fe}\cdots\text{Fe}$ contacts per sphere.[‡] This number is lower for compound **4** than for **5**, due to the presence of six centres that do not effectively contribute to paramagnetism, *i.e.*, that are effectively non-magnetic. A uniform statistical distribution of the non-magnetic centres over the 30 icosidodecahedron vertices results in 38 $\text{Fe}\cdots\text{Fe}$ contacts compared to the 62 contacts of a hypothetical all-iron configuration including 60 icosidodecahedron edges and 2 distinct bridges to the adjoining spheres in the chain. Thus, proceeding from the value $\theta(\mathbf{5}) = -21.6 \text{ K}$, we obtain $\theta(\mathbf{4}) = 38/62 \times \theta(\mathbf{5}) = -13.2 \text{ K}$, which is in excellent agreement with the value experimentally determined.

It is of interest to compare the case of uniform distribution of effectively non-magnetic centres with other distribution patterns, for example, the arrangement of all the non-magnetic centres on neighbouring sites of the icosidodecahedron. In this case, the Weiss temperature should increase to -18 K . Thus, the calculated $\theta(\mathbf{4})$ value perfectly reflects the uniform distribution of the magnetic centres in each individual sphere (with a ratio of the numbers of magnetic to non-magnetic positions equal to 24 : 6). If the average ratio equal to 24 : 6 is retained, while the magnetic to non-magnetic centre ratio in different spheres can be different, this situation cannot strictly correspond to the determined Curie–Weiss parameter. It is noteworthy that, because the Weiss temperature reflects the ordering and the distribution of the non-magnetic centres over the thirty possible positions, this value can be used to draw structural conclusions that cannot be obtained from the single crystal X-ray structure analysis.[§]

3. General outlook

Now we consider an interesting result related to the chemistry of extended structures. Spherical molybdenum-oxide based keplerate-type clusters possess a number of interesting features,²⁸ in particular, they can be used as building blocks in the development of various extended structures and nanomaterials. The linking of nano-sized spherical capsule-type objects, for instance, can lead to one-dimensional chains *via* a room-temperature solid-state reaction which can be regarded as a type of crystal engineering process. In view of the fact that we are dealing with spherical capsules of the type $(\text{Pentagon})_{12}(\text{Linker})_{30}$ ($\text{Linker} = \{\text{Fe}(\text{H}_2\text{O})\}^{3+}$, see Refs 33, 34, $\{\text{MoO}(\text{H}_2\text{O})\}^{3+}$, see Ref. 36), the linkers L can be changed stepwise with the option to change the surface properties. For example, by changing appropriately the degree of electron density on the surface of cluster **3**, by increasing in the present case the number of $\{\text{MoO}(\text{H}_2\text{O})\}^{3+}$ groups, the nucleophilicity of this cluster can correspondingly be increased, which could lead to different types of inter-sphere condensation reactions. In summary, the type of linking of the spherical units depends on the $\text{MoO}^{3+}/\text{Fe}^{\text{III}}$ ratio.

In addition, the presence of two $\text{Fe}^{\text{II}}\cdots\text{Mo}^{\text{VI}}$ and $\text{Fe}^{\text{III}}\cdots\text{Mo}^{\text{V}}$ couples with very close redox potentials makes compounds **3** and **4** especially interesting. In particular, this type of electronic structure can induce a temperature-dependent electron transfer in **4a**. In this context it is important to realize that the Fe and Mo atoms

[‡] This result follows from the standard expression for θ determined for systems with a single exchange constant.

[§] Single-crystal X-ray structure analysis does not allow one to distinguish between the situation of all spherical units having the same composition (as in the present case) and the situation where certain spheres have different compositions but also yield altogether for the whole compound the same $\text{Fe}^{\text{III}}/\text{Mo}^{\text{V}}$ average ratio of 24 : 6.

in solid metal oxides which occupy octahedral positions obey the following equilibrium:³⁸



The mentioned type of electron transfer is similar to electron delocalisation or hopping in ‘heteropoly blues’.¹ This was confirmed by quantum-chemical calculations for electron transfer transitions in substituted (at the metal) polyoxometallates and by Mössbauer spectroscopy data for the iron-substituted cerium salt of 12-molybdenophosphoric acid, containing 0.6 Fe^{II} atoms as the counter-cations and 0.9 Fe^{II} atoms in the Keggin part.³⁹ The Mössbauer spectrum of this compound measured at room temperature differed from the spectrum recorded at very low (4.2 K) temperature.³⁹ Other examples of electron hopping and delocalisation in mixed-valence oxometallate clusters have also been reported.⁴⁰

Finally, the 3 → 4 transformation and the resulting products are just one of a myriad of options that can be achieved in the future investigations of ‘our’ POM system.

IV. Extending the structural variety

1. General aspects

Nature’s evolution from the primordial earth to the present overwhelming variety of macroscopic forms and functionalities, the formation of which is directed by their molecular ‘counterparts’, *i.e.*, nano-sized biomolecules, should stimulate thoughts about the potential of material systems in general and the related first principles, *i.e.* natural laws.

We refer to processes based on reservoir systems containing appropriate building blocks, the linking of which can lead to an overwhelming or even, in a kind of combinatorial explosion, to practically an infinite number of molecular forms. This process is particularly valid on passing to the nanocosmos size category. The nanocosmos as such does not show the variety-limiting translational symmetry restriction of macroscopic crystalline materials but offers — unlike the microcosmos with its small molecules — the possibility of existence of larger arrays with local symmetries which are not in agreement with the overall symmetry. This is a well-known situation for spherical viruses with their hexagonal arrays. Figure 6 shows a model of the protein subunits of the Tomato Bushy Stunt Virus (TBSV) as an icosadeltahedron.^{41, 42}

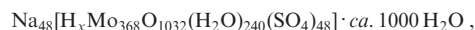
In order to get a huge variety of structures the appropriate fragments chosen as building blocks should display a certain type of flexibility, which is a prerequisite for an extreme linking versatility of course not reaching by far that of amino acids.[†] This condition is well fulfilled by molybdenum-oxide based fragments which are collected as (virtual) building units in a ‘dynamic library’ with a potential to participate in a sort of ‘split and link’ processes depending on slight alterations of the relevant boundary conditions.

Remarkable in this context is the synthesis of a rather unusual giant molybdenum-oxide based nanocluster with the size of hemoglobin containing 368 metal and 1880 non-hydrogen atoms. The cluster has been formed by linking 64 {Mo₁}-, 32 {Mo₂}- and 40 {Mo(Mo₅)}-type units. The formation process was accompanied by a remarkable symmetry breaking process, which is nicely recognisable at the cluster surface. The preparation of the {Mo₃₆₈} nanocluster can be considered as the starting point for the synthesis of quite a number of other clusters with a comparable or even larger size. Referring to the present discovery we would like to attract attention to the momentous and far-

reaching step into the nanocosmos with perspectives for nano-chemistry (*via* symmetry breaking), molecular topology and surface sciences with catalytical relevance. The above-mentioned symmetry breaking can be considered in relation to a transition from positive to negative surface areas, *i.e.*, the monotony breakdown.

2. Synthesis and structure

The reduction of a molybdate solution acidified by sulfuric acid gives the dark blue compound¹⁷



6

which contains the giant mixed-valence cluster anion **6a** (Fig. 7).



6a

with {Mo(Mo₅)}' ≡ {Mo₆O₂₁(H₂O)₆}; {Mo(Mo₅)}'' ≡ {Mo₆O₂₁·(H₂O)₃(SO₄)}; {Mo₂}' ≡ {Mo₂O₃(H₂O)₂}; {Mo₂}'' ≡ {Mo₂(O_t)₂·(O_{br})₃(SO₄)}; {Mo₂}''' ≡ {Mo₂(O_t)₄(O_{br})(SO₄)}; {Mo₁} ≡ {MoO(H₂O)}; *x* ≈ 16.

Compound **6** crystallises in the space group *I4mm*, its unit cell comprises two giant blue lemon-like cluster anions **6a** with approximate *D*₄ symmetry; the anion has a nearly spherical {Mo₂₈₈O₇₈₄(H₂O)₁₉₂(SO₄)₃₂} central fragment (**B**) and two {Mo₄₀O₁₂₄(H₂O)₂₄(SO₄)₈} capping areas (**C**). As the average degree of reduction of the caps **C** is lower than the central fragment **B**, it is reasonable to suggest that the pathway to anion **6a** includes the initial formation of a fragment that resembles in shape the central fragment (**B**) of **6a** while owing to its more nucleophilic nature, it in turn gets capped by two more electrophilic caps **C** in course of the growth process (this refers to a relative consideration). The fragments **B** and **C** have local symmetries (see Fig. 7a), *D*_{8d} and *C*_{4v}, respectively. Figure 7a shows a clearly well-defined cross-section where the symmetry breaking^{43–45} occurs and a negative curvature is generated. It should be noted that the linking of fragments **B** and **C**, characterised by different local symmetry, occurs through vertices rather than edges of the corresponding polyhedra. This was to be expected, as this pattern ensures a higher flexibility.

More precisely, the anion **6a** is built up by the six well-defined building units mentioned above, namely, {Mo(Mo₅)}', {Mo(Mo₅)}'', {Mo₂'}, {Mo₂}'', {Mo₂}''' and {Mo₁} (see Fig. 7a), which are linked to produce the giant molecular container (vase) of **6a** with a giant cavity (diameter *d* ≈ 2.5 × 4.0 nm at the most extended points). This cavity can accommodate an enormous number (~400) of water molecules. Of the 1000 (crystal) water molecules indicated in the formula of **6**, 400 molecules are encapsulated inside the cavity.

The presence of the bidentate SO₄²⁻ ligands is indicated in the vibrational spectrum by a typical splitting of the ν₃(F₂)-type vibrational bands (1191, 1122 and 1060 cm⁻¹), while the presence of Mo^V centres along with the Mo^{VI} centres causes the IVCT (intervalence charge transfer) band at ~740 nm. As can be seen from the above formula, the anion **6a** incorporates two types of {Mo(Mo₅)} building units differing in the type of ligands. Thirty two {Mo(Mo₅)}' blocks containing SO₄²⁻ ions are present in fragments **B** and eight {Mo(Mo₅)}'' blocks which do not contain these ligands are located in the caps **C**. The binuclear {Mo₂} building units differ not only by the type of ligands but also by the type of coordination. Thus both Mo atoms of the {Mo₂}''' fragments located at the ends of both caps **C** contain two terminal oxygen atoms. This situation seems to be characteristic of growth termination. The {Mo₁} units are of the classical type, {OMo^V(H₂O)}³⁺; they contribute significantly to the highly reduced state of anion **6a** (64 of the 112 Mo^V atoms belong to these fragments). The remaining 48 Mo^V-type centres are formally

[†]This special situation of versatility could lead us, using a term from J-M Lehn’s lectures, to the category ‘Multiple Expression of Molecular Information’, a statement which can be related to the formation of the variety of giant clusters obtained from relevant substance ‘libraries’.



Figure 6. Drawing of an icosadeltahedron ($T = 3$) as a model for the topologically identical protein coat subunits of the Tomato Bushy Stunt Virus (TBSV). The drawing was taken from Ref. 41. The orange lobes are packed about the icosadeltahedron fivefold axes, whereas the blue and green lobes alternate about its local sixfold axes, not allowed for an icosahedral symmetry group.

distributed over several parts of the cluster areas which causes a widespread delocalisation of Mo(4d) electrons.

The structure of **6a** can be considered as a hybrid between the giant ring-shaped cluster of the $\{\text{Mo}_{176}\}$ type^{5–7} and the spherical $\{\text{Mo}_{102}\}$ -type cluster.³⁶ In the cluster **6a**, one can find both: the $\{\text{Mo}(\text{Mo}_5)\}$ and $\{\text{Mo}_1\}$ fragments, typical for the spherical $\{\text{Mo}_{102}\}$ cluster, as well as the $\{\text{Mo}(\text{Mo}_5)\}$ and $\{\text{Mo}_2\}$ fragments, typical for ring-shaped systems. The hybrid character of cluster **6a** also becomes obvious due to the presence of 24 $\{\text{Mo}_{11}\}$ groups with C_5 symmetry and 16 $\{\text{Mo}_{10}\}$ groups with C_s symmetry, containing one MoO_6 octahedron less (Fig. 8).⁷ (Note that the two groups have 56 MoO_6 octahedra in common; see Fig. 7a.) The $\{\text{Mo}_{11}\}$ groups with C_5 symmetry are identical to those of the spherical clusters,⁷ and the $\{\text{Mo}_{10}\}$ groups are identical to the $\{\text{Mo}_{10}\}$ fragment encountered in ring-shaped clusters, *i.e.* the $\{\text{Mo}_{11}\}$ group without the displaced MoO_6 octahedron.[†]

[†] The spherical- ($n = 12$) and ring-type ($n = 14, 16$) cluster species can be expressed by the same basic type of stoichiometry $\{\text{Mo}_{11}\}_n$, *i.e.*, they differ only in numbers n ; this was categorised by us as a Pythagorean harmony.⁷

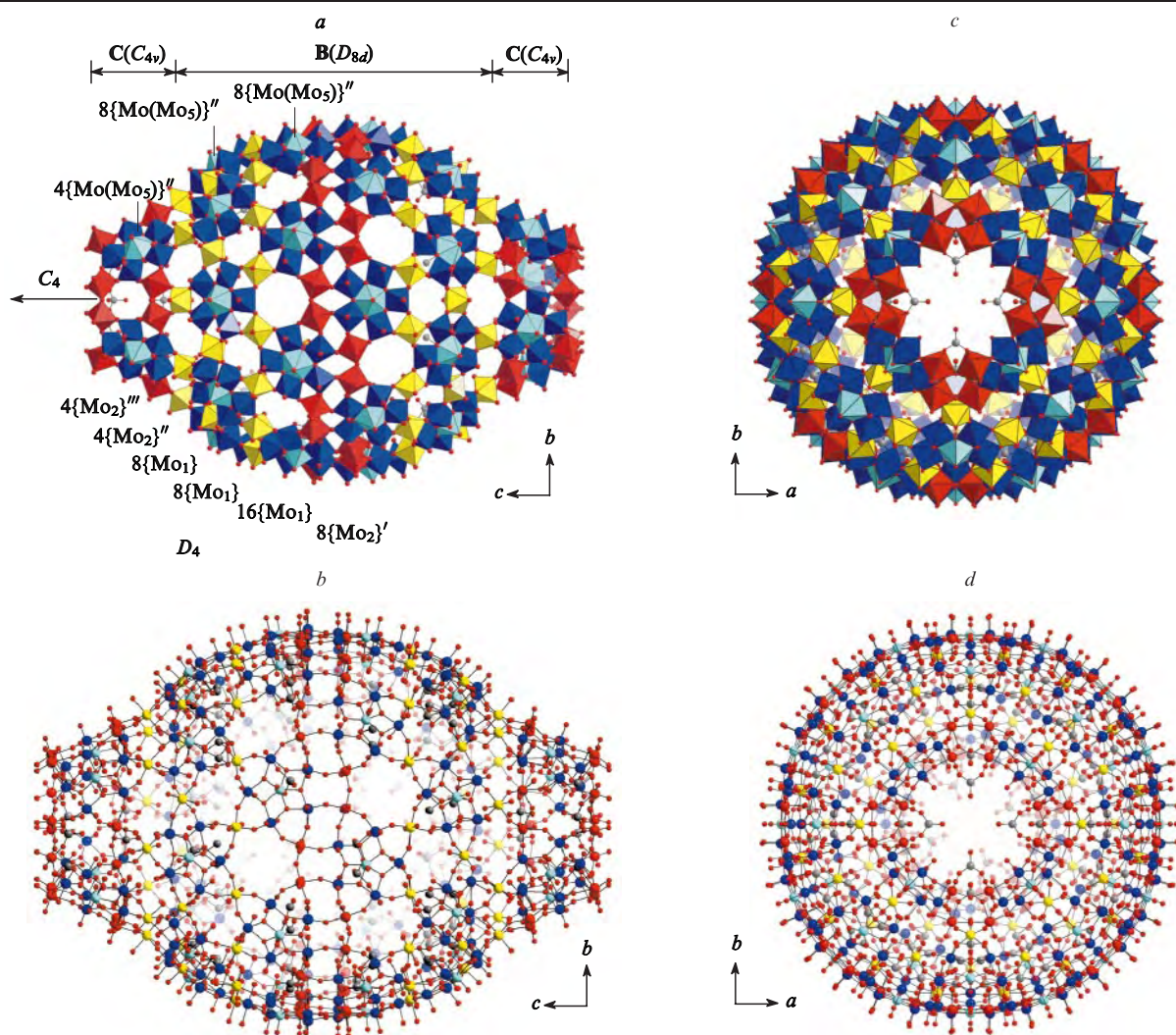


Figure 7. Structure of **6a** in crystals of **6** in polyhedral (*a, c*) and atomic (*b, d*) representations perpendicular to the C_4 axis (*a, b*) and along the C_4 axis (*c, d*). Building units: $\{\text{Mo}_1\}$, yellow; $\{\text{Mo}_2\}$, red; $\{\text{Mo}(\text{Mo}_5)\}$, blue with blue-turquoise pentagonal bipyramids; the O atoms are small red spheres, the S atoms are grey spheres. Note that one capping part is turned against the other by $360/16^\circ$. Different building blocks and the arrays of different local symmetry are marked. This drawing was first published in Ref. 17.

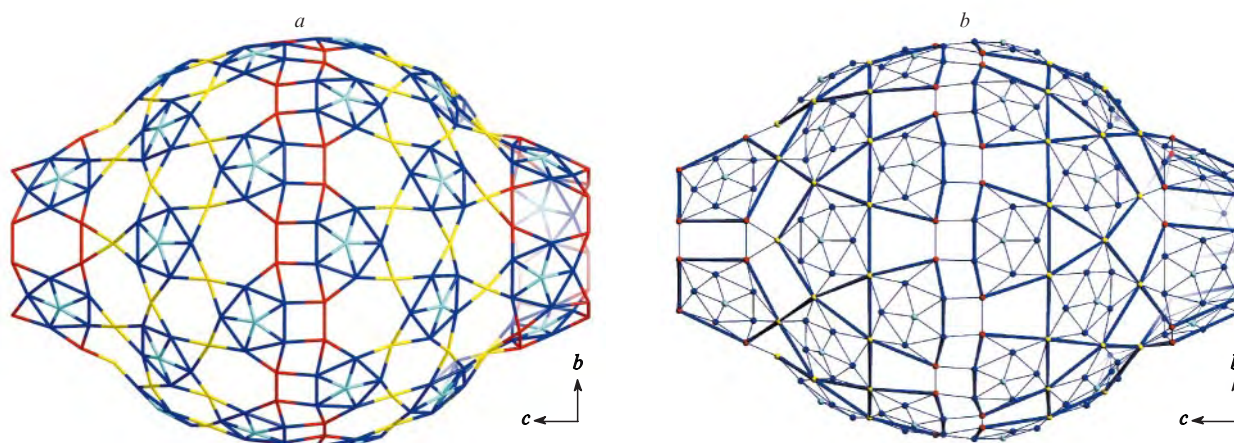


Figure 8. $\{\text{Mo}_{368}\}$ metal atom framework of **6a** in wire-frame (a) and atomic (b) representations. For colour designations, see Fig. 7a. The $\{\text{Mo}_{11}\}$ and $\{\text{Mo}_{10}\}$ building blocks in (b) are emphasised through thick lines.

The high degree of reduction (about 112 Mo^{V} and 256 Mo^{VI}) of **6a**, which is much higher than that in the ring systems (for example, 28 Mo^{V} and 126 Mo^{VI})⁵ indicates that the cluster growth is promoted by reducing conditions. The largest cluster obtainable in an acidified molybdate solution in the absence of a reducing agent is the rather small $\{\text{Mo}_{36}\}$ anion,[‡] which, however, ‘starts growing’ upon the addition of a reducing agent.⁵ It is also significant that the higher the negative charge of the anion, the less probable is its uncontrolled linking but it initiates further protonation, which is a prerequisite for further linking. The high negative charge of anion **6a** is also influenced by the presence of SO_4^{2-} ligands coordinated to the intermediates and to the final cluster species. When the reaction is performed in the presence of the weakly coordinating ligands such as Cl^- or ClO_4^- (which do not appear in the cluster when HClO_4 or HCl are used as acidification agents, instead of H_2SO_4), the reaction affords only ring-like molybdenum-oxide based species⁵ rather than the hybrid cluster **6a**. It is also worth mentioning that, although the coordination capacity of SO_4^{2-} is higher than those of Cl^- or ClO_4^- , it is still not too strong; thus, it provides a coordination flexibility and, as a consequence, generation of a variety of different appropriate building blocks. The average degree of reduction of the two $\{\text{Mo}_{40}\}$ -type caps (**C**) in cluster **6a** is lower than that of the central fragment **B**. This observation agrees with our hypothesis that growth processes in polyoxometallate-type systems are mostly based on nucleophiles which form the initial fragment of the cluster and direct the formation of electrophiles by which they get capped (electrophiles and nucleophiles in a relative consideration).

As examples of such growth, one can consider the transition from a hypothetical extremely negatively charged V^{IV} -type Keggin ion to the stable cluster formed upon capping the Keggin ion with six additional VO^{2+} groups;^{1,2,47} the transition from the $\{\text{Mo}_{57}\}$ -type cluster to the extended $\{\text{Mo}_{63}\}$ cluster (via linking of $\{\text{Mo}_{57}\}$ to six MoO^{4+} groups⁴⁸); and the transition from the $\{\text{Mo}_{176}\}$ -type cluster anion to the $\{\text{Mo}_{248}\}$ anion via linking of $\{\text{Mo}_{176}\}$ to two neutral $\{\text{Mo}_{36}\}$ fragments.⁴⁹ A further example refers to remarkable processes occurring during the formation of the unusual unsymmetrical molybdenum-oxide based $\{\text{Mo}_{37}\}$ cluster. After a highly reduced ϵ -Keggin-type $\{\text{Mo}_{12}^{\text{V}}\}$ unit is capped by four electrophilic $\{\text{MoO}_3\}$ groups, these groups get reduced while the resulting $\{\text{Mo}_{16}\}$ species is capped by the positively charged $\{\text{Mo}_{11}\}$ and $\{\text{Mo}_{10}\}$ fragments. Often, processes of this type result in a lowering of the unusually high negative charge of the intermediates. In each of the examples described

above, the central nucleophilic core appears to have directed the formation of electrophilic fragments.

3. Perspectives

The knowledge of structural details of cluster **6a** will probably be the starting point for the synthesis of many other systems of comparable sizes as well as for the development of a new type of nanochemistry characterised by performing well-defined reactions at specified sites of well-defined nanoobjects and also includes their handling as intact units for instance for the preparation of composites, e.g., with silica and additionally surfactants to give micelles, films, and even liquid crystals.^{10–14, 50, 51} (The possibility of these studies is indicated by the syntheses and use of the giant spherical and ring clusters mentioned above.) The present results with the cluster having a giant surface also seem to be of relevance for some aspects of catalysis, as it is still a challenge to understand the details of the interaction mechanisms of substrates with the surfaces of heterogeneous catalysts.^{52–55} In the case of transition metal oxides, like MoO_3 , which play an important role in selective oxidation processes,^{54, 55} it would be a tremendous step forward to consider the surfaces of discrete and well-defined giant molybdenum-oxide based clusters for modelling catalytic reactions [note that the large surface of **6a** contains only $\text{Mo}=\text{O}$ and $\text{Mo}(\text{H}_2\text{O})$ groups].⁸ This would help to understand the surface properties for related catalytically active bulk materials which are difficult to investigate.⁵⁶

Another interesting aspect is the possibility of performing reactions within the cavity of the giant molecular container **6a**, the largest structurally well-defined one known, while for instance encapsulation-type reactions resulting in a novel type of supramolecular compounds are known for even smaller spherical clusters.^{28, 57} This type of nanochemistry/nanotechnology and supramolecular engineering^{58, 59} is based on the use of thoroughly characterised objects obtained by the ‘bottom-up’ method.

Symmetry breaking,^{43–45} observed in many natural processes, can be modelled by the present reaction. The symmetry breaking occurs here due to the presence of different local symmetry areas on the surface of **6a** as in the case of Fowler’s Phantasmagorical Fullerenes, due to the presence of negative and positive curvatures. Symmetry breaking is also relevant for the understanding of patternings in the macrocosmos including those cases where the antagonistic effects are important.^{60–65} This phenomenon was described long ago by D’Arcy Thompson in his famous book ‘*On Growth and Form*’.⁶² A remarkable example of symmetry breaking

‡ When the paper⁴⁶ dealing with the structure of $\{\text{Mo}_{36}\}$ was published, it was considered to be the largest inorganic anion(!).

§ The presence of the large number of $\{\text{O}=\text{MoO}_6\}$ -type pentagonal bipyramids in **6a** is interesting as this group is considered to be responsible for important types of selective oxidations based on molybdenum oxide catalysts.⁵³

was discussed by L. Addadi and S. Weiner.⁶⁶ They considered the formation of asymmetrical shapes during the growth of crystalline structures. The authors refer in this context to the famous Curie symmetry principle⁶⁷ (see also Refs 68, 69), which, as the authors state, cannot be generalised. It is also not fulfilled in our particular case, *i.e.*, when fragment **B** is regarded as inducing the ‘growth’ of the other fragment **C**. Addadi and Weiner⁶⁶ consider the above-mentioned process to be the first step towards understanding asymmetry in biology.

It would be a breakthrough if rather large nanoareas, such as **B** and **C** with different symmetries, could be further extended. In particular, this should be of course more easily possible under dissipative conditions.

The formation of **6a** under conservative conditions shows a type of patterning, emergence, and complexity at a nanolevel, not as is mostly considered at a macrolevel case, as, for instance, in the situations of dissipative self-organisation model processes leading to Bénard convection cells and to Belousov–Zhabotinsky-type reactions.⁶¹ The novelty of the present nanoobject is that symmetry breaking is observed during growth, *i.e.* self-assembly. This is caused by different distributions of a rather large number of different negative and positive vertices with polygons ranging from triangles to heptagons (Fig. 9). The complexity of the structure of cluster **6a** can be demonstrated by comparison with the Archimedean solids having only one type of vertex.

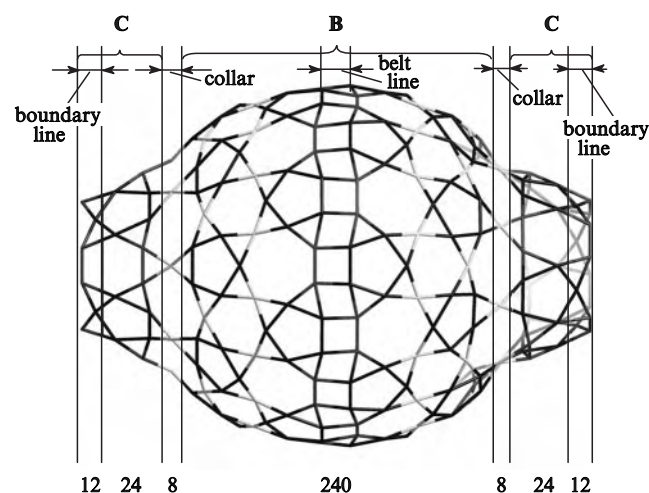


Figure 9. The four regular polyhedron depicting the surface of **6a**, consisting of $328 = 368 - 40$ Mo atoms (*i.e.*, without the Mo atoms of the pentagonal bipyramids). The polyhedron has 240 vertices in the central fragment **B**. 64 vertices are in the belt region, 32 vertices with the vertex configuration [3,4,4,5], 32 of the type [3,4,4,7]; 16 + 8 of the type [3,5,3,7], 8 of the type [3,5,3,6], and 16 of the type [3,6,3,7] are in each of the two **B** regions next to the belt and another two times 16, 8, and 16 with a vertex configuration of the type [3,5,3,6], [3,6,3,7], and [3,5,3,7], respectively, are next to the two collars, altogether 16 of type [3,7,3,7] along the two collars, 8 of types [3,6,3,7], [3,5,3,7], and [3,5,3,6] each in the interior of the two capping regions, and 4 of type [3,5,3] and 8 of type [3,6] along each of the two boundary lines. This drawing was first published in Ref. 17.

4. Combinatorial topology of the polyhedral structure of nanoclusters: relevance for the present symmetry breaking processes

This Section explains first of all the topological nature of the surface of **6a** but it could also be useful for a chemist in constructing rather large patterns showing positive and negative curvatures. Combinatorial analysis of the four regular polyhedral net formed by the Mo atoms in **6a**, as shown in Fig. 9 (for simplicity, the Mo atoms within the interior of the pentagonal

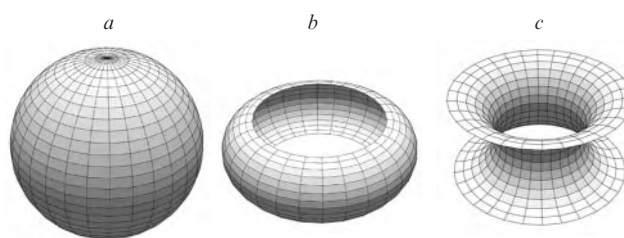


Figure 10. Shapes of positively (*a, b*) and negatively (*c*) curved surfaces. The sphere and the outer part of a torus are paradigms of surfaces exhibiting positive curvature (*a, b*); the saddle and the inner part of a torus are paradigms of surfaces exhibiting negative curvature (*c*).

bipyramids are omitted), reveals a clear correspondence between the overall distribution of positively and negatively curved surface segments (for illustration, examples of positively and negatively curved surfaces are given, Fig. 10) and the distribution of vertices with positive and negative combinatorial curvature. This is in line with the well-known Euler's theorem,⁷⁰ interpreted as a discrete version of the Gauss–Bonnet theorem.

Indeed, the surfaces of the central fragment **B** with D_{8d} symmetry and two capping regions **C** with C_{4v} symmetry are positively curved. The fragments **B** and **C** are connected by the two narrow collars exhibiting a strong indentation, thus creating two ring-shaped surface components of large negative curvature of relevance for the symmetry breaking. Additional negative curvature is ‘hidden’ in the jaggedness of the two circular boundary lines (see Fig. 9). Indeed, straightening them out into circles would create shapes that would each mimic the shape of a neck, *i.e.*, one half of the negatively curved inner part of a torus (see Fig. 10). The important role of pentagons and heptagons in the case of Fowler's Phantasmagorical Fulleroids is clearly illustrated by Fig. 11. Any fulleroid with icosahedral symmetry consisting of only pentagons and heptagons contains exactly $12 + 60N$ pentagons and $60N$ heptagons for some positive integer N . There are two such fulleroids with $N = 1$. In one of them, 72 pentagons are grouped in 12 sets each containing 6 pentagons. Each set generates the outcrops of a high positive curvature counterbalanced by a network of negatively curved channels built from its 60 heptagons, which results in a net positive curvature of four as required. The other one consists of 12 separate pentagons and 20 sets of three pentagons each, which are also connected by a network of negatively curved channels built from the heptagons exhibiting, however, a much smoother geometry because of the much better local balance of positive and negative curvature. Figure 11 shows the structures of two Fowler's Phantasmagorical Fulleroids, illustrating how areas

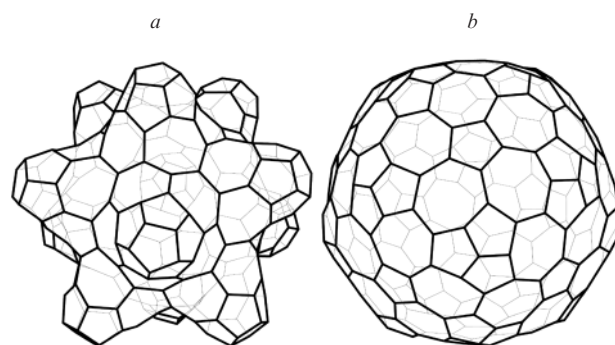


Figure 11. Fowler's Phantasmagorical Fulleroid structures (see Ref. 17 with related references).

exhibiting strongly positive curvature can be intertwined with areas exhibiting negative curvature to produce a surface of only moderately positive curvature.

V. Conclusion

The use of the cluster building blocks present in solutions of polyoxometallates and linking of special fragments such as the pentagonal-type $\{\text{Mo}(\text{Mo}_5)\}$ units by different types of linkers, e.g. paramagnetic (open shell) centres opens up new fascinating perspectives for nano-, supramolecular, solid-state and magnetochemistry. 'Playing' with pentagons not only can result in several giant spherical, quasi-spherical and circular species, but it is also of interest because of their role in the history of culture, virology, the geodesic domes of Fuller, and certain aspects of solid-state physics (see the fascinating quasicrystals). A special challenge will be, for instance, to fill the cavities and pores of nanoobjects such as of the spherical $\{\text{Mo}_{132}\}$ cluster with a variety of different guests and also to place molecules inside the cavities of ring-shaped clusters, resulting in different reactivities compared to those of the discrete (isolated nano-sized) ones.

We believe that the title of this review is justified, as our topic allows an unusual type of nanochemistry by performing controlled reactions at well-defined sites of structurally well-defined nanoobjects. Since such nanoobjects can be used as building blocks for the construction of extended structures based on crystal engineering, this field opens up new perspectives for solid-state chemistry, which becomes defined and accurate even up to the atomic level. It has been a long and thorny but successful way in polyoxometallate chemistry since 1956, when Jonassen and Kirschner published a review referring to the knowledge of that time and to the major earlier contributions of important chemists like Rosenheim, Werner, Pfeiffer, Pauling and Keggin.⁷¹

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Some new views on the tautomerisation mechanism

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Abstract. Published data on the prototropic tautomerism of some carbonyl and nitrogen-containing acyclic and heterocyclic compounds are systematised. Mechanisms of intramolecular and intermolecular proton transfer in tautomerisation reactions are considered. On the basis of the results of semiempirical and *ab initio* quantum-chemical calculations, preference is given to an intermolecular collective (dimeric, trimeric, tetrameric or oligomeric) mechanism. A new approach to the description of the solvent effect on the prototropic tautomeric equilibrium is proposed. The bibliography includes 107 references.

I. Introduction

Since the discovery of prototropic tautomerism, its nature and essence have attracted much attention. Studies performed for more than a hundred years led to the general conclusion that many processes typical of chemical reactions involve the tautomeric interconversion. Hence, the latter serves as a convenient model for studying the reaction mechanisms. In this connection, it is pertinent to mention the appropriate statement by Bilobrov¹ that tautomeric interconversions of molecules are one of the reasons for a striking diversity of the world of chemical reactions.

It is known that the more polar keto form dominates in the keto–enol equilibrium and the mobile hydrogen atom is transferred as the ion. However, in the case of acetylacetone and benzoylacetone, the equilibrium is almost completely shifted to the enol form. It is still unclear whether this fact is an exception from the general situation with the keto–enol tautomeric equilibrium or there are no general regularities at all. When discussing this problem, one might reason that there is no need to reveal the general regularities of this phenomenon. It is only necessary to establish the character of a particular process reliably and

unambiguously by chromatographic and spectroscopic methods and quantum-chemical calculations. The tautomeric equilibria can be quantitatively described with the advantageous use, for example, of intensities of stretching vibrations of the carbonyl (ν_{CO}) and hydroxy (ν_{OH}) groups in the IR spectra² and chemical shifts of the protons and carbon nuclei of the corresponding functional groups in the ¹H and ¹³C NMR spectra.³ Of theoretical methods, semiempirical^{4,5} and *ab initio*⁶ quantum-chemical methods find wide application. These methods allow one to calculate the energy, electronic and structural characteristics of individual tautomeric forms and estimate the tautomeric equilibrium constants (K_{T}). It should be noted that a necessary condition for the quantitative description of the tautomeric equilibrium is the existence of two rather deep minima in the plot of the proton-transfer energy vs. the reaction coordinate.

Investigations on tautomeric processes were surveyed in the reviews^{7–10} and considered in more recent detailed studies cited below.

The present review considers new views in the theory of prototropic tautomerism, in particular, the intermolecular mechanism of proton transfer, and a new approach to the determination of tautomeric equilibrium constants and quantitative description of the influence of the solvent on the equilibrium. The results of quantum-chemical calculations of prototropic tautomeric equilibria and their examination by spectroscopic methods are discussed in particular sections.

II. Keto–enol tautomerism

The keto–enol tautomerism is the most well-studied type of prototropic rearrangements. Since individual tautomeric forms can be readily detected by different methods, measurements of the equilibrium constants of this process present no difficulties. Due to the high affinity of the carbonyl oxygen atom for the proton, keto–enol tautomerism is observed in many compounds. The tautomeric equilibrium constants for various β -dicarbonyl compounds were estimated by Meyer¹¹ back in the early 20th century with the use of bromometric titration. These results are still scientifically useful. The constants K_{T} determined by Meyer correlate with the polarities of the solvents, which were determined by spectroscopic methods many decades later.

Modern studies of the keto–enol equilibrium confirmed the earlier views that the keto form is thermodynamically more stable than the enol form. This is evidenced, for example, by calculations

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of the relative stabilities of the keto and enol forms and energy barriers to enolisation of ketones MeCOR ($\text{R} = \text{Me}, \text{H}, \text{F}, \text{CN}$).¹²

With the aim of studying the effect of substituents on the keto–enol tautomerism, the reaction coordinates and activation energies for enolisation of aldehydes XCH_2CHO ($\text{X} = \text{H}, \text{BH}_2, \text{NH}_2, \text{OH}, \text{F}, \text{CN}, \text{NC}, \text{Cl}$) were calculated by *ab initio* methods. The results of calculations at different levels of theory showed that the keto forms of the compounds under study are thermodynamically more stable than the corresponding enol forms.¹³

The *ab initio* calculations of the ethenethiol–thioacetaldehyde tautomeric interconversion demonstrated that ethenethiol in the gas phase is $2.6 \text{ kcal mol}^{-1}$ less stable than thioacetaldehyde.¹⁴

The position of the keto–enol equilibrium depends, among other factors, on the polarity of the solvent. Thus, the molecular modelling of the photoinduced transformation of the excited enol tautomeric form of 7-hydroxy-8-morpholinomethylquinoline into the keto form demonstrated that an intramolecular hydrogen bond between the protonated morpholine nitrogen atom and the deprotonated hydroxy group in cyclohexane hinders the proton transfer. By contrast, an intermolecular hydrogen bond is formed in 1,4-dioxane, and the morpholine nitrogen atom serves as a proton carrier.¹⁵

The tautomeric equilibrium in methyl esters of para-substituted benzoylactic acids was studied by ^1H NMR spectroscopy¹⁶ and the dependences of the equilibrium constants K_T on the solvent and the nature of the substituent were found.

The third-order terms were measured for the concerted acid–base catalysis of enolisation of simple aldehydes and ketones to form substituted acetic acids. It was concluded that aldehydes undergo enolisation under the conditions of base catalysis. The isotopic effect of the solvent in enolisation of aldehydes under the conditions of concerted acid–base catalysis shows that the transition state with proton transfer to the carbonyl group is formed more readily than that in the case of ketones.¹⁷

Until recently, the dielectric permeability of the medium has been used as the main parameter describing the influence of the solvent on the tautomeric equilibrium.^{18–20} However, Prezhdo *et al.*²¹ reasonably noted that the dielectric permeability of the solvent cannot be considered as a universal characteristic of interactions between molecules and the medium. To obtain a more adequate estimate of the polarity of the solvent, the dipole moment, polarisability, molar volume and specific and non-specific interactions should also be taken into account.^{22, 23}

In 1963, Dimrot *et al.*²³ proposed the empirical polarity parameters (E_T) for organic solvents. These parameters are estimated on the basis of the energy of electron transfer corresponding to long-wavelength absorption bands in the UV-vis spectra of *N*-phenoxypyrimidine dyes exhibiting negative solvatochromism.

The experimental constants K_T for acetoacetic ester in different solvents, which were determined by spectroscopic, kinetic, refractometric and bromometric methods, were published in the study.²¹ The plot of the constants K_T vs. E_T for 12 solvents, including acetoacetic ester (**1**), exhibits a hyperbolic character (Fig. 1). Analogous qualitative and quantitative characteristics were found for acetoacetic ester (**1**) and acetylacetone (**2**) by titrimetry, liquid chromatography and NMR spectroscopy.^{3, 24}



The experimental curves also indicate that the constants K_T are inversely proportional to E_T .

The proton transfer in keto–enol tautomerism can occur along the intermolecular hydrogen bond between the oxygen atom of the carbonyl group and the proton at the α position in the cyclic dimer of carboxylic acid.²⁵ This is somewhat contradictory to the concept according to which the involvement of the hydrogen atom in hydrogen bonding requires high electronegativity of the atom to which this hydrogen atom is bound. The IR

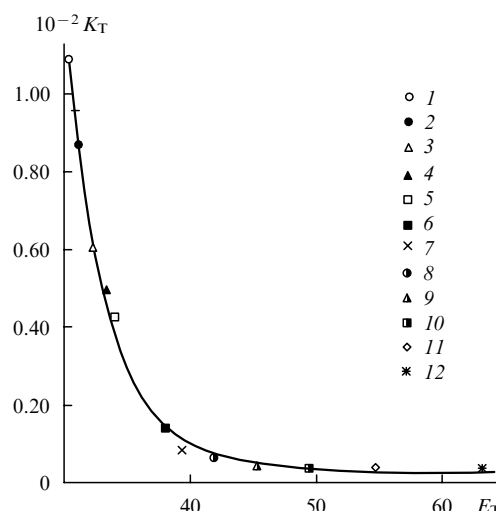
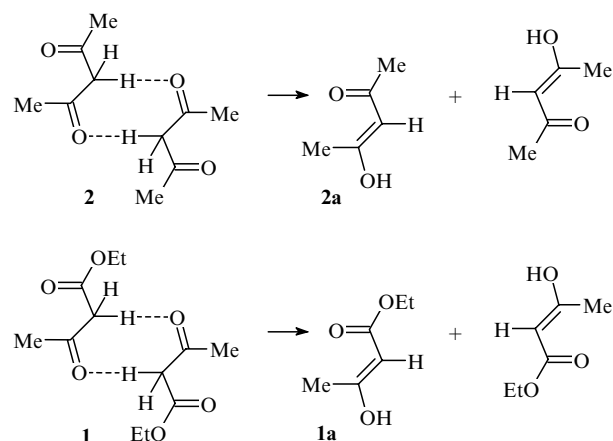


Figure 1. Tautomeric equilibrium constant K_T of acetoacetic ester vs. the polarity parameter of the solvent E_T .

(1) cyclo- C_6H_{12} ; (2) $n\text{-C}_6\text{H}_{14}$; (3) CCl_4 ; (4) CS_2 ; (5) Et_2O ; (6) MeCO_2Et ; (7) CHCl_3 ; (8) Me_2CO ; (9) MeCN ; (10) acetoacetic ester (**1**); (11) MeOH ; (12) H_2O .²¹

spectroscopic study²⁶ performed by one of the authors of the present review showed that a proton of the methyl group can be involved in intermolecular hydrogen bonding in acetophenone. In the studies,^{27, 28} preference was given to the mechanism of proton transfer through intramolecular hydrogen bonding, although the activation barrier for this process is rather high. In some early studies^{25, 29} and in more recent investigations,^{30–37} evidence was reported for the formation of dimeric associates through two-proton transfer in the case of carbonyl and nitrogen-containing acyclic and heterocyclic compounds in which intramolecular hydrogen bonding is energetically and geometrically unfavourable.

We proposed that the mechanism of tautomerisation involving dimers be used to obtain quantitative estimates of the energy of proton transfer and constants K_T for acetoacetic ester (**1**) and acetylacetone (**2**) upon transformations into the corresponding enol forms **1a** and **2a**.



We carried out calculations to establish the dependence of the enthalpy on the reaction coordinate (R_{CH}), which allowed us to construct the energy diagram for the two-proton transfer in the dimer of acetoacetic ester (**1**), *i.e.*, the dependence of ΔH on R_{CH} for the $\text{C} \cdots \text{H} \cdots \text{O}$ triad corresponding to an intermolecular hydrogen bond (for R_{CHO} , the value of $2.60 \text{ \AA}$ was assumed). From this diagram, we determined the activation enthalpies of the two-proton transfer $\Delta\Delta H^\ddagger = 91.1 \text{ kJ mol}^{-1}$ and heats of reaction $\Delta\Delta H = 32.2 \text{ kJ mol}^{-1}$, which have reasonable values for this

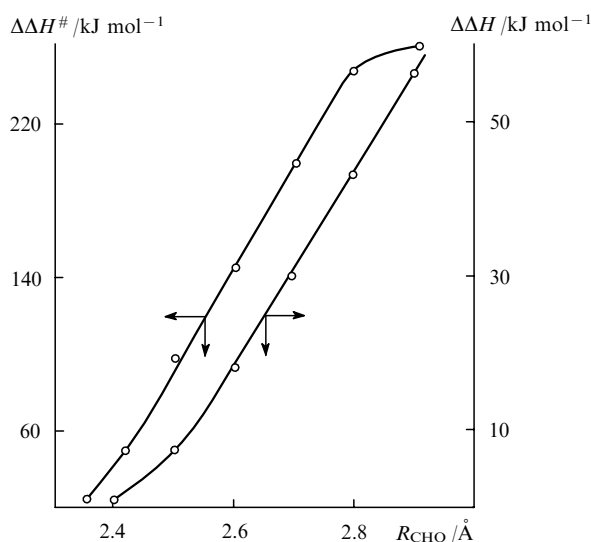


Figure 2. Activation enthalpy $\Delta\Delta H^\ddagger$ and heat of reaction $\Delta\Delta H$ for the proton transfer vs. the length of the CHO triad corresponding to an intermolecular hydrogen bond (R_{CHO}) in acetoacetic ester (**1**) (our data).

process. The $\Delta\Delta H^\ddagger$ and $\Delta\Delta H$ values depend on R_{CHO} . As can be seen from Fig. 2, $\Delta\Delta H^\ddagger$ and $\Delta\Delta H$ can be considered as average values based on the reference points in the middle of the linear region, although the linearity of the plot is disrupted in the vicinity of the boundaries. Analogous results were obtained for acetylacetone (**2**) (Fig. 3). In particular, at $R_{\text{CHO}} = 2.60$ Å, the activation enthalpy $\Delta\Delta H^\ddagger = 103.7$ kJ mol⁻¹ and the heat of reaction $\Delta\Delta H = 23.7$ kJ mol⁻¹.

The choice of the calculation method for estimating the constant K_T is of great importance. Since the thermodynamic equation $\ln K_T = -\Delta\Delta H/RT$ is independent of the reaction mechanism (in the case under consideration, on the mechanism of proton transfer), it is of little use for the adequate estimation of K_T . Besides, this equation describes the overall process of two-proton transfer, although if tautomeric interconversions of different nature take place (for example, in nucleic bases), the constants

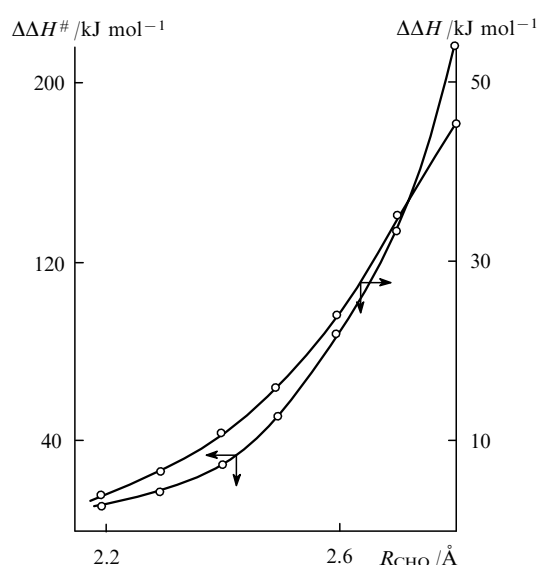


Figure 3. Activation enthalpy $\Delta\Delta H^\ddagger$ and heat of reaction $\Delta\Delta H$ for the proton transfer vs. the length of the CHO triad corresponding to an intermolecular hydrogen bond (R_{CHO}) in acetylacetone (**2**) (our data).

K_T for each proton depend differently on the structural changes. We propose a new approach to estimating the tautomeric equilibrium constants according to which the constant K_T can be represented as a function of the orders of the bonds that are cleaved and formed in the course of proton transfer.³⁸ In the case of the keto–enol tautomerism proceeding through a cyclic dimer, the proton transfer is accompanied by an increase in the O–H (P_{OH}) bond order to the maximum value (~ 0.900) and a decrease in the C–H (P_{CH}) bond order to zero, i.e., the latter bond is cleaved. Simultaneously, the order of the C=O double bond (P_{CO}) decreases to the single-bond order (~ 1.000), while the order of the C–C (P_{CC}) single bond increases to the order of the C=C double bond (~ 1.600). Hence, the double bond is shifted from the carbonyl group to the adjacent C–C bond giving rise to the enol tautomeric form. The bond orders under consideration (P_{CH} , P_{OH} , P_{CO} , and P_{CC}) would change in parallel with changes in the percentage of the keto and enol forms in the course of proton transfer. On going from the first to the second energy term, the percentages of the keto and enol forms can be described by Eqn (1):

$$\frac{P_{\text{OH}}^1}{P_{\text{CH}}^1} E_n + \frac{P_{\text{CO}}^1}{P_{\text{CC}}^1} Kt = \frac{P_{\text{OH}}^2}{P_{\text{CH}}^2} E_n + \frac{P_{\text{CO}}^2}{P_{\text{CC}}^2} Kt, \quad (1)$$

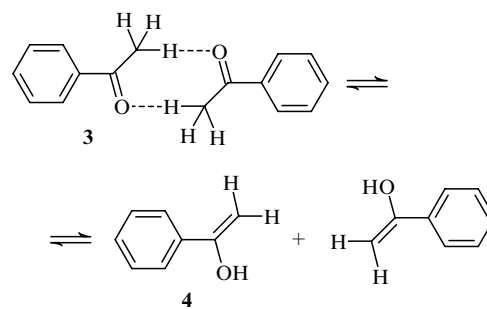
where E_n and Kt are the initial contributions (in %) of the enol and keto forms, and P_{ij}^1 and P_{ij}^2 are the orders of the corresponding bonds in the first and second terms.

After dividing both sides of Eqn (1) by Kt taking into account that $K_T = E_n/Kt$ followed by simple algebraic transformation, we get Eqn (2) for the constant of the keto–enol tautomeric equilibrium.

$$K_T = \frac{P_{\text{CH}}^1 P_{\text{CH}}^2 (P_{\text{CO}}^1 P_{\text{CC}}^2 - P_{\text{CO}}^2 P_{\text{CC}}^1)}{P_{\text{CC}}^1 P_{\text{CC}}^2 (P_{\text{CH}}^1 P_{\text{OH}}^2 - P_{\text{CH}}^2 P_{\text{OH}}^1)}. \quad (2)$$

The value of K_T calculated according to Eqn (2) is independent of the external factors and depends only on the electronic structures of the molecules involved in tautomeric interconversions.

An analogous approach was applied to the quantitative description of the tautomerisation of acetophenone (**3**) to the enol form **4**.



The dependences of $\Delta\Delta H^\ddagger$ and K_T on R_{CHO} thus obtained are consistent with those for acetoacetic ester (**1**) and acetylacetone (**2**). A decrease in the length of the triad to $R_{\text{CHO}} = 2.60$ Å in the dimer of acetophenone leads to a decrease in $\Delta\Delta H^\ddagger$ from 405.0 to 120.4 kJ mol⁻¹ and a decrease in $\Delta\Delta H$ from 110.8 to 41.0 kJ mol⁻¹, the constant K_T being increased from 0.024 to 0.107.

A model was constructed for the quantitative description of the effect of the solvent on K_T . The plots of K_T vs. R_{CHO} for acetoacetic ester (**1**) (Fig. 4) and acetylacetone (**2**) calculated by Eqn (2) (Fig. 5) are hyperbolic curves, i.e., the constants K_T are inversely proportional to R_{CHO} . For compounds **1** and **2**, the constant K_T is also inversely proportional to the polarity parameter of the solvent E_T (Figs 6 and 7, respectively). A comparison of these dependences shows that the dimers are extended in more polar solvents and compressed in less polar solvents. Actually, the plots of R_{CHO} vs. E_T for compounds **1** and **2** (Figs 8 and 9,

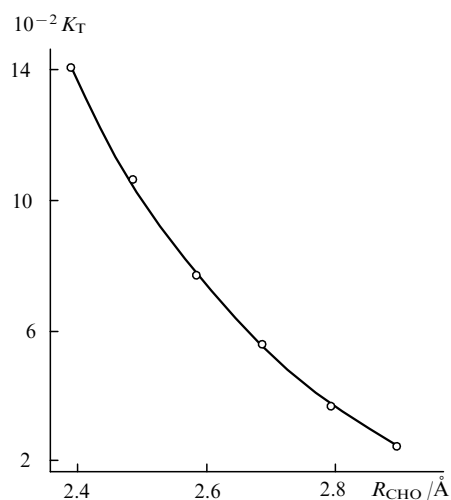


Figure 4. Plot of the constant K_T of acetoacetic ester (1) vs. the length of the CHO triad corresponding to an intermolecular hydrogen bond (R_{CHO}) (our data).

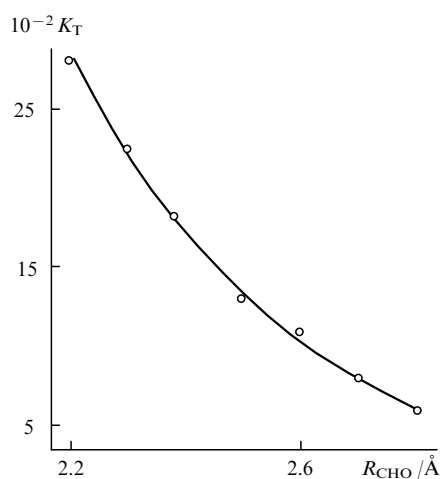


Figure 5. Plot of the constant K_T of acetylacetone (2) vs. the length of the CHO triad corresponding to an intermolecular hydrogen bond (R_{CHO}) (our data).

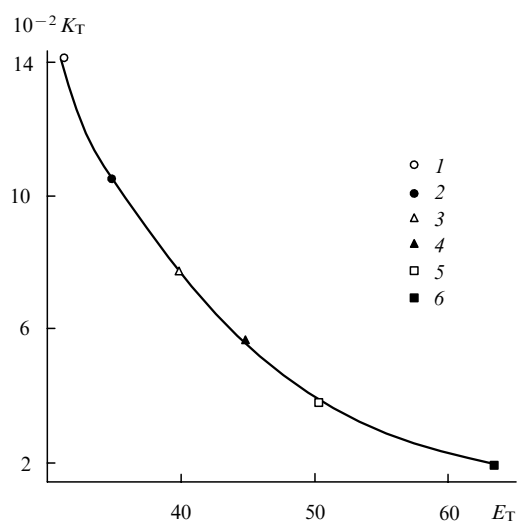


Figure 6. Plot of the tautomeric equilibrium constant of acetoacetic ester (1) vs. the polarity parameter of the solvent E_T . (1) $n\text{-C}_6\text{H}_{14}$; (2) Et_2O ; (3) CHCl_3 ; (4) MeOH ; (5) EtOH ; (6) H_2O (our data).

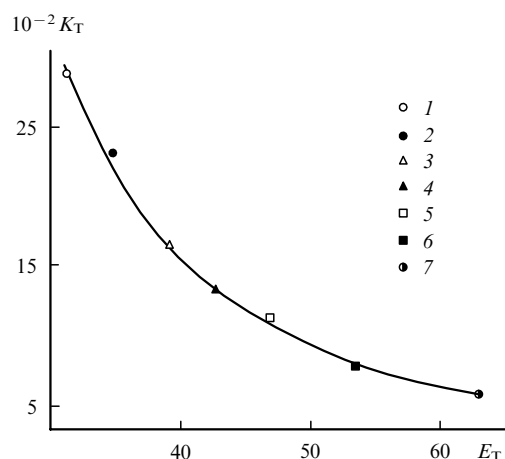


Figure 7. Plot of the tautomeric equilibrium constant of acetylacetone (2) vs. the polarity parameter of the solvent E_T . (1) $n\text{-C}_6\text{H}_{14}$; (2) Et_2O ; (3) CHCl_3 ; (4) Me_2CO ; (5) MeCN ; (6) EtOH ; (7) H_2O (our data).

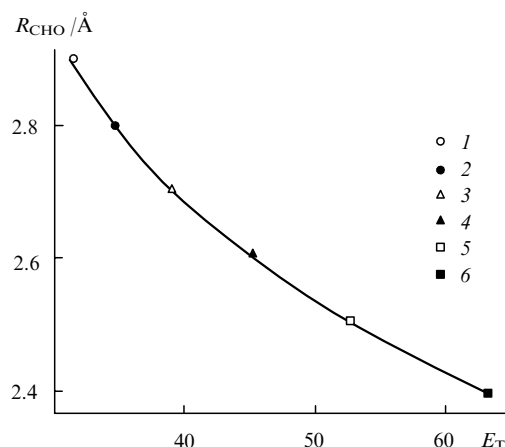


Figure 8. Length of the CHO triad of an intermolecular hydrogen bond (R_{CHO}) in the dimer of acetoacetic ester (1) vs. the polarity parameter of the solvent E_T . (1) $n\text{-C}_6\text{H}_{14}$; (2) Et_2O ; (3) CHCl_3 ; (4) Me_2CO ; (5) MeCN ; (6) EtOH ; (7) H_2O (our data).

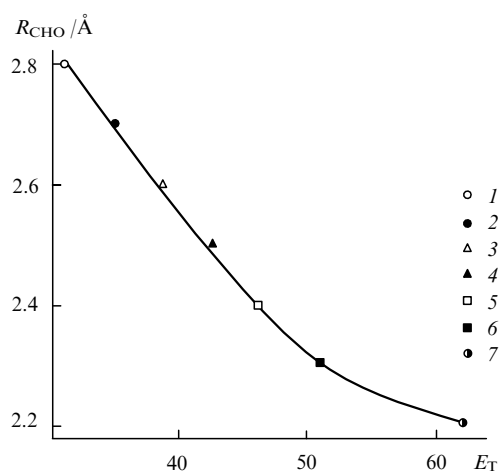
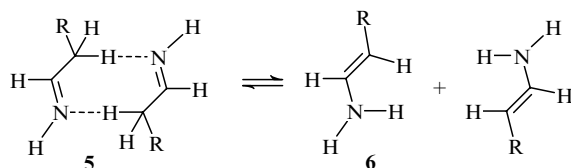


Figure 9. Length of the CHO triad of an intermolecular hydrogen bond (R_{CHO}) in the dimer of acetylacetone (2) vs. the polarity parameter of the solvent E_T . (1) $n\text{-C}_6\text{H}_{14}$; (2) Et_2O ; (3) CHCl_3 ; (4) Me_2CO ; (5) MeCN ; (6) EtOH ; (7) H_2O (our data).

respectively) indicate that the length of the triad corresponding to an intermolecular hydrogen bond is inversely proportional to the polarity of the solvent. This model can be used to advantage for the quantitative description of the effects of external factors on some biologically important processes (see below).

III. Imine–enamine tautomerism

Tautomerisation involving the proton bound to the nitrogen atom is a key step in reactions of heterocyclic compounds. The possibility of the transformation of imines into the corresponding enamines was first studied by Lawer.³⁹ This classical reaction can be represented as the intermolecular proton transfer in the dimer of imine **5** to form enamine **6**.



The influence of the α - and β -substituents on the position of the imine–enamine tautomeric equilibrium was estimated quantitatively. In particular, the percentage of the enamine form in α -substituted derivatives of the $R^1CH=C(Me)NHR^2$ type changes from 50% to 70%,⁴⁰ whereas this percentage in β -substituted analogues is in the range of 30%–100%.⁴¹

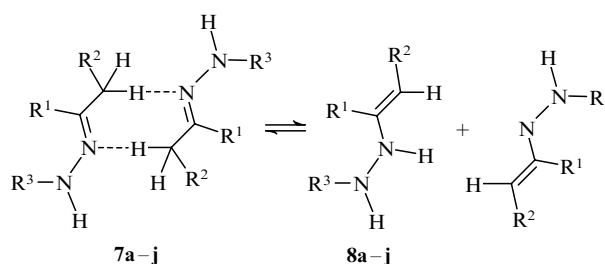
The investigation of the tautomerism in analogous *N*-substituted imines showed that an increase of the charge on the nitrogen atom⁴² as well as an increase in the volume of the substituent at the same atom^{42,43} led to a decrease in the percentage of imine in the equilibrium mixture. An attempt was made to find the dependence of the percentage of enamine on its pK_a ⁴⁴ assuming that the mobility of the proton of the amino group should facilitate an increase in the percentage of enamine. However, no correlation was revealed.

The study of the effect of the solvent on the imine–enamine equilibrium⁴⁵ demonstrated that the percentage of enamine increases in the series of the solvents $CHCl_3 < PhH < MeNO_2 < MeCN < MeCOMe < C_5H_5N < MeSOMe$. This series does not correlate with a change in the polarity parameter E_T of the solvent,²³ which accounts for all types of interactions. Apparently, this inconsistency results from experimental errors.

In 1971, using *N*-methylphenylhydrazone of ethyl pyruvate as an example, Ahlbrecht⁴⁶ discovered the hydrazone–enehydrazine interconversion as a special case of the imine–enamine tautomerism. The examination of the characteristic features of the transformation of hydrazone into enehydrazine is of great importance for the target synthesis of indole derivatives.⁴⁷ It was assumed that the hydrazone–enehydrazine tautomerisation is the rate-determining step of Fischer indolisation,⁴⁸ although we do not share this opinion.³⁶

The results of qualitative and quantitative studies of the imine–enamine tautomerism and, in particular, the hydrazone–enehydrazine tautomerism, were comprehensively discussed in the review.⁴⁹ Shainyan and Mirskova⁴⁹ believed that the proton transfer in these processes occurs through an intermolecular mechanism. It was also noted that the hydrazone form is more stable in the absence of conjugation with an electron-withdrawing substituent.⁵⁰ In the presence of an electron-withdrawing substituent in any position, conjugation with this substituent stabilises enehydrazine (due to the predominance of the negative mesomeric effect), which was confirmed by quantum-chemical calculations of the tautomerisation of acetophenone hydrazone to the corresponding enehydrazine.⁵¹

In our opinion, the tautomerisation of phenylhydrazones of some carbonyl compounds **7a–j** into the corresponding enehydrazines **8a–j** proceeds through the formation of cyclic dimers.



To confirm this assumption, the activation enthalpies ($\Delta\Delta H^\ddagger$), heats of reaction ($\Delta\Delta H$) and tautomeric equilibrium constants (K_T) for the above-considered reaction were calculated (Table 1).³⁸

Table 1. Activation enthalpies ($\Delta\Delta H^\ddagger$ /kJ mol^{−1}) and heats of reaction ($\Delta\Delta H$ /kJ mol^{−1}) for the hydrazone–enehydrazine tautomerism in phenylhydrazones **7a–j**.

Compound	R ¹	R ²	R ³	K_T	$\Delta\Delta H^\ddagger$	$\Delta\Delta H$
a	H	H	Ph	0.05	185.2	171.3
b	Me	H	Ph	0.04	150.0	130.4
c	Et	H	Ph	0.04	124.1	92.0
d	CO ₂ Et	H	Ph	0.05	145.5	128.4
e	Ph	H	Ph	0.05	134.2	98.2
f	4-MeC ₆ H ₄	H	Ph	0.05	133.3	97.0
g	4-NO ₂ C ₆ H ₄	H	Ph	0.05	140.0	107.8
h	Ph	H	4-MeC ₆ H ₄	0.04	133.8	98.0
i	Ph	H	4-NO ₃ C ₆ H ₄	0.05	134.8	98.0
j	(CH ₂) ₄		Ph	0.09	83.2	46.0

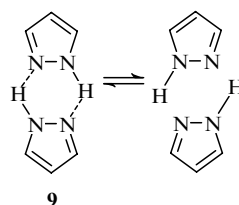
The constants K_T were calculated by Eqn (3).

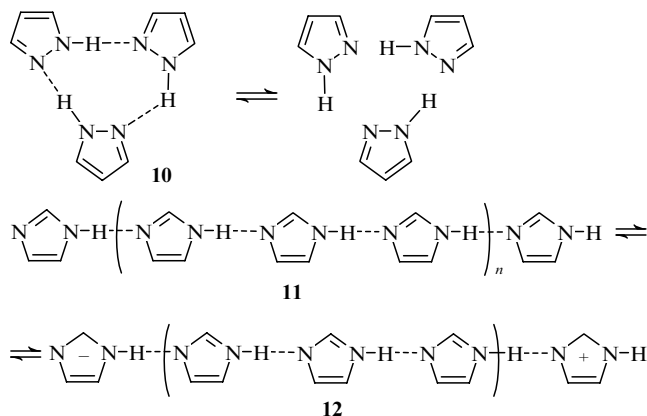
$$K_T = \frac{P_{CH}^1 P_{CH}^2 (P_{NC}^1 P_{CC}^2 - P_{NC}^2 P_{CC}^1)}{P_{CC}^1 P_{CC}^2 (P_{CH}^1 P_{NH}^2 - P_{CH}^2 P_{NH}^1)} \quad (3)$$

As can be seen from Table 1, the constants K_T for phenylhydrazones **7a–i** have virtually equal values, whereas the constant for cyclohexanone phenylhydrazone **7j** is twice as large as these values. The electron-withdrawing (NO₂) and electron-donating (Me) substituents in the para position of the benzene ring of both the hydrazone and carbonyl fragments (compounds **7f–i**) exert only a slight effect on K_T and $\Delta\Delta H^\ddagger$, although it is known⁵² that these substituents have a substantial effect on the kinetics of indolisation. In our opinion, this is evidence that the hydrazone–enehydrazine tautomerisation is not a rate-determining step of Fischer indolisation of arylhydrazones.

IV. Tautomerism in diazoles

Tautomerism in the series of azoles is associated with the mobility of the hydrogen atom of the amino group.⁵³ In the study,⁵⁴ it was demonstrated that the tunnelling proton transfer can occur through an intermolecular hydrogen bond between the NH group of one pyrazole molecule and the lone electron pair of the nitrogen atom of the second molecule. Collective mechanisms involving dimers (**9**) and trimers (**10**) of pyrazole and oligomers of imidazole **11** were proposed.⁵⁴

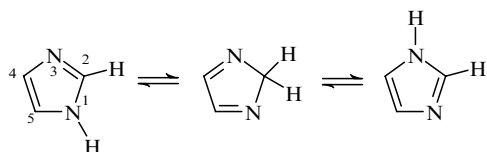




However, the existence of an oligomeric structure of imidazole **12** seems to be unlikely because the IR spectra have no absorption bands of the N^+H group, which must be present in the structure of **12**.⁵⁵ Based on the ^1H NMR spectroscopic data,⁵⁶ it was suggested that solutions of N-derivatives of imidazole contain associates as stacks, which are stabilised by interplanar interactions due to overlapping of the π -electron clouds of the adjacent molecules. Later on, the possibility of the intermolecular proton transfer in imidazole and pyrazole proceeding through the tunnelling mechanism was demonstrated by Nesmeyanov *et al.*⁵⁷ by ^1H and ^{13}C NMR spectroscopy. However, an intermolecular structure was not described. In investigations of the proton transfer in imidazole, preference is given to an intermolecular mechanism. An intramolecular mechanism is energetically unfavourable, which was demonstrated by quantum-chemical calculations⁵⁸ and ^{13}C NMR spectroscopy.⁵⁹ Recently, the proton conductivity in crystalline imidazole was studied by ^{14}N NMR spectroscopy and the so-called migration and reorientation mechanisms were proposed for processes occurring in oligomeric chains.⁶⁰ This conclusion about the formation of oligomeric chains is in contradiction with the results of another study.⁵⁵ It is difficult to give preference to a particular investigation. However, it can be assumed that oligomeric chains can exist in the excited states, due, among other factors, to the difference in the potentials in measurements of the proton conductivities of the imidazole systems. It should be noted that the equilibrium constants depend substantially on the basis set used in *ab initio* quantum-chemical calculations.⁶¹

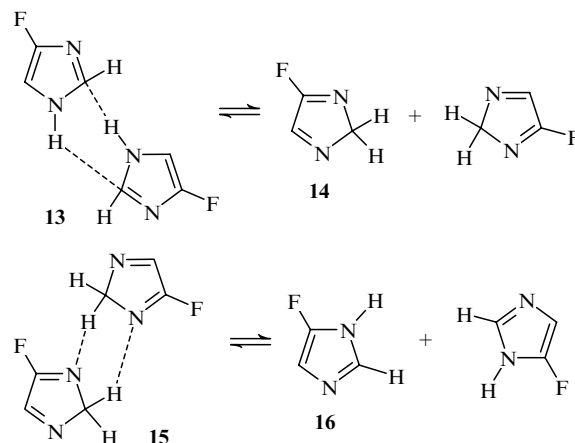
The ability of imidazole derivatives to occur in a particular tautomeric form depends on many factors. Thus, both the NH and 3-OH tautomeric forms of 2,4,5-triphenylimidazole 3-oxide were observed in aqueous solutions, whereas only the latter form was found in non-polar solvents.⁶² Quantum-chemical calculations⁶³ demonstrated that 4- and 5-nitroimidazoles are equally stable in the gas phase, whereas the 4-nitro isomer prevails in solutions. The self-associations of imidazole and 1-, 2-, 4-, and 5-methylimidazoles in aqueous solutions were studied by UV spectroscopy and it was demonstrated that these compounds are prone to dimerisation and polymerisation.⁶⁴

As mentioned above, the intramolecular proton transfer in imidazole is energetically unfavourable. The intermolecular H^1-H^3 proton transfer in the dimer is sterically hindered.⁶⁵ Hence, it was proposed that the tautomerisations of imidazole might proceed through a two-step mechanism involving the H^1-H^3 proton transfer.⁶⁶



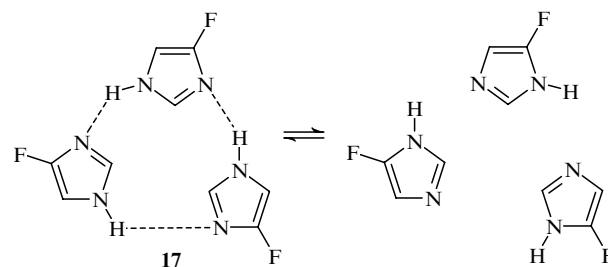
This complex process can occur in two steps through the proton transfer in dimer **13** from position 1 to position 2 to give

H^2 -tautomer **14** followed by the proton transfer in dimer **15** from positions 2 to position 3 to form 3H-tautomer **16**.



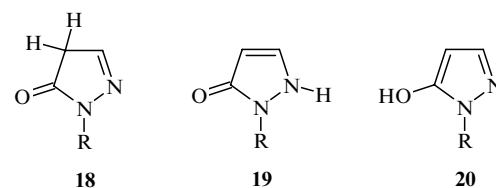
We calculated the activation enthalpies of these steps and the heat of reaction for 4-fluoroimidazole **13**. The activation enthalpies of the first and second steps are 170.5 and 116.6 kJ mol⁻¹, respectively. The heat of the overall reaction ($\Delta\Delta H$) is -50.6 kJ mol⁻¹, *i.e.*, the H^1-H^3 tautomeric transformation in 4-fluoroimidazole is an exothermic process. The equilibrium constants for the first and second steps calculated by Eqn (3) are 2.87×10^{-2} and 3.96×10^{-2} , respectively.

The one-step H^1-H^3 proton transfer in 4-fluoroimidazole can also occur in trimer **17**.



To obtain a quantitative description of the simultaneous transfer of three protons, we calculated the energy, electronic and structural characteristics of these processes in the reaction coordinate mode (R_{NH}).⁶⁵ The high activation enthalpy ($\Delta\Delta H^\ddagger = 454.4$ kJ mol⁻¹) and low heat of reaction ($\Delta\Delta H = 3.8$ kJ mol⁻¹) provide evidence that the tunnelling proton transfer in the trimer of imidazole can occur. The tautomeric equilibrium constant ($K_T = 10^{-2}$) was calculated.

The tautomeric equilibrium for pyrazoles was systematically studied by Elguero and co-workers.⁶⁶⁻⁶⁸ Spectroscopic studies demonstrated that 1-substituted 5-hydroxypyrazoles in non-polar solvents exist predominantly in 4H form **18** with a small admixture of NH form **19**. In aqueous solutions, these compounds exist predominantly in NH form **18** with an admixture of OH form **20**.

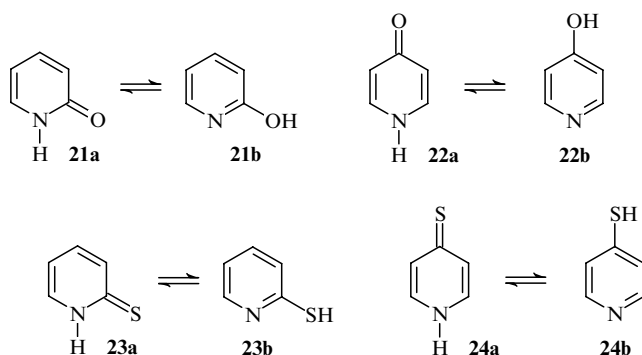


In early studies, it was assumed that the long-range proton transfer takes place in pyrazole.^{66,69} Later on, the dynamics of the intermolecular tautomerisation of pyrazole derivatives in the solid state was studied by NMR spectroscopy and X-ray diffraction analysis.⁶⁷⁻⁶⁹ It was concluded that these compounds can exist as cyclic trimers. In the recent review by Japan researchers,³⁴ the results of subsequent studies performed by Elguero and co-

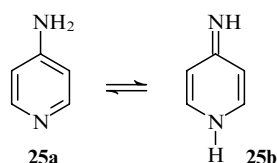
workers were discussed. In these studies, the dimeric,⁷⁰ trimeric^{71–73} and tetrameric^{74,75} mechanisms of proton transfer in pyrazoles through intermolecular hydrogen bonds were examined. Based on the results of NMR spectroscopy and X-ray diffraction analysis, it was concluded that the proton transfer in the compounds under study can proceed through so-called collective mechanisms.

V. Tautomerism in pyridines

In the reviews,^{9,76} it was reported that 2- (**21a**) and 4-pyridones (**22a**) as well as 2- (**23a**) and 4-thiopyridones (**24a**) in aqueous and polar solvents occur predominantly in the oxo and thioxo forms.



However, the amino rather than imino form is typical of 4-aminopyridine (**25a**).



Katritzky attributed this difference in the behaviour of these compounds to stabilisation of ionic intermediates.⁷⁶

It was demonstrated⁷⁷ that stability of tautomeric forms is associated with low enthalpies. Studies of the effect of the solvent on the tautomeric equilibrium led to the conclusion that the ratio between the hydroxy and oxo forms increases linearly as the polarity of the solvent increases.

In the review,⁷⁸ the influence of the structural and external factors, including the possible formation of intra- and intermolecular hydrogen bonds, on the tautomeric equilibrium in pyridine derivatives was examined by spectroscopic and quantum-chemical methods and by investigating individual tautomers.

The position of the tautomeric equilibrium in pyridine derivatives often depends on the concentration of the solutions used. In particular, the constant K_T for 2-pyridone (**21a**) decreases by a factor of 7 upon a 100-fold dilution of a solution in cyclohexane.²⁹ This is attributable to self-association of the molecules. Hence, it was suggested that 2-pyridone (**21a**) might occur as a dimer and 4-pyridone (**22a**) might exist as a chain associate.

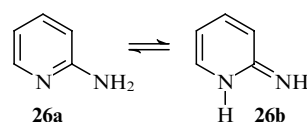
With the aim of studying the effect of the nature of substituents on the tautomeric equilibrium in α -substituted 4-pyridones, the constants K_T were determined by UV spectroscopy. It was demonstrated that K_T depends linearly on the Hammett σ -constant of the substituent.⁷⁹ It was also found that the electron-donating and electron-withdrawing substituents led to increases and decreases in $\log K_T$, respectively.

An intramolecular mechanism of proton transfer was proposed for the lactam–lactim tautomerism in 2-pyridone (**21a**).⁸⁰ The activation barrier calculated by the CNDO/2 quantum-chemical method is 145 kJ mol^{−1}. It should be noted that this method is of little use for the estimation of the energy indices. The value calculated by this method is substantially overestimated. Actually, the activation energy determined in the study on the tautomeric equilibrium in 6-methoxy-2-pyridone⁸¹

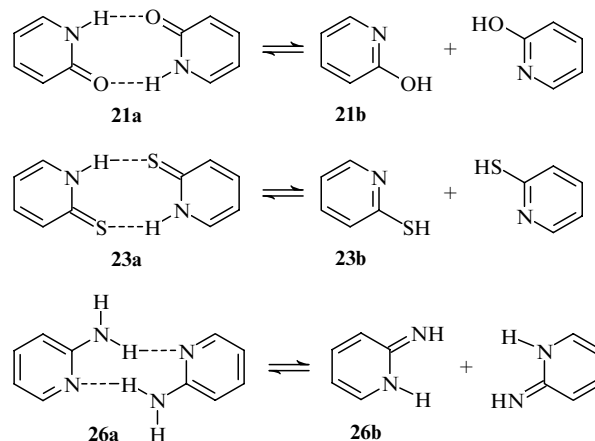
(46 kJ mol^{−1}) is three times lower, which casts some doubt on the energetically unfavourable intramolecular mechanism of proton transfer proposed in the study.⁸⁰

Quantum-chemical methods find wide use for studying the tautomeric equilibria in pyridine derivatives. Thus, the relative stabilities of tautomers of monosubstituted (OH, SH, NH₂) pyridines were studied by the MNDO method.⁸² It was noted that the lactam form is energetically more favourable in all cases, which is in good agreement with the experimental data. Schlegel *et al.*⁸³ calculated the energies of tautomerisation of 2- and 4-pyridones by semiempirical and *ab initio* quantum-chemical methods. The calculations by the semiempirical CNDO/2 and MINDO/3 methods gave unreasonable results, whereas the results of *ab initio* calculations depend substantially on the basis set used. However, in some cases, the calculated values are close to the experimental data. Noteworthy is the study⁸⁴ in which the proton transfer in the lactim–lactam tautomerism in 2-pyridone (**21a**) was examined by *ab initio* methods. Three types of proton transfer were considered, *viz.*, those proceeding by intramolecular and self-association mechanisms and the proton transfer due to the addition of a water molecule. The authors of the cited study believed that the mechanisms, in which the proton transfer occurs either in a dimer or through the addition of a water molecule, are the most reasonable. The enthalpies (ΔH) of tautomerism in 2-, 3- and 4-pyridones were calculated by the semiempirical AM1, MNDO and PM3 methods.⁸⁵ The results obtained by different methods differ substantially from each other and from the experimental data. A good agreement with experiment was achieved only with the use of the AM1 method ($\Delta H = 32.5$ and 30.1 kJ mol^{−1}). The influence of the solvents on the tautomeric equilibrium in 2- and 4-pyridones was studied by the AM1 method,⁸⁶ for which purpose the dielectric permeability of the solvent was introduced into the equation for the total energy. The constant K_T thus calculated is in good agreement with experiment. It should be noted that the calculated and experimental constants K_T depend linearly on the Onsager parameter $\varepsilon - 1/2\varepsilon + 1$, where ε is the dielectric permeability of the solvent.

To obtain a quantitative description of the tautomerism **21a** → **21b**, **22a** → **22b**, the enthalpies (ΔH) and orders of the bonds that are changed (P_{ij}) were calculated by the AM1 and MNDO quantum-chemical methods.

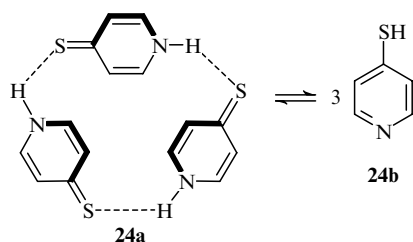
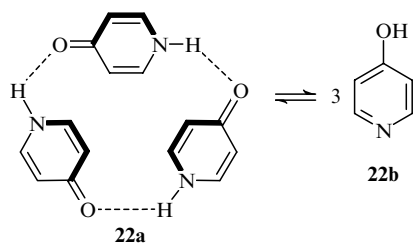


For 2-substituted pyridines **21a**, **23a** and **26a**, the proton transfer was calculated with the use of a dimeric mechanism in the reaction coordinate mode (R_{NH}).⁸⁷



For the tautomerisation of 4-substituted pyridines **22a** and pyridinethiones **24a**, the proton transfer through a dimeric mech-

anism is sterically hindered. In this connection, we proposed a trimeric mechanism for the proton transfer in compounds **22a** and **24a**. In the trimeric forms, the pyridine rings are located perpendicular to the plane of the figure, which excludes repulsions between the hydrogen atoms at positions 2, 3, 5 and 6.



We calculated the equilibrium constants for all types of proton transfer occurring in the course of this process by Eqn (4). (For pyridinethiones, the oxygen atom is replaced by the sulfur atom.)

$$K_T = \frac{P_{\text{NH}}^1 P_{\text{NH}}^2 (P_{\text{CO}}^1 P_{\text{CN}}^2 - P_{\text{CO}}^2 P_{\text{CN}}^1)}{P_{\text{CN}}^1 P_{\text{CN}}^2 (P_{\text{NH}}^1 P_{\text{OH}}^2 - P_{\text{NH}}^2 P_{\text{OH}}^1)} \quad (4)$$

The activation enthalpies ($\Delta\Delta H^\ddagger$), heats of reaction ($\Delta\Delta H$) and equilibrium constants (K_T) for the tautomerisation reactions under study are given in Table 2. It can be seen that the 4-pyridone–4-hydroxypyridine tautomerisation (**22a** → **22b**) with proton transfer through a trimeric mechanism is characterised by a rather high activation enthalpy (446.5 kJ mol^{−1}) and low heat of reaction (9.2 kJ mol^{−1}). This indicates that the proton transfer in this process can proceed through a tunnelling mechanism. The 4-pyridinethione–4-thiopyridine transformation (**24a** → **24b**) is an exothermic process characterised by a substantial heat evolution and a large equilibrium constant. The largest constant K_T was found for the 2-pyridinethione–2-thiopyridine equilibrium (**23a** → **23b**) characterised by small energy indices $\Delta\Delta H^\ddagger$ and $\Delta\Delta H$. It can also be seen from Table 2 that the tautomeric equilibrium constant is inversely proportional to the activation enthalpy. The fact that the known dependence persists in this case provides evidence that the approach used is suitable for the quantitative description of prototropic tautomerism.

Table 2. Activation enthalpies, heats of reactions and equilibrium constants for tautomerisation of substituted pyridines.

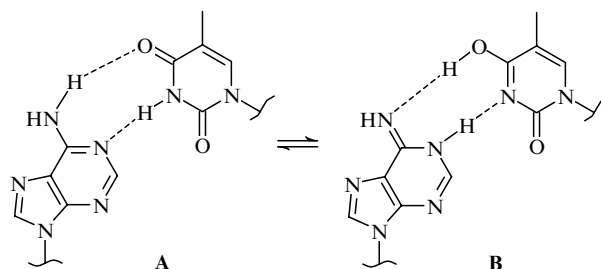
Tautomerisation	$\Delta\Delta H^\ddagger$ /kJ mol ^{−1}	$\Delta\Delta H$ /kJ mol ^{−1}	$10^{-2} K_T$
23a → 23b	44.3	23.4	13.0
24a → 24b	102.0	−99.1	5.2
21a → 21b	195.5	29.7	3.8
26a → 26b	196.6	106.6	4.4
22a → 22b	446.5	9.2	1.8

In conclusion, let us mention the study⁸⁸ in which the vibrational spectrum of 2-hydroxypyridine in an argon matrix was studied by Fourier IR spectroscopy and the constant for the 2-pyridone–2-hydroxypyridine tautomeric equilibrium **21a** → **21b** was estimated. This value (0.4) differs substantially

from all known constants K_T , which were determined both by theoretical and experimental methods.

VI. Tautomerism in nucleotide bases

From the very beginning of molecular genetics, it has been discussed that mutations in DNA replication arise from the ability of nucleic acid bases to occur in rare tautomeric forms involved in mutagenesis.⁸⁹ The keto–amine tautomers **A** are the dominant forms of base pairs (for example, of the adenine–thymine pair) in DNA duplexes. However, each base pair can be transformed into its minor, while still quite stable, enolimine tautomer **B**.⁹⁰ Löwdin⁹¹ attributed the formation of rare tautomeric forms of nucleic acid bases to the concerted transfer of two protons within the base pair linked by a hydrogen bond.



If the ratio between the tautomer **B** and canonical tautomer **A** is larger than 10^{−4}–10^{−5} and the rare tautomer remains stable over time necessary for DNA replication, the double proton transfer may play an important role in spontaneous mutations.^{92–94} Rapid proton transfer between bases can make a contribution to the physical properties of DNA, such as duplex flexibility, protein recognition or stability in DNA replication, etc.⁹⁰ The accuracy of the *in vitro* replication per base pair is 10⁸–10¹⁰ (Ref. 95). A possible reason for mismatches in DNA replication is the formation of hypothetical structures including thermodynamically unfavourable tautomers of natural bases in mismatched pairs, such as AC or GT.⁹⁶ The typical frequency of mismatches upon the insertion of mismatching bases was estimated at 10^{−4}–10^{−6} (see Ref. 96), which is in good agreement with the experimental values (10^{−6}–10^{−10}, see Ref. 85).

In spite of importance of tautomerisation in nucleic acid bases, this process is not characterised experimentally, because studies of the superfast and reversible proton transfer between specific base pairs present difficulties.⁹⁷

The parameters of the tautomeric equilibrium in nucleic acid bases and dynamics of proton transfer are estimated by numerous calculation methods.^{98–101}

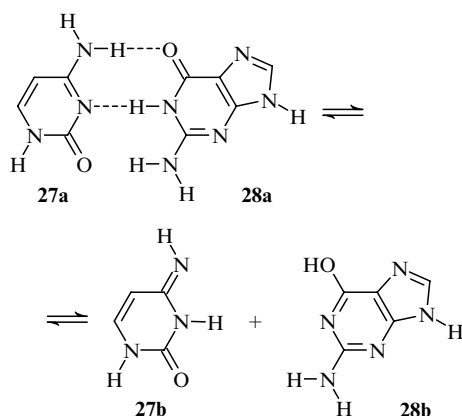
For example, the internal energies of isolated tautomeric forms of guanine and cytosine were calculated by an *ab initio* quantum-chemical method¹⁰² ($\Delta E = 84.6$ kJ mol^{−1}). The authors of the cited study proposed also the equation for calculations of the corresponding equilibrium constants. This equation includes the ratio of the standard state functions of individual tautomeric forms as the preexponential factor.

$$K_{aa'} = \frac{f_a}{f_{a'}} \exp\left(-\frac{\Delta E_{aa'}}{RT}\right),$$

where $K_{aa'}$ is the equilibrium constant of the tautomeric conversion $a \rightarrow a'$; f_a , $f_{a'}$ are the standard state functions of the tautomeric forms a and a' , respectively, and $\Delta E_{aa'}$ is the activation energy of the tautomeric conversion.

Calculations of isolated tautomeric forms of nucleic acids as applied to the quantitative description of the proton transfer in complementary base pairs of DNA do not necessarily provide adequate results. For example, one can calculate the activation enthalpy ($\Delta\Delta H^\ddagger$) of the simultaneous transfer of two protons in the cytosine (**27a**)–guanine (**28a**) complementary pair to form tautomers **27b** and **28b** (equilibrium processes are better described

by the enthalpy difference than by the total energy difference, which is a standard practice in *ab initio* calculations).



However, in this case, two tautomeric conversions, *viz.*, amine–imine (27a → 27b) and lactam–lactim (28a → 28b), take place and their equilibrium constants can have different values and depend on structural changes in DNA. Consequently, these constants K_T cannot be determined with the use of one thermodynamic equation, which is, in addition, invariant with respect to the mechanism of proton transfer.

An intermolecular mechanism was proposed for proton transfer in isolated mono- and dihydrated guanine complexes on the basis of the results of *ab initio* quantum-chemical calculations.¹⁰³ By contrast, an intramolecular mechanism of proton transfer from the amido group with the activation energy of 150 kJ mol^{−1} was suggested in another study¹⁰⁴ also on the basis of *ab initio* quantum-chemical calculations. In our opinion, the formation of such an intramolecular hydrogen bond is impossible from the viewpoint of geometry, although the energy barrier is rather low.

We calculated the activation enthalpies, heats of reaction and constants of the amine–imine (K_T^{AI}) and lactam–lactim (K_T^{LL}) tautomeric equilibria in the cytosine–guanine pair for different lengths of the triad group corresponding to the intermolecular hydrogen bond (R_{NHN} or R_{NHO}) by the semiempirical AM1 method in the reaction coordinate mode R_{NH} . The equilibrium constants were calculated by Eqns (5) and (6).

$$K_T^{AI} = \frac{P_{NH}^1 P_{NH}^2 (P_{CN}^1 P_{CN}^2 - P_{CN}^2 P_{CN}^1)}{P_{CN}^1 P_{CN}^2 (P_{HN}^1 P_{NH}^2 - P_{HN}^2 P_{NH}^1)}, \quad (5)$$

$$K_T^{LL} = \frac{P_{NH}^1 P_{NH}^2 (P_{CO}^1 P_{CN}^2 - P_{CO}^2 P_{CN}^1)}{P_{CN}^1 P_{CN}^2 (P_{NH}^1 P_{OH}^2 - P_{NH}^2 P_{OH}^1)}. \quad (6)$$

Based on the calculated data, we construct the plot of ΔH vs. R_{NH} for $R_{NHN} = 2.8$ Å, which is an energy curve with two minima. The first minimum or term corresponds to the amine and lactam tautomeric forms, and the second term corresponds to the imine and lactim tautomeric forms. The results of complete calculations are given in Table 3. It can be seen that $\Delta\Delta H^\#$ decreases linearly with decreasing R_{NHN} (R_{NHO}). An excellent correlation ($r = 0.99$) achieved in this case indicates that this approach is adequate for the quantitative description of proton exchange between the nucleotides under study. The dependence of K_T^{AI} (K_T^{LL}) on R_{NHN} is a hyperbolic curve, which indicates that the equilibrium constant is inversely proportional to the length of the triad describing an intermolecular hydrogen bond.

According to the opinion that the mutation frequency N_m can be determined from the product of the concentrations of rare tautomeric forms of nucleotides,^{90,92} this parameter can be calculated by Eqn (7)

$$N_m = K_T^{AI} K_T^{LL}, \quad (7)$$

Table 3. Activation enthalpies ($\Delta\Delta H^\#$ /kJ mol^{−1}), heats of reaction ($\Delta\Delta H$ /kJ mol^{−1}), amine–imine (K_T^{AI}) and lactam–lactim (K_T^{LL}) equilibrium constants and mutation frequencies (N_m) depending on R_{NHN} (R_{NHO}) of the proton exchange in the cytosine–guanine pair.

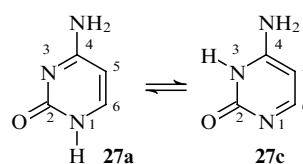
R_{NHN} (R_{NHO})	$\Delta\Delta H^\#$	$\Delta\Delta H$	K_T^{AI}	K_T^{LL}	N_m
3.00	282.6	65.6	1.51	2.16	0.33
2.95	274.6	75.2	1.90	3.00	0.57
2.90	238.7	75.2	2.19	3.38	0.74
2.85	211.5	64.2	2.34	4.28	1.00
2.80	183.1	66.9	3.15	4.83	1.52
2.75	157.6	58.5	3.35	5.50	1.84
2.70	140.9	66.0	4.17	6.70	2.79

because the constants K_T^{AI} and K_T^{LL} give the ratios between the imine and amine or lactim and lactam forms, respectively.

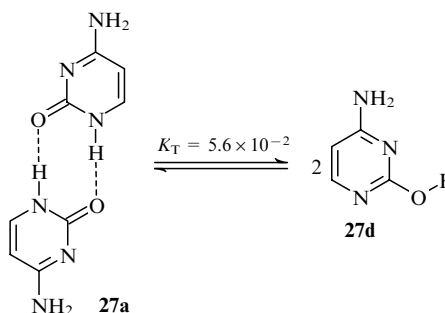
For some R , the mutation frequencies calculated by this equation (see Table 3) are substantially higher than the experimental values reported in the study.⁹⁶ However, it is known that experimental data obtained in studies of rapid processes proceeding at low concentrations of the compounds are sometimes of low accuracy.

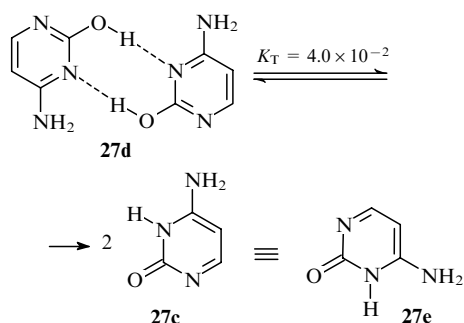
The influence of the solvent on the tautomeric equilibrium of nucleotide bases can be manifested in a deformation of the solvation cavity of the cytosine–guanine dimer, in particular, in a change in the length of the triad corresponding to an intermolecular hydrogen bond [R_{NHN} (R_{NHO})]. As can be seen from Table 3, a decrease in the length of the triad group in the dimer leads to a decrease in $\Delta\Delta H^\#$ resulting in an increase in K_T^{AI} and K_T^{LL} and, consequently, in an increase in N_m . However, the tautomeric equilibrium constant is inversely proportional to the polarity parameter E_T . Consequently, a nucleotide dimer is extended along the intermolecular hydrogen bond in a more polar solvent, whereas this dimer might be contracted in a less polar solvent. Hence, it can be concluded that more polar solvents decrease the spontaneous mutation frequency, whereas this frequency increases in less polar solvents. Since water serves as the solvent in mutation processes in DNA, this approach to modelling the influence of the solvent on the tautomeric equilibrium (see Section II) cannot be applied in the case under consideration. However, this approach may be useful for the qualitative description of scientifically created conditions.

In addition to prototropic tautomerism in DNA, prototropic rearrangements proceeding directly in nucleic acid bases deserve notice. Thus, the amine–imine equilibrium (27a → 27c) in cytosine was considered.^{105, 106}



It is not difficult to understand that the $H^1 \rightarrow H^3$ proton transfer can proceed only through an intermolecular mechanism. In our opinion, this process involves two steps.





The first step represents the keto–enol (lactam–lactim) tautomerisation in compound **27a** with the proton transfer from the amino group to the carbonyl group through a dimeric mechanism. The second step involves the enol–ketone (lactim–lactam) tautomerisation in tautomer **27d** with the proton transfer from the hydroxy group to the imine N(3) atom. The activation enthalpies ($\Delta\Delta H^\ddagger$) of the first and second steps are 157.8 and 107.8 kJ mol^{−1}, respectively. The total enthalpy of the overall process ($\Delta\Delta H^\ddagger$) is 168 kJ mol^{−1}. The heat of reaction ($\Delta\Delta H$) is −5.0 kJ mol^{−1}. Consequently, the 1H → 3H proton transfer is an exothermic process. The rotation of tautomer **27c** about the C(2)–C(5) axis by 180° gives rise to an isomer of cytosine, viz., 2-oxo-6-aminopyrimidine (**27e**). Hence, this transformation can be formally considered as the 1,3-shift of the amino group and a new type of a molecular rearrangement.

VII. Conclusion

It is often assumed that the proton transfer as well as other molecular rearrangements involved in prototropic tautomerisation proceed through an intramolecular mechanism. The results of modern studies show that this mechanism of proton transfer is sometimes both energetically and geometrically unfavourable. From this viewpoint, the so-called collective (dimeric, trimeric, tetrameric or oligomeric) mechanism seems to be more reasonable. The mechanism involving dimers works well in the case of the proton transfer to the *ortho* position. For the proton transfer to the *para* position, trimeric models are more adequate from the viewpoint of geometry. By contrast, a two-step proton transfer is more suitable for the description of tautomerism in compounds containing functional groups in the *meta* positions (as was accepted, for example, for imidazole).

The quantitative description of the prototropic equilibrium by purely chemical methods presents certain difficulties,¹⁰⁷ because the experimental parameters, which are necessary for calculating the equilibrium constants, are sometimes impossible to determine with a high degree of accuracy for compounds present at low concentrations. In this connection, the representation of K_T as a function of the orders of the bonds, which are cleaved and formed in the course of proton transfer, can be used for estimating the reliability of experimental data.

It should be noted that the approach proposed to modelling the influence of the solvent on the prototropic equilibrium is, to a certain extent, formal. However, the K_T – E_T correlation taking into account the polarity parameter of the solvent may be of practical use.

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Determination of the three-dimensional structure for weakly aligned biomolecules by NMR spectroscopy

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Abstract. The key achievements and the potential of NMR spectroscopy for weakly aligned biomolecules are considered. Due to weak alignment, it becomes possible to determine a number of NMR parameters dependent on the orientation of biomolecules, which are averaged to zero in usual isotropic media. The addition of new orientational constraints to standard procedures of 3D structure determination markedly increases the achievable accuracy. The possibility of structure determination for biomolecules using only orientation-dependent parameters without invoking other NMR data is discussed. The methods of orientation, experimental techniques, and calculation methods are systematised. The main results obtained and the prospects of using NMR spectroscopy of weakly aligned systems to study different classes of biomolecules and to solve various problems of molecular biology are analysed. Examples of biomolecules whose structures have been determined using orientation-dependent parameters are given. The bibliography includes 508 references.

I. Introduction

The advances achieved in implementation of the programme of the human genome decoding marked a new stage in investigations of the structure and functioning of living organisms. Study of the human genome entailed the research into the genomes and gene products of many other organisms. The primary structures of many biomolecules have already been determined; however, for understanding of the functioning mechanisms, one should know the spatial structure of these molecules.

The key experimental methods used to determine the three-dimensional structures of biomolecules include X-ray crystallography (X-ray) and nuclear magnetic resonance spectroscopy (NMR).

Currently, The Protein Data Bank (PDB)¹ stores the results of structural studies for ~19 000 proteins and their complexes; however, only ~6000 structures are different and of these, ~1000 structures have essentially different homologies. The 3D structures for an enormous number of proteins are still to be determined.

By the end of 2002, ~83% of the structures of known biomolecules have been determined by X-ray, ~16%, by NMR, and ~1%, by other methods (mainly, by neutron diffraction). The proportion of structures determined using NMR steadily grows. Indeed, by the end of 1997, 1008 structures of various biomolecules had been determined using NMR; during the following four years, this number doubled, and by the end of 2002, it trebled. Moreover, for ~75% of these biomolecules, no data on the crystal structure was included in the PDB.² Nuclear magnetic resonance proved especially efficient for investigation of nucleic acids. It was used to determine more than one-third of all DNA structures and 60% of RNA structures.

Comparison of numerous structural data obtained by NMR and X-ray diffraction methods showed a high degree of compliance, indicating that NMR is a worthy companion for X-ray, although the latter remains the predominant method used to determine the spatial structures of biomolecules. However, many proteins (for example, most of membrane proteins) cannot be crystallised; therefore, X-ray diffraction is inapplicable to them. In addition, to elucidate the role of proteins in various processes, one should know not only their structures but also the dynamic behaviour, furthermore, under conditions resembling, as close as possible, the environment [either liquid or liquid-crystalline (LC)] in which these proteins exist as well as the structures and dynamic behaviour of their partners and complexes. First of all, this refers to processes such as enzymic catalysis, immune response, signal transduction, regulation of protein synthesis, *etc.* These problems can be solved by using NMR spectroscopy, while X-ray diffraction is not always suitable for this purpose.^{3,4}

Despite the fact that NMR and X-ray techniques are based on different kinds of physical phenomena, they have much in common, first, investigation objects; second, computation software that allows processing of both X-ray and NMR data; and third, databases which accumulate, archive and annotate the obtained structural information of biomolecules. Therefore, it is not a surprise that most of the new NMR research centres are established at large functioning sources of synchrotron radiation,

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which is used most often in structural studies. The resolution achieved in both methods is 1.0–1.5 Å and the amount of specimen required is 30–50 mg. Currently, NMR techniques are still much inferior to X-ray as regards the time and cost of determination of one structure. However, owing to the fast development of research using NMR, these parameters may soon become comparable for both methods.

The progress made due to the use of synchrotron radiation, automated systems for sample crystallisation and handling, effective array detectors for data collection and processing, and development of the multiwavelength anomalous diffraction method has transformed X-ray into a fast and convenient method for determining the structures of biomacromolecules. The NMR spectroscopy methods are used predominantly only at a few research centres. In particular, NMR spectroscopy is becoming the major component in investigations of the 3D structures of biomolecules in at least several large research centres.^{2,5} For example, twenty high-frequency NMR spectrometers were installed last year at the RIKEN Genomic Sciences Centre in Japan. It is evident that NMR spectroscopy will be the main tool of investigating the structure–biological functions relationships for proteins.

The modern structural NMR spectroscopy has formed in two phases. The first phase (1985–1995) was characterised by vigorous development and active use of multidimensional Fourier Transform spectroscopy methods[†] for the study of structures of biomolecules.^{6–21} Initially, the measurements were carried out in liquid isotropic solutions using two- or three-dimensional homonuclear NMR methods based on the nuclear Overhauser effect (NOE), and the weights of macromolecules did not exceed 10 kDa.

Further progress of the research was held up by two restrictions of principle. First, the widths of resonance lines in the NMR spectrum in solution are inversely proportional to the spin–spin relaxation time T_2 , which decreases as the size of the molecule increases, and to the rotational correlation time. This diminishes the sensitivity of the pulse sequences used, as long delays are required for coherence transfer.

Second, larger molecules give rise to more complicated spectra, because the numbers of NMR-active nuclei and interactions between them increase.

In the early 1990s, methods of selective $^{15}\text{N}/^{13}\text{C}$ -enrichment of biomolecules as well as multidimensional heteronuclear spectroscopy and triple resonance spectroscopy with pulse gradients were developed. Thus the mass of eligible proteins was increased to 25 kDa.²² With the progress in a NMR hardware (the appearance of high-frequency spectrometers operating at 700, 800 and 900 MHz, probes with magnetic field pulse gradients, *etc.*) and with the advent of procedures for partial and selective deuteration of biomolecules, it became possible to study molecules with higher masses, up to 35–40 kDa.^{23–25} Combination of triple resonance spectroscopy with $^{15}\text{N}/^{13}\text{C}$ -enrichment and perdeuteration allows investigation of proteins weighing up to 50–60 kDa. The up-to-date TROSY (Transverse Relaxation Optimized Spectroscopy) and CRINEPT (Cross-Correlated Relaxation-Enhanced Polarisation Transfer) methods^{26–33} have increased this value to more than 100 kDa.^{34–36} For instance, the structure of an octameric protein with a 110 kDa mass has been determined.³⁷ Certainly, this is not the limiting value. For example, the segment-by-segment isotope labelling procedure reported recently,^{38,39} the decrease in the rotational correlation time by using low-viscosity solvents,⁴⁰ and the use of cryogenic probes and high-frequency NMR spectrometers (with an operating frequency of 1 GHz or higher) provide the possibility of increasing substantially the size

of molecules that can be studied, especially resorting to new, in principle, ideas and approaches.^{3,41}

The second phase in the study of the structures of biomolecules by NMR spectroscopy, which started in 1995, was marked by the advent of a new approach. It was proposed to use the orientation of biomolecules on exposure to the spectrometer magnetic field.^{42,43} For aligned molecules, one can determine additional parameters of NMR signals that bear structural information, first of all, the residual dipolar coupling constants (RDC).⁴⁴ However, even in strong magnetic fields, the orientation of biomolecules was very weak; therefore, it was possible to measure only the RDC for directly linked nuclei in biomolecules with highly anisotropic magnetic susceptibility. The accuracy of structure determination in these experiments was not inferior to that in NOE-based experiments but still left much to be desired.

Tjandra and Bax⁴⁵ proposed using micellar solutions and dilute LC phases for the orientation of biomolecules. In these media, the degree of alignment of biomolecules can be easily controlled by changing experimental conditions, for example, component concentrations and temperature. In this case, one can select the optimal values of the order parameters and to simplify the spectra.

By using NMR methods, one can determine a number of physical characteristics bearing information on the interatomic distances and angles in the molecule. Most of these values are orientation dependent, *i.e.*, they depend on the orientation of biomolecules relative to the direction of the magnetic field; in usual isotropic solutions, they are averaged to zero due to the fast rotation of molecules. Nevertheless, there exist some parameters containing indirect information on the distances between the magnetic nuclei and on dihedral angles which can be elucidated in experiments with isotropic solutions. For example, these are nuclear spin relaxation times in NOE experiments depending on the dipole–dipole couplings between them; the spin–spin coupling constants through three covalent bonds (^3J) or cross-correlated relaxation rates depending on the dihedral angle between these bonds. In addition, the chemical shifts of some protons and carbon atoms depend crucially on the environment and can be useful for determining the tertiary structure of proteins.

Despite the low accuracy of the results, the complexity and high cost, NOE experiments are widely used to determine the spatial structures of biomolecules in solutions. Recently, several other parameters characterising specific properties of various types of relaxation were added to the known parameters, ^3J and chemical shifts. However, by using isotropic parameters, one can establish only the local structure, whereas the use of orientation-dependent values allows determination of both the local and long-range structures.

Direct quantitative measurement of orientation-dependent parameters, for example, RDC, from the splitting observed in the spectra of oriented molecules is certainly preferable to rough evaluation of these parameters in NOE experiments using qualitative analysis of cross-peak intensities for isotropic solutions. In the former case, we are dealing with an effect that can be interpreted using only the first-order perturbation theory; in the latter case, experimental results can be interpreted only by resorting to higher-order perturbation theory (*i.e.*, a much rougher approximation); moreover, they can be masked by other effects. In addition, RDC can be measured faster and more accurately (and between a much larger number of different nuclei) in the spectra of oriented specimens than only between protons in NOE experiments. This means that RDC are more suitable for structural studies, as was brilliantly demonstrated in a publication⁴⁶ in which the 3D structure of a protein backbone was determined using only residual dipolar couplings without invoking the data of NOE experiments. This publication marks a change in the priority in the structural studies of biomolecules by NMR spectroscopy: cumbersome NOE-based experiments in isotropic media with approximate estimation of the distances between some close

[†] In 1991, Ernst (Switzerland) was awarded the Nobel Prize in chemistry for these studies.

protons are replaced by fast and efficient experiments with measurement of more informative and diverse parameters for oriented molecules directly related to their geometry.

A number of methods for the measurement of orientation-dependent NMR parameters have now been developed and development of new methods is in progress. They are based on investigations of biomolecules, either completely aligned in the solid phase or partially aligned in a liquid or LC medium. These methods are equally good for investigating both the structures of biomolecules and conformational changes, for determining the relative orientation of the domains, the formation of intermolecular complexes and for investigation of dynamic processes.^{47, 48} Experiments with weak alignment of biomolecules have been most successful so far, although it is expected that solid-state NMR techniques for highly oriented biomolecules (in the solid state) would prove to be more efficient in the study of structures and functions of membrane proteins.⁴⁹

In modern approaches, the new methods mentioned above are combined with 'classical' methods based on the NOE, the use of vicinal ^3J constants, chemical shifts and relaxation times. This permits reliable determination of the structures of proteins with a mass of up to 100 kDa and even more. The research of biomolecules by NMR spectroscopy can be classified into three groups of studies carried out in parallel:^{18–21}

- in liquid isotropic media;
- in weakly aligned media;
- solid-state experiments with magic angle spinning.

This review describes the scope of NMR spectroscopy of weakly aligned biomolecules in solutions. The procedures used in NMR studies of non-aligned molecules are also outlined. The ways of orienting biomolecules, the types of orientation-dependent parameters, experimental procedures, and calculation methods are described in detail; the main results and prospects for the use of NMR spectroscopy of weakly aligned molecules in the research of proteins, nucleic acids and oligosaccharides are analysed.

II. Methods of investigation of the structure of non-oriented biomolecules in solution

The structure of a biomolecule can be represented by either a set of Cartesian coordinates (x, y, z) of each atom or by a set of intrinsic coordinates [for proteins, these are bond lengths and angles $\phi, \psi, \omega, \chi_1$, and χ_2 for each amino-acid residue (Fig. 1)].

1. Nuclear Overhauser effect and its use in structural studies

Nuclear magnetic resonance techniques based on NOE have been used successfully for more than 20 years to elucidate the three-dimensional structures of biomolecules in solutions. NOE parameters are determined in 2D and 3D experiments and are used subsequently to calculate the interatomic distances. The studies of

small proteins, transport RNA, oligonucleotides and interactions of proteins with ligands and nucleic acids are described in detail in many publications.^{7–25, 50}

The NOE is underlain by the fact that the rate constant for the dipole cross-relaxation is inversely proportional to the sixth power of the distance between the interacting nuclei. The intensities of NOE cross-peaks, which are proportional to the rate constants for cross-relaxation are determined in experiments. Thus, if one distance between protons (R_0) is known (for example, from the trivial covalent geometry of the molecule), the other, unknown R_x can be determined from the relation

$$R_x = \left(\frac{I_0}{I_x} \right)^{1/6},$$

where I_0 and I_x are the integral intensities of the corresponding cross-peaks.

A 2D (or 3D) NMR spectrum of a protein contains numerous NOE cross-peaks corresponding to different pairs of protons. Depending on the intensity, they are classified into strong, medium-intensity and weak. Strong cross-peaks correspond to protons neighbouring *via* covalent bonds (for example, geminal protons in the methylene groups or vicinal protons in aromatic rings) and to neighbouring protons in a regular secondary structure of the protein (for example, H^N-H^α along the chain, $H^\alpha-H^\alpha$ and H^N-H^α in β -sheets). The medium-intensity cross-peaks usually correspond to H^N-H^α pairs in helices. Even for proteins with a mass below 10 kDa, the number of these responses is about 100; this is sufficient for determining the spatial structure of the protein globule. The structures of many proteins with masses of up to 100 kDa have now been determined using several hundred (in some cases, above several thousand) cross-peaks.

The major advantage of these studies over X-ray studies is that the structure of a biomolecule is determined in a solution rather than in a single crystal. The structures of some biomolecules are known to change upon crystallisation; therefore, structure determination in solution is preferred, in particular, for physicians and biologists. In addition, the molecules in the crystal are exposed to anisotropic crystal fields; therefore, discrepancy between the structures determined in the crystal state and in solution does not mean by itself that either of these structures is erroneous.

However, the NOE arises only between closely spaced (not more than 5–6 Å) magnetic nuclei (mainly, protons), whereas X-ray diffraction analysis allows determination of the position of any atom. Yet another important difference between these methods is manifested in investigations of mobile molecules. The crystal structure determined by X-ray is a simple superposition of all molecules present in the crystal, whereas NOE experiments provide certain averaged $(\langle r_{ij}^{-6} \rangle)^{-1/6}$ values rather than the distances themselves. This implies that in the former case, the contributions of all fluctuations to the distances between the nuclei in the crystal structure are identical, while in the latter case, the contributions of states with closely located protons to the measured distances are much greater than the contributions of states with remote protons, resulting in apparent shortening of the averaged distance.

Nuclear Overhauser effect experiments successfully supplement X-ray studies, especially in those cases where crystal data are not readily available, in a comparative study of oligonucleotides with different sequences, and in a study of transitions between various DNA conformations.

Until recently, data on the geometry of biomolecules in solutions have been mainly gained in NOE experiments. However, the knowledge of distances between protons found in these experiments does not suffice for structure determination. Therefore, the use of any additional information is useful both for structure refinement and for facilitating the structure determination procedure.

As the mass of the biomolecule increases, the NOE signals are broadened, which may result in line coalescence in the spectra.

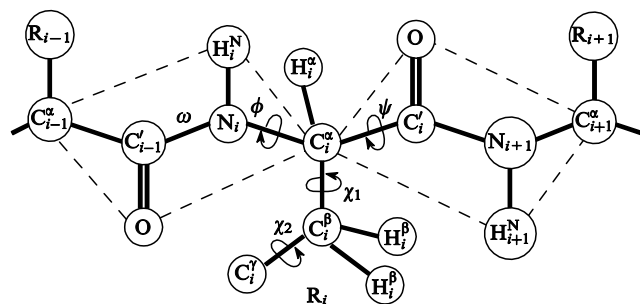


Figure 1. Fragment of the protein polypeptide chain. Dashed lines designate the peptide planes. The backbone conformation is determined by the angles ϕ and ψ for each amino acid residue R and the side chain conformations are determined by the angles χ_1 and χ_2 .

This phenomenon can be controlled by using partial deuteration; however, this markedly decreases the number of NOE signals and increases the cost of structure determination. This makes the additional information obtained in other experiments even more significant.

2. Spin–spin coupling constants

The use of spin–spin coupling constants through three bonds ^3J in structural studies is based on the fact that they obey an empirical dependence on the dihedral angle θ described by Karplus:^{10, 13}

$$^3J(\theta) = A\cos^2\theta + B\cos\theta + C.$$

The coefficients A , B and C depend on the types of particular nuclei forming the dihedral angle; they are determined during optimisation of experimental ^3J constants and the angles found from high-resolution X-ray diffraction data for a multitude of molecules. There are several of these constants for protein molecules. The constant $^3J(\text{H}^N - \text{H}^\alpha)$ directly related to the torsion angle ϕ of the peptide chain is the most convenient for structural studies, as it can be determined rather simply and accurately. Data on the other torsion angle of the peptide chain ψ are contained in the $^3J(\text{N} - \text{H}^\alpha)$ and $^3J(\text{N} - \text{N})$ constants, but, unfortunately, they are both small and, moreover, change the sign. In return, data on the conformations of side chains, in particular on the torsion angle χ_1 , can be derived from the spin–spin coupling constants for different pairs: $\text{H}^\alpha - \text{H}^\beta$, $\text{N} - \text{H}^\beta$, $\text{C}' - \text{H}^\beta$, $\text{H}^\alpha - \text{C}^\gamma$, $\text{N} - \text{C}^\gamma$, $\text{C}' - \text{C}^\gamma$.

The possibility of using the spin–spin coupling constants through one or two bonds in structural research has been barely studied until recently. However, the advent of NMR spectroscopy of weakly aligned molecules brought about the necessity of separating the contributions of the coupling constants and RDC through one bond to the observed splitting because a researcher measures a spin–spin coupling constant every time he determines a RDC. At first glance, these constants provide little information and are measured with a too low accuracy, but they can still be used. For example, the $\text{C}^\alpha - \text{H}^\alpha$ and $\text{C}^\alpha - \text{C}^\beta$ constants proved to be ‘sensitive’ to the torsion angle ψ of the peptide chain.⁵¹ The number of spin–spin coupling constants suitable for conformational studies of nucleic acids and carbohydrates is greater and their information content is higher; therefore, they have been better studied.⁵² In addition, the knowledge of spin–spin coupling constants is important due to the fact that they allow one to plan NMR experiments with coherence transfer *via* the corresponding bonds.

3. Chemical shifts

The chemical shifts of nuclei depend on their local environment and, actually, they bear all information needed to determine the 3D structure of the molecule. However, calculation of a 3D structure using chemical shifts alone has not been performed so far, although some progress along this line has been achieved.^{53, 54}

The chemical shifts of the ^1H , ^{15}N , ^{13}C and ^{31}P nuclei are widely used as constraints in determining the structure of a biomolecule. Empirical correlations between the ϕ and ψ angles, which determine the conformation of a section of the peptide chain, and the H^N , H^α , ^{15}N , $^{13}\text{C}'$, $^{13}\text{C}^\alpha$ and $^{13}\text{C}^\beta$ chemical shifts are known.⁵⁵ For example, the $^{13}\text{C}^\alpha$ and $^{13}\text{C}^\beta$ chemical shifts in the α -helices and β -sheets are markedly different, which allows reliable identification of these elements of the protein secondary structure. Similar correlations have been found for nucleic acids.⁵²

The structural information contained in these chemical shifts duplicates to some extent the information obtained using ^3J constants (for example, data on ϕ angles). However, not all the ^3J constants can be measured (because they are too small or because of broadening or overlap of spectral lines), whereas chemical shifts can be determined for any atom.

The signal assignment and chemical shift determination procedures are almost entirely automated; they are performed at an initial stage of structural studies. When these values are known,

one can establish and locate rather reliably the elements pertaining to the secondary structure of the biomolecule,⁵⁶ which is important for further analysis.

The chemical shifts of nuclei are determined not only to obtain tentative data concerning the structure; their changes during functioning of the biomolecule can serve as a fast-response tool suitable for investigating biochemical processes, screening low-molecular-mass ligands, and determining the sites of their binding to the biomolecule. The results of these studies are required, first of all, for the development of drugs.

4. Determination of constants through one hydrogen bond

Hydrogen bonds are the key stabilising factor which determines the secondary and tertiary structures of biomolecules. Until recently, the existence of hydrogen bonds could be inferred only indirectly from the NMR parameters, for example, from the rates of proton exchange, ^1H and ^{15}N chemical shifts, isotope shifts or the spatial proximity of partners.

However, it was found that the constants through one hydrogen bond can be determined rather easily for the molecules of nucleic acids or proteins. In particular, the $^2J_{\text{N} \cdots \text{HN}}$ constants between the ^{15}N atoms of the purine and pyrimidine bases in the Watson–Crick pairs have been measured for both RNA⁵⁷ and DNA.²⁷ The spin–spin coupling constants found are rather high ($^2J_{\text{NN}}$ is about 6–7 Hz); they depend on the length of the hydrogen bond.⁵⁸ Therefore, measurement of the through-hydrogen-bond constants is not only indicative of the presence of this bond (this can also be inferred indirectly from the chemical shifts) but also allows one to determine the bond length.^{59, 60} Smaller constants ($^1J_{\text{HN}}$ of about 2–4 Hz) have been found between the imine group proton and its ^{15}N acceptor in the Watson–Crick pairs.

For proteins, the $^3J_{\text{CO} \cdots \text{HN}}$ constants have also been found.^{61–63} They are equal to 0.2–1.0 Hz and also depend on the length of the hydrogen bond.⁶³

5. Relaxation parameters

One relaxation parameter, the intensity of NOE peaks, has been mentioned above.

The times of heteronuclear relaxation contain information on the intramolecular dynamics. For example, the spin–spin relaxation time T_2 for a ^{15}N nucleus is a function of both frequency-dependent and frequency-independent constituents of the spectral density, and the spin–lattice relaxation time T_1 is a function of only frequency-dependent components. Due to anisotropy of rotational diffusion in the absence of large-amplitude motions in the molecule (and, hence, without broadening of NMR lines), the T_1/T_2 ratio for the ^{15}N nuclei in a protein molecule with an axially symmetrical diffusion tensor depends only on three variables: the angle between the vector of the $\text{N} - \text{H}$ bond and the principal axis of the diffusion tensor and the parallel and perpendicular components of the diffusion tensor. This fact can be used to determine the orientation of the $\text{N} - \text{H}$ bond vector, and the T_1/T_2 ratio can be included as an independent variable into the group of varied parameters for determining the structure of a biomolecule.^{64, 65}

In recent years, methods based on cross-correlation (or interference) of the relaxation mechanisms related to the dipole–dipole interaction (DD) and chemical shift anisotropy (CSA) have been used for gaining structural and dynamic information on biomolecules.⁶⁶ These methods are based on elucidation and use of DD–DD,^{67–69} DDI–CSA^{70–73} or CSA–CSA⁷⁴ type cross-correlations. One more type of cross-correlation is found in paramagnetic proteins, namely, that between the DD and the Curie spin, which is the net magnetic moment of the system of interacting nuclei and the unpaired electron.⁷⁵ These tensor correlations are very convenient for studying the dynamics⁷⁶ and determining various torsion angles in biomolecules.^{77, 78}

For example, to find the ψ angle in proteins, one can measure the following relaxation rates: DD($\text{C}^\alpha - \text{H}^\alpha$)–DD($\text{N} - \text{H}^N$),^{68, 69} DD($\text{C}^\alpha - \text{H}^\alpha$)–CSA(^{15}N),⁶⁸ DD($\text{C}^\alpha - \text{H}^\alpha$)–CSA($^{13}\text{C}'$)^{70, 71} and

$\text{CSA}(^{13}\text{C}') - \text{CSA}(^{13}\text{C}')$.⁷² The use of cross-correlated $\text{DD}(\text{C}-\text{H}) - \text{CSA}(^{31}\text{P})$ relaxation has been proposed for determining the angles in the phosphodiester chain of RNA.⁷³

The cross-correlation of relaxation parameters has also been used to study the glycoside bond in polysaccharides,⁶⁹ to explore the intramolecular dynamics in proteins^{76,79} and to determine the conformations of the sugar rings in RNA⁸⁰ and the geometry of metal binding in zinc-containing protein molecules.⁸¹ The research making use of relaxation parameters is only at the beginning but encouraging results have already been obtained.^{82,83} For instance, TROSY spectroscopy has been embodied owing to these studies.

III. Study of membrane proteins by solid-state NMR spectroscopy

Studies into the structure of biomolecules by solid-state NMR spectroscopy carried out by several research groups are currently in progress.^{84–91}

Biomolecules are oriented to the greatest extent in the solid phase; however, due to the absence of rotational or translational degrees of freedom, the NMR spectra exhibit lines corresponding to interactions of magnetic nuclei not only within the molecule but also with the magnetic nuclei of neighbouring molecules. This makes the spectrum more complicated; it contains a large number of overlapping lines. In addition, the protein molecules forming a crystal unit cell are oriented in different ways relative to the crystal axes, and, hence, the RDC for the same pairs of nuclei are different in the magnetic field of the spectrometer.

In order to simplify the NMR spectra, one can use the LC phases of the studied substances. In an ideal case, the spectra should exhibit only intramolecular interactions, while intermolecular interactions should be averaged to zero. However, the mere use of LC phases would not ensure a full success due to the same problem: there are too many magnetic nuclei in a biomolecule. Nevertheless, the fact that intermolecular interactions are not manifested in the spectra is a step forward. By using methods for simplification of NMR spectra with allowance for the fact that the principal axes of molecules are unidirectional, it becomes possible to interpret the results obtained much more accurately than with crystals. This new line of research is currently vigorously developing, especially in investigations of insoluble membrane proteins.

Membrane proteins participate in important processes in cells (intercellular bonds, signal transduction, toxin secretion, transport of ions and nutrients); therefore, they are of interest as potential targets for drugs. It is difficult to determine the spatial structure of a membrane protein by X-ray or liquid-state NMR. These proteins virtually do not crystallise and are almost insoluble; even if a crystal or a solution is obtained, the protein structure may no longer correspond to the native structure. In addition, for understanding of the mechanism of functioning of a membrane protein, it is important to know the positions of elements of the secondary structure of the protein itself relative to the membrane.

Only several dozens of structures for membrane proteins have now been determined by X-ray with a resolution of 0.3 nm, while for soluble proteins, this number is more than 3000 for the same resolution. The structures of several more membrane proteins have been established using electron microscopy of two-dimensional crystals obtained by crystallisation of protein-containing lipid bilayers. However, this does not provide a satisfactory resolution. Thus, NMR spectroscopy appears to be the most promising technique for large-scale determinations of the structures of membrane proteins.

Solid-state NMR is convenient for investigations of membrane proteins in lipid bilayers, because both the tertiary structure of the membrane-embedded protein and the protein orientation relative to the membrane surface can be determined simultaneously.

Membrane proteins are oriented in the same way with respect to the membrane but are arranged chaotically on its surface. Actually, both the membrane and the protein are in the LC state, the degree of alignment of biomolecules being very high. This accounts for the multiple dipolar splittings of lines, which makes the resultant spectrum unresolved, like the spectra of usual organic crystals. However, in the case of membrane proteins, in view of the fact that the proteins are similarly oriented on the membrane, there is a unique opportunity to prepare specimens in which the membranes themselves are also aligned. Such a specimen would be suitable for investigation by solid-state NMR techniques.

In most of these techniques, magic-angle spinning of the oriented specimen is combined with other NMR tools (multi-dimensional spectroscopy, multi-quantum experiments, *etc.*). In this case, the orientation-dependent information is lost (due to averaging), but it can be restored by analysing, for example, the spinning sidebands.^{92–94}

In order to decrease the RDC value for highly aligned molecules and to simplify the NMR spectrum, magic-angle spinning in the spin space is used; this is attained by using special pulse sequences.

Magic-angle spinning (or spinning at a very similar angle) results in virtually complete averaging of relatively small RDC from remote nuclei, leaving only the contributions from non-averaged large RDC, which are usually due to directly linked or very close nuclei. Since the distances between such nuclei are often known with high accuracy (the distances between the nuclei at the sites of contact of different chain sections are an exception), the experimental RDC values can be used to find the orientation of each pair of nuclei relative to the magnetic field. The set of these parameters called orientational constraints determines the conformation of the biomolecule in space. This method developed in a number of studies^{95–99} can be successfully used to determine the structure and polymorphism of the membrane proteins.

Up till now, solid-state experiments have been carried out using the RDC of a covalently bonded $^{15}\text{N} - ^1\text{H}$ pair which lies in the plane of the peptide bond. Potentially suitable are the RDC for the directly linked $^{13}\text{C} - ^1\text{H}$, $^{17}\text{O} - ^{13}\text{C}$, and $^{15}\text{N} - ^2\text{H}$ heteronuclear pairs,^{96,100} the $^{13}\text{C} - ^{13}\text{C}$ and $^{15}\text{N} - ^{15}\text{N}$ homonuclear pairs, and the ^2H -quadrupole couplings.⁹⁷ The first attempts were undertaken using the $^1\text{H} - ^1\text{H}$ coupling constants for exchanging protons. They were determined by the homonuclear dipole–dipole decoupling technique in the MAS (Magic Angle Spinning) spectra of highly deuterated proteins and peptides.^{101,102}

The $^{15}\text{N} - ^1\text{H}$ dipolar coupling constants are mainly determined in SLF (Separated Local Field)¹⁰³ and PISEMA (Polarisation Inversion with Spin Exchange at the Magic Angle) experiments.¹⁰⁴ The procedures of these experiments make it possible to exclude the homonuclear proton–proton constants and to increase sharply the resolution of spectra. These procedures are vigorously developing now.^{85,105,106} The known REDOR (Rotational Echo Double Resonance) procedure has started to be used in the solid-state investigations of biomolecules.^{103,107,108}

The PISEMA spectra as well as the usual heterocorrelated $^1\text{H}/^{15}\text{N}$ NMR spectra exhibit readily diagnosable cross-peaks, which form resonance patterns called PISA-Wheel, because they correspond to α -helices or β -sheets that are somewhat tilted in the membrane body. These resonance patterns serve as excellent and clearly visible indicators for the presence of secondary structure elements (α -helix or β -sheet) and their orientation with respect to the membrane.^{109–112} For visualisation and reliable identification of this type of spectral images and for numerical simulation of the spectra of proteins, a very convenient SIMMOL program,¹¹³ integrated into the SIMPSON program,¹¹⁴ used for the analysis of the solid-state protein spectra, has been developed.

Note that usual methods of NMR spectroscopy in the liquid state are also applicable to membrane proteins provided they are placed in, for example, micelles.^{115,116} The NMR spectra of solutions of these encapsulated membrane proteins resemble the

spectra of soluble proteins. For increasing the relaxation times, one can use low-viscosity solvents or reversed micelles.⁴⁰ This procedure was used to establish the structure of the transmembrane domain of membrane protein A from *E. coli* embedded in dodecylphosphocholine micelles¹¹⁷ (the structure proved to be identical to the structure determined by X-ray diffraction analysis in n-octyltetraoxyethylene micelles) and the OmpX membrane protein from *E. coli* in dihexanoyl phosphatidylcholine micelles.³³

Gramicidin A is the first membrane protein whose structure has been determined by solid-state NMR using isotope labels.^{96, 118–120} Subsequently PISEMA experiments were used to sequence the structure of the transmembrane M2 segment of the nicotine acetylcholine receptor,^{121, 122} which is a single helix arranged at an angle of 12° to the membrane normal. A membrane pore designed in molecular modelling accommodated five of these helices. It was established in similar experiments that the M2 protein of the influenza virus A forms an ion channel out of four helices located at a 35° angle to the membrane normal,^{123, 124} while the Vpu protein forms a similar channel in the HIV-1 membrane at an angle of 15°.¹²⁵ Structural and topological studies of some other membrane proteins have been reported.^{126–128}

The results of numerical modelling of the high-resolution solid-state NMR spectra of uniformly isotope-enriched membrane proteins, rhodopsin and porin, in oriented lipid layers made it possible to increase the efficiency of the experimental procedures used.¹²⁹

The structures of only two membrane proteins have now been deposited with the PDB, namely, gramicidin A and M2 of the acetylcholine receptor. The intensive development of solid-state NMR spectroscopy provides every reason for hoping that the number of these structures will increase within the next few years.

Encouraging results were also obtained in the development of procedures for determination of the structures of single-crystalline specimens of ¹³C- and ¹⁵N-enriched peptides.^{88, 130}

The high degree of alignment of molecules in solid specimens brings about specific problems; the procedures used to solve these problems allow one to diminish artificially the effects of the high degree of alignment down to acceptable values which normally correspond to weakly aligned molecules. Weak alignment of molecules can also be attained in the liquid phase.

IV. Methods for alignment of biomolecules in solutions

The idea of the orientation of molecules for gaining structural information sprang up in the early 1960s. Later, this was implemented in practice with the advent of the method for the orientation of molecules by placing them in an LC medium; this method has been used to determine the structures of small organic molecules.¹³¹ Other ways of orientation appeared non-competitive at that time due to low degrees of alignment achieved and the limitation on the number of magnetic nuclei in the molecule, which had to be not more than 10–12; otherwise, interpretation of the NMR spectrum became impossible due to overlap of lines.

At that time, the possibility of studying biomolecules in this way seemed impracticable. However, the idea to use weakly aligned molecules for structural purposes, paradoxical at first glance, made it possible to simplify the NMR spectrum and to eliminate the limitation on the number of magnetic nuclei in the molecule. In addition, the lines in the NMR spectra of weakly aligned biomolecules, unlike the lines of highly aligned molecules, are not virtually broadened due to faster reorientation.

Weak alignment of biomolecules can be attained by a much greater number of methods than high alignment. The type of alignment depends on the specific interactions of the biomacromolecule with the orienting forces or particles; therefore, the orientation mechanisms in different media can differ in principle; this is important for selecting the optimal experimental condi-

tions, more facile data interpretation, and for automation of experiments and calculations.

The simplest methods used for orientation of biomolecules include exposure to magnetic or electric fields or pressure, stretching or straining of microporous matrices, flow and gradient of velocity in the flow. Lyotropic liquid crystals, polymer gels, zeolites and so on can be used as media for the orientation. Virtually all of these methods have been covered in a review.¹³² Orientation by particles is accomplished due to stereospecific interactions of the biomolecules with highly anisotropic particles shaped like discs (bicelles, membrane fragments) or rods (phages, viruses) which are readily aligned under the action of a magnetic field. The molecules of the orienting media can be either oriented (additionally oriented, reoriented) under the action of the magnetic field of a spectrometer or retain their initial orientation.

The media that can be oriented due to steric interactions are preferred because they have no influence on the rotational correlation time and, hence, the line widths in the NMR spectrum remain constant. The orientation on complex formation often affects appreciably the mechanisms of rotational correlation, and, hence, T_2 . The orienting properties of various media have been described in detail in reviews.^{133–135} Currently, intensive search for new methods for the orientation of biomolecules is in progress. Figure 2 sketches different types of LC media used for weak alignment of biomolecules in NMR spectroscopy.

1. Alignment induced by an external magnetic field

Molecules with a non-zero anisotropy of magnetic susceptibility can be aligned on exposure to an external magnetic field. The orientation of molecules in solution obeys the Boltzmann law, the degree of alignment being proportional to the magnetic field strength squared.¹³⁶ In practice, the degree of alignment of molecules is slight and cannot be observed under usual conditions.

The partial alignment of molecules induced by a magnetic field, resulting in new or additional line splittings in high-resolution NMR spectra, was first observed by Bothner-By and coworkers.^{137, 138} They studied the paramagnetic complex bis[(*p*-tolyl)-tris(pyrazolyl)borato]cobalt(II). The orientation under the action of a magnetic field was very weak and took place only for some of the molecules, mainly complexes with paramagnetic metals. With the progress in NMR hardware, the magnetic fields in the spectrometers have become stronger; therefore the orientation effects are observed more and more frequently¹³⁹ and they should be taken into account for precise determination of spin–spin coupling constants.

It was shown⁴² that biological molecules, for example, DNA duplexes and quadruplexes can also be aligned in the magnetic field of the spectrometer. In particular, the researchers observed rather substantial changes in the ¹J_{CH} constants in DNA dodecamers upon an increase in the magnetic field strength. It was proposed to use this effect in structural studies.

The research group headed by Prestegard⁴³ demonstrated the orientation of molecules of a paramagnetic protein, cyanomethmyoglobin, on exposure to a magnetic field. The measured ¹J_{NH} values differed from the known ones. The difference between the constants (–1 to 5 Hz) was attributed to the residual ¹⁵N–¹H dipolar coupling.

Tjandra *et al.*¹⁴⁰ observed magnetic field-induced orientation even for the diamagnetic ¹⁵N-enriched human ubiquitin protein. The anisotropy of magnetic susceptibility of this protein is an order of magnitude lower than those for cyanomethmyoglobin or DNA dodecamers; correspondingly, the residual constants are also lower (< 0.3 Hz). The studies were carried out using three NMR spectrometers with different magnetic fields. The constants ¹J_{NH} were measured using two procedures. A constant was found to comprise two components: an orientation-independent component caused by the dynamic frequency shift and orientation-dependent component caused by the ¹⁵N–¹H RDC. The residual ¹³C–¹H dipolar couplings for the same protein enriched in ¹³C have been measured.¹⁴¹ The measurements were carried out using

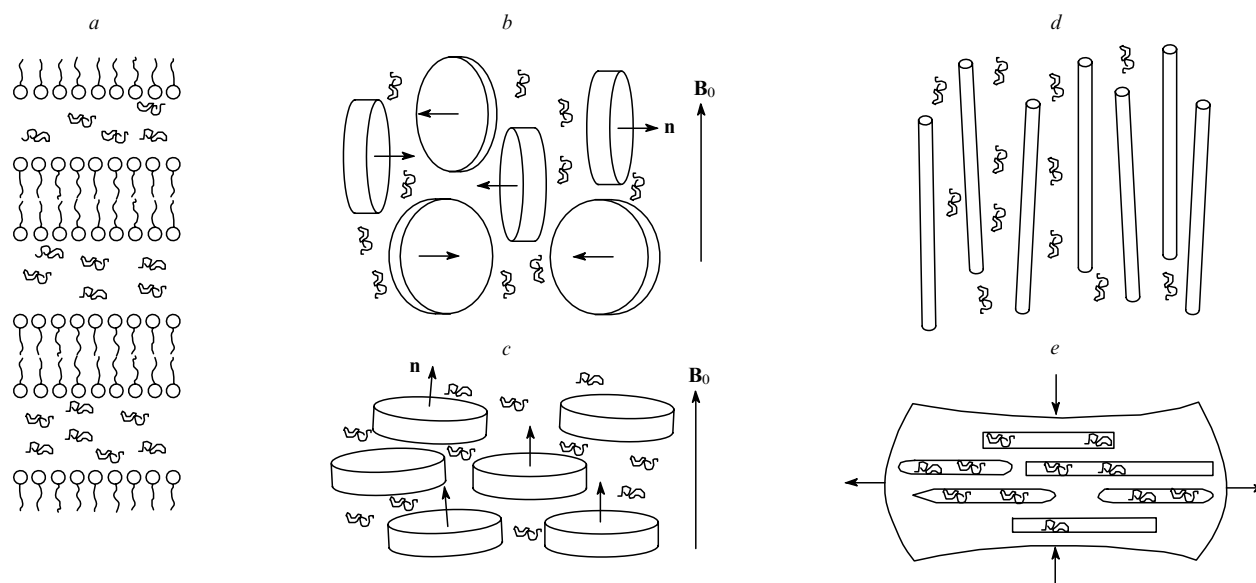


Figure 2. Schematic view of the media for weak alignment of biomolecules.

(a) Helfrich lamellar phases with bilayers remote from one another; (b) aqueous solution of disc-like particles with a negative anisotropy of diamagnetic susceptibility orienting with their normal $\mathbf{n}$ perpendicular to the magnetic field $\mathbf{B}_0$; (c) aqueous solution of the same particles with a positive anisotropy of diamagnetic susceptibility orienting parallel to the magnetic field $\mathbf{B}_0$; (d) aqueous solution of rod-like particles (suspensions of filamentous phages and viruses, cellulose crystallites), which align with their long axis parallel to the field; (e) stretched or compressed porous polymer gels.

two spectrometers operating at 360 and 750 MHz. However, the residual dipolar couplings were relatively weak (due to the weak degree of alignment of the biomolecule) and inapplicable for structural studies.

The complexes of proteins with DNA or with paramagnetic metals are aligned much better on exposure to a magnetic field.

2. Alignment induced by paramagnetic ions

To enhance the alignment of biomolecules in a magnetic field, it is necessary to increase the anisotropy of magnetic susceptibility of these molecules or the orienting system (membranes, media, and so on). This can be done, for example, by adding paramagnetic metal ions (mainly, lanthanide ions). These ions form a paramagnetic complex with a studied molecule, which is aligned more efficiently in the magnetic field of the spectrometer. This was shown for the first time using the paramagnetic complex of myoglobine.⁴³ The degree of alignment thus attained is not very large and is inferior to that attained in dilute LC media but it is quite sufficient for structural investigations.

A paramagnetic ion can be linked to the studied biomolecule in several ways. Some proteins initially contain paramagnetic ions, for example, the myoglobine mentioned above and heme-containing proteins. In other metal-containing biomolecules, diamagnetic metal ions can be replaced by paramagnetic ions. The proteins devoid of metal can be built up by attaching a protein fragment containing metal atoms to one of its ends. The orientation of the biomolecule would be different depending on whether the paramagnetic label is attached to the C- or N-end. This provides additional structural information and proves fairly useful for removing the degeneracy of orientation data in determining the three-dimensional structure of a biomolecule. By successive replacement of several different ions in a biomolecule, one can attain its multiple orientations.

The position of the Eu^{3+} in the Eu–DNA quadruplex system was determined by using magnetic orientation induced by the paramagnetic ion.¹⁴²

As a result of orientation induced by replacement of the Ca^{2+} ion in calcium-containing biomolecules by lanthanide ions^{143–147} [in particular, by Tb^{3+} (see Ref. 144) or by Ce^{3+} (see Ref. 146)], it became possible to observe the dipole splitting and to determine the structures of a number of proteins. The same replacement

made it possible to measure the RDC for pairs of nuclei in the NH_2 groups and to study the conformational mobility of the side chains in the asparagine and glutamine residues in the molecule of the Ca_2 -calbindin protein.¹⁴⁵

A situation where two aligning factors, for example, a paramagnetic ion and an LC medium, compete with each other is favourable for structure determination. In these cases, the resulting RDC is equal to the sum of the RDC for the initial diamagnetic protein molecule induced by the LC phase and that induced by the paramagnetic ion. When the diamagnetic ion in the protein is replaced by different paramagnetic ions, the alignment tensor can be determined unambiguously.¹⁴⁸

The method in which a standard paramagnetic label is attached to the N- or C-end of the protein molecule is promising. Various small proteins and protein tags have been proposed as labels, for example, the Zn-finger protein in which the diamagnetic Zn^{2+} ion can be replaced by paramagnetic Co^{2+} and Mn^{2+} ions,¹⁴⁹ or the terminal fragment of the EF-hand oncomodulin protein consisting of 12 amino acid residues in which Co^{2+} can be replaced by paramagnetic lanthanide ions.¹⁵⁰ The range of these labels is broad.¹⁵¹ Donaldson *et al.*¹⁵² proposed the shortest sequence, consisting of only three amino acid residues, binding the Cu^{2+} ion for adding a paramagnetic label to the N-end of a studied protein. The protein molecules containing a paramagnetic label exhibit a substantial anisotropy of paramagnetic susceptibility and are efficiently aligned in a magnetic field, whereas the orientation of a diamagnetic protein is very weak. By recording the NMR spectra before and after the substitution, one can determine the dipolar constants and the dipolar shifts. If in paramagnetic relaxation experiments, the Mn^{2+} ion is replaced by a paramagnetic ion, it is possible to determine the distance between the unpaired electron and the proton of the amide group. When these distances and the dipolar shifts of the amide protons are known, one can calculate the z coordinates for these protons.¹⁴⁹

In addition to the orientation (or reorientation) effect in the magnetic field and the possibility of measuring RDC, the presence of a paramagnetic ion in a biomolecule allows one to measure other parameters containing structural information also. In particular, these are the paramagnetic shifts of nuclei, the constants of cross-correlated relaxation between the electron and

nuclear spins^{153,154} and between nuclear spins and the Curie spin.^{75,155,156}

The pseudocontact shifts caused by the dipolar coupling between the magnetic moments of the electron and the nucleus also carry structural information and can be used as additional parameters for structure determination of a protein.¹⁵⁷ The paramagnetic heme-containing protein of the rat cytochrome *b*₅ in the paramagnetic (oxidised) and diamagnetic (reduced) states was studied in this way.¹⁵⁸ The structures determined from the data obtained in NOE-based experiments, by means of RDC, and using information on the pseudocontact shifts are in good agreement.

Using data on dipolar coupling, one can determine the anisotropy of the magnetic susceptibility of the whole protein. In particular, comparison of the dipolar couplings and the anisotropies of the magnetic susceptibility of cytochrome-*c*' from *Rhodobacter capsulatus* in the paramagnetic and diamagnetic states found by different methods with one another and with published results^{159,160} showed good agreement of these values. It was also shown that the protein exists in solution in the monomer form.

Taking into account the self-orientation of cytochrome *b*₅₉₂ molecules from *E. coli* containing heme in the oxidised state, Arnesano *et al.*¹⁶¹ were able to refine the structure of this protein and to separate the diamagnetic and paramagnetic contributions from the total magnetic anisotropy of the molecule.

3. Alignment induced by an electric field

An electric field can be used as an orientation factor; however, this restricts the possible electrochemical and electroconvective processes involving biomolecules in aqueous and salt-containing aqueous solutions.^{162,163}

An electric field was first used to align the *p*-nitrotoluene molecules.¹⁶⁴ This study was undertaken to determine the sign of the spin–spin coupling constant.

The orientation of molecules on exposure to an electric field has an obvious advantage over the magnetic field-induced orientation: there is no need to carry out measurements using at least three NMR spectrometers to distinguish between the orientation effects and those caused by dynamic frequency shifts; it is sufficient to employ only one spectrometer but three different electric field strengths.

It has been proposed^{165,166} to use an alternating pulse electric field synchronised with a sequence of radiofrequency pulses. In this case, multidimensional NMR experiments can be carried out with the electric field being switched on and off at particular time instants. The researchers cited developed two 2D experimental procedures for determination of the RDC. In one experiment, the electric field was applied only in the second dimension to observe the dipolar splitting, while the isotropic chemical shifts were observed in the direct dimension. In the other experiment, the electric field was switched on only during mixing; as a consequence, cross-peaks were observed only for the pairs connected by dipolar coupling. In these experiments, alternating electric fields with a frequency of 28.5 kHz and a strength of 40–70 kV cm^{−1} were used.

A similar 2D ²H NMR experiment for observing the correlation between the isotropic chemical shift and the residual anisotropic couplings (in this case, quadrupole coupling induced by a pulse-modulated constant electric field) has been proposed.¹⁶⁷ For decreasing the influence of the molecular motion on the measured signal, multiquantum filtration is used.^{168,169} This technique is equally suitable for dipole-coupled systems with a spin of 1/2.

In these experiments, nitrobenzene thoroughly purified from ionic impurities was used as an orienting compound. The molecules of some proteins have higher dipole moments than nitrobenzene; however, it is still unknown to what extent the method involving orientation in an electric field is applicable to biomolecules. These studies are only at the beginning.

4. Orientation in liquid-crystalline media

The self-orientation of biomolecules (except for the molecules containing paramagnetic centres) even on exposure to strong magnetic and electric fields is very low. A higher degree of alignment can be attained by placing a biomolecule in the LC medium, which is oriented in a magnetic field and thus aligns the biomolecules it contains. This medium should meet a number of requirements: it should be miscible with water, not interact chemically with the studied molecule, accommodate high concentrations of the biomolecules under study and the required buffer components and also to be stable for a long time over a broad temperature range. However, every LC possesses a high degree of alignment; therefore, the main difficulty in searching for these systems is the requirement of weak alignment of the biomolecules, *i.e.*, several orders of magnitude weaker than the degree of alignment of the LC molecules.

Systematic search resulted in a number of LC systems suitable for structural studies of biomolecules. For weak alignment of biomolecules, first, traditional lyotropic LC systems were tested, for example, solutions in quarternary ammonium, pyridinium,^{170,171} and other salts in aqueous alcohol. Mere dilution by water allows one to decrease somewhat the degree of alignment in these systems but only to certain critical concentrations below which the system is no longer liquid-crystalline and, hence, aligned. Liquid-crystalline media based on cetylpyridinium chloride–hexanol¹⁷⁰ and cetylpyridinium bromide–hexanol proved to be the systems of choice.¹⁷¹ These systems form lamellar phases of the Helfrich type consisting of double layers, which can be moved apart by adding a solvent, so that the distance between them will markedly exceed the thickness of the bilayer itself (see Fig. 2*a*). These lyotropic phases are very convenient and simple systems, relatively stable over a broad range of temperatures and concentrations. They withstand the concentrations of salts optimal for the existence of biomolecules and are stable for a long period of time. The magnetic anisotropy of the pyridinium rings determines the orientation of lamellae in a magnetic field: the symmetry axes of the lamellae are arranged along the field direction.

A new non-ionic lyotropic LC medium based on alkyl poly(ethylene glycols) and alkanols, which has certain advantages, has been proposed.¹⁷² In particular, the solution can be prepared outside the magnetic field of the spectrometer. The specimen has a low viscosity and can be transferred into the ampoule just by a pipette. In a magnetic field, the system is rapidly oriented. The components of this system are commercially available and inexpensive compared to the components of other systems used to study biomolecules by NMR spectroscopy techniques. They can be used with equal efficiency to study both proteins and nucleic acids. Advantages of these systems include low sensitivity to the pH and to high concentrations of salts and the protein.

5. Orientation by disc-like particles

a. Bicelles

Disc-like particles (bicelles, membrane fragments, *etc.*) can also be oriented in a magnetic field, form ordered LC media and align biomolecules that occur together with them in a solution.

Ram and Prestegard¹⁷³ were the first to propose disc-like mixed micelles as a model membrane system for NMR investigations. Bicelles, which are formed in aqueous solutions of lipids and surfactants and represent discrete bilayer disc-shaped structures, proved to be most convenient for this purpose.¹⁷⁴ They are equally applicable to studies of membrane proteins, which are incorporated and fixed in bicelles, by solid-state or liquid-state NMR and to NMR studies of water-soluble proteins in the presence of bicelles which are aligned in a magnetic field and align the protein molecules due to specific interactions with them.^{175–179}

The researchers' attention to bicelles as a medium for the study of biomolecules was enhanced when it was found that enzyme activity is retained in this medium.¹⁶⁷ Tjandra and Bax^{45,177} proposed using a dilute solution of bicelles as an orienting solvent

for biomolecules. Even the first results demonstrated that the distances and angles determined using ^1H – ^{15}N , ^1H – ^{13}C and ^{13}C – ^{13}C RDC in the molecules of human ubiquitin in dilute bicellar LC media were in agreement with the corresponding parameters determined in their crystal structure.¹⁷⁸

Bicelles (especially, those containing phospholipids) are much more similar to native membranes than small micelles. Therefore, the structure determined for membrane proteins encapsulated into bicelles is more plausible.¹⁸⁰ (However, data on micelle-induced bending of biomolecules have been reported.¹⁸¹) If the bicelle discs are small, they are freely and rapidly reoriented in solution and are not oriented under the action of a magnetic field. Such bicelles can form an ideal system for the investigation of encapsulated membrane proteins by conventional high-resolution NMR techniques used to study water-soluble proteins.¹⁸² In addition, a bicelle is oriented much more easily by a magnetic field than a spherical micelle with an embedded protein. This allows one to use procedures based on residual dipolar couplings in the studies of membrane proteins encapsulated in bicelles.

An anisotropic bicelle with a high ratio of the radius to the thickness can be oriented on exposure to an external magnetic field. By varying the composition and component ratio and their concentration in an aqueous solution, one can change gradually the degree of bicelle orientation and, hence, the degree of alignment of the studied biomolecules (which occur in the aqueous phase or inside the bicelles).

Studies of membrane proteins and peptides encapsulated in bicelles are usually carried out with high concentrations of phospholipids. This method was used to determine the orientation of the N-terminal fragment of the ARF1 protein relative to the surface of a bicelle oriented in a magnetic field¹⁸³ and to compare the orientation of the same fragment relative to micelle or bicelle surfaces.¹⁸⁴

Below we consider the use of bicelles for the studies of biomolecules only in solutions. By varying the component concentrations, one can change the degree of alignment of the dissolved biomolecules in these systems over broad ranges in order to attain the desired values of residual dipolar splitting. Various additives can be used to improve the properties of the system.

Bicelles consist of a mixture of at least two phospholipids with short and long hydrophobic tails; long-chain phospholipids form the flat surface of the disc, while the short-chain ones form the rounded edges. A typical thickness of a lipid bilayer is 40–50 Å. The dimensions of the bicelles increase with an increase in the molar ratio of the long-chain to short-chain lipids.¹⁸⁵ An important feature of such systems is the ability to pass from the nematic LC state into an isotropic state on changing the temperature; as this takes place, one can record the spectra of the dissolved molecules in both states of the system, which is necessary for determining the dipole contributions to the observed splitting. In particular, the transition of the basic DMPC–DHPC system (DMPC is dimyristoylphosphatidylcholine, DHPC is dihexanoylphosphatidylcholine) from the nematic to isotropic state takes place at 35 °C. This system is used most widely. It forms an alignable LC phase at very low bicelle concentrations ($\approx 3\%$ – 5%). The distances between separate bicelles in solution reach 300 Å; this is quite sufficient for biomolecules to fit between them. The disc radius is directly proportional to the [DMPC]/[DHPC] ratio and is inversely proportional to the total concentration of phospholipids in water with their ratio remaining constant.¹⁸⁶

The procedures for sample preparation for NMR studies and the properties of the basic DMPC–DHPC bicellar system have been described in detail in the literature. The dependences of the stability and the orienting properties of this medium on the temperature, pH, salt composition, the relative concentrations of components and additives have been studied.^{187–189}

The properties of bicelles (size, shape, surface charge, the anisotropy of diamagnetic susceptibility or the anisotropy of

dielectric constant) can be varied over broad ranges. Usual bicelles are stable only in narrow ranges of temperatures and pH. Charged lipids¹⁹⁰ or aromatic surfactants¹⁹¹ can be added to bicellar systems in order to extend the temperature range, increase the stability, enhance the orienting ability and change the type of orientation. The additives counterbalance the destructive influence of high salt concentrations on the system and minimise the interactions between the macromolecule under study and the bicelle. This effect shows itself with both positively and negatively charged additives. The addition of cationic lipids imparts to the system a low positive charge, which has an influence on the alignment of proteins caused by electrostatic and steric forces.¹⁹²

A large number of compositions able to form aqueous bicellar solutions under certain conditions have now been found.¹⁷⁹ The most promising among them are DLPC–CHAPSO¹⁹³ [DLPC is dilaurylphosphatidylcholine, CHAPSO is 3-(chloroamidopropyl)dimethylammonio-2-hydroxy-1-propane sulfonate] for studies over a broad temperature range and DIODPC–CHAPSO¹⁹⁴ (DIOIPC is 1,2-di-*O*-dodecyl-*sn*-glycero-3-phosphocholine) for studies of macromolecules in highly acidic media. Struppe *et al.*¹⁹⁵ have modified the DMPC–DHPC system by adding 25 mass % of dimyristoylphosphatidylserine (DMPS) or dimyristoylphosphatidylglycerol (DMPG). These ‘acidic’ bicelles are stable at pHs from 5.5 to 7 and are suitable for use in NMR studies of membrane proteins, because natural membranes are often charged, as they contain negatively charged lipids.

Many bicellar systems are susceptible for hydrolysis, which hampers long-term experiments (taking many days). Ottiger and Bax¹⁹⁶ proposed replacing diacyl phospholipids by dialkyl analogues in order to make the bicelles stable against hydrolysis. New bicelle systems are similar in orienting properties to DMPC–DHPC type systems but they are suitable for operation in both acidic and alkaline media. The DIODPC–CHAPSO system is also stable against hydrolysis.¹⁹⁴

The mechanism of orientation of biomolecules by bicelles is complicated and includes, apart from steric repulsion, electrostatic interactions and adsorption on the bicelle surface. The steric interactions are usually rather weak and can be easily modelled.¹⁹⁷

Bicelles can be oriented in different ways: by attaching an additional peptide tail to the C-end of the protein molecule, for example, so-called peptide Hi-tag; by changing pH; by adding cationic lipids, which would make the system slightly positively charged; by adding particles with highly anisotropic diamagnetic susceptibility or paramagnetic ions.¹⁹² The orientation of the director of the bicellar LC phase can also be varied by rotating the sample.¹⁹⁸

Usually, the degree of alignment of bicelles and transition of a bicellar LC system into the isotropic state are detected by measuring the quadrupole splittings in the spectra of heavy water, which is the major component of the system. Another method for measuring the degree of alignment of phospholipid bicelles in a magnetic field based on ^{31}P NMR spectroscopy has been proposed.¹⁹⁹

The morphology of three lyotropic LC phases — bicellar phase, a mixture of pentaethylene glycol monododecyl ether with hexanol and the cetylpyridinium bromide–hexanol system — was studied in detail in translational diffusion anisotropy experiments.²⁰⁰ Bicelles remain stable in the studies under elevated pressures. The interest in these studies is increasing at present.²⁰¹

Thus, lyotropic bicellar systems are very convenient media for investigating aligned proteins. However, there exist a number of proteins that destroy bicelles when interacting with them; therefore, study of the structures of these proteins using bicelles is problematic.^{178,202}

b. Orientation of biomolecules in bicelles doped with lanthanide ions

Bicelles are usually oriented in a magnetic field in such a way that their normal is perpendicular to the field direction,²⁰³ while the planes of the discs are located chaotically. This orientation can be changed by adding paramagnetic ions or by incorporating into the

bicelles an aromatic compound or macromolecules with a great anisotropy of diamagnetic susceptibility.

The orienting properties of bilayer membranes doped with lanthanide ions^{204–207} are rather attractive not only for investigating membrane proteins but also for investigating proteins encapsulated in them in solutions.^{150, 208, 209} This system combines two mechanisms for the ordering of biomolecules, namely, the influence of the membrane and the effect of paramagnetic ions. In the presence of Er^{3+} , Eu^{3+} , Tm^{3+} , or Yb^{3+} ions, the negative diamagnetic anisotropy of bicelles increases and their symmetry axis becomes parallel to the magnetic field. The biomolecules in the bicelles are also reoriented.^{204, 205} The transition accompanied by the change in the orientation of the bicellar system with respect to the magnetic field from the perpendicular to the parallel upon the addition of paramagnetic ions, as well as the formation of the LC phase upon increasing the bicelle concentration are cooperative phenomena depending on the interactions between the bicelles and on the temperature. In some cases, two types of alignment have been observed, the equilibrium between them being dependent on the concentrations of the paramagnetic ions and bicelles.²⁰⁸

The systematic research of mixtures of phospholipids with long and short chains over a broad range of concentrations and temperatures by small-angle neutron scattering showed the presence of phases with different morphologies such as lamellae, multilamellae, monolamellar vesicles and bicellar discs.²¹⁰

However, the large concentration of paramagnetic ions in the system results in undesirable line broadening and line shifts in the NMR spectra, which hampers their analysis. When chelating phospholipids are added in an equimolar amount with respect to paramagnetic ions,²⁰⁶ the ions form chelates incorporated in the membrane, and the paramagnetic effects are levelled. In addition, due to the alignment of the lanthanide chelates in the membranes, the total anisotropy of the diamagnetic susceptibility increases to such an extent that the lanthanide ion concentration needed for the reorientation of bicelles can be decreased. The possibility of inducing substantial changes in the type of bicelle orientation and, hence, the orientation of biomolecules by adding paramagnetic ions is also attractive due to the fact that a second set of RDC can be obtained rather easily. Owing to the new set, the number of RDC is actually doubled; on the one hand, this markedly increases the accuracy of the determined structure and, on the other hand, eliminates the ambiguity of the order parameters (see below).

If phospholipids containing, for example, a biphenyl group²⁰³ in one of the long chains, are added instead of nonlipid amphiphilic aromatic compounds or paramagnetic ions, it is possible to create bicellar systems with positive anisotropy of magnetic susceptibility ($\Delta\chi$).^{211, 212}

Study of a number of hydrophobic membrane proteins in solution became possible due to the effect of binding of lanthanide ions to protein-containing micelles.²¹³ The use of bicelles, membrane fragments and viruses for this purpose is problematic because membrane proteins change appreciably the structures of these particles when react with their lipids. This influences the quality of NMR spectra.

c. Purple membrane fragments

A method for aligning water-soluble biomolecules in the presence of purple membrane fragments (PM) was proposed almost simultaneously in two publications.^{214, 215} Purple membrane fragments are prepared from halobacteria, which form wide disc-like particles consisting of bacteriorhodopsin and some residual lipids when occurring in an aqueous solution with a concentration of $1–10 \text{ mg ml}^{-1}$. These particles are stable on sharp changes in the temperature, pH and ionic strength of the solution. They have great negative charges and, therefore, they can induce orientation of biomolecules (due to electrostatic interaction), which can be controlled by changing the concentrations of the PM fragments or by adding cations for reducing the electrostatic interaction between the macromolecule and the membrane.²¹⁵ These systems

are highly stable against temperature or pH variations and represent an excellent alternative to bicelles.

The orientation of biomolecules induced by PM fragments was demonstrated using two proteins, namely, human ubiquitin and p53. The maximum values of the $^1\text{H}–^{15}\text{N}$ RDC were $\sim 20 \text{ Hz}$. It is worth mentioning that in this case, too, the axial and rhombic components and the direction of the principal axis of the alignment tensor differ appreciably from the corresponding values in bicelles and other orienting media, which makes the membrane fragments a convenient medium for determining the additional set of RDC. The presence of several sets of RDC in which the principal axes of the corresponding diagonalised tensors are arranged at substantially different angles allows one to construct the complete 'triangulation' system of biological macromolecules in solution (see below).

A solution of PM fragments is not a liquid-crystalline system. Typical PM fragments are several micrometers in diameter and are $45 \text{ \AA}$ thick. Their alignment in a magnetic field is due to seven α -helices of bacteriorhodopsin. In a magnetic field, PM fragments are oriented in such a way that the normal to the membrane is parallel to the magnetic field direction and, due to high concentration of bacteriorhodopsin, the degree of alignment is extremely high.²¹⁴

The concentration of liquid crystals in solution cannot be lower than the value where the LC phase is formed; conversely, the concentration of the aligning particles in a suspension can be arbitrarily low. The alignment can be monitored based on quadrupole splitting of deuterium in the spectrum of heavy water.

The use of lanthanide ions, as in the case of bicelles, allows one to change the direction of the predominant orientation of biomolecules in the presence of PM fragments.²¹⁶ In a study dealing with the structure of a membrane protein,²¹⁷ an oxygen molecule has been used as a paramagnetic probe.

6. Orientation by rod-like particles

It should be borne in mind that bicelles are stable only in narrow temperature and pH ranges (beyond this range, hydrolysis of the ester bond can take place) and that many proteins interact with bicelle membranes to destroy them. Therefore, it is more preferable to use solutions of more stable particles that can be oriented and to orient the dissolved biomolecules without destroying their structure. This role can be played by any rigid, charged, rod-like macromolecular ensembles consisting, for example, of rod-shaped viruses and bacteriophages of the filamentous phage family, inorganic filamentary crystallites, polymeric crystallites and other relatively rigid filamentary polymeric structures (for example, polytetrafluoroethylene whiskers).

a. Liquid-crystalline colloid suspensions of rod-shaped viruses

Widely known suspensions of bacteriophage fd and the tobacco mosaic virus,²⁰² bacteriophage Pf1 or M13²¹⁸ were among the first systems to be proposed as alternatives to bicelles. These systems are very convenient for attaining medium degrees of alignment of the dissolved biomolecules; moreover, it is possible to control the orientation parameters by adding the bacteriophage Pf1 subject to magnetic alignment.^{218, 219} This procedure was used to determine the $^1\text{H}–^1\text{H}$, $^1\text{H}–^{13}\text{C}$ and $^1\text{H}–^{15}\text{N}$ RDC of various proteins and oligosaccharides. The orientation of the molecular alignment tensor in these systems differs substantially from the orientation in the medium of usual bicelles; this allows the measurements to be taken simultaneously in both media.

The procedure of preparation of the bacteriophage Pf1 specimen for the partial alignment of biomacromolecules has been described in detail elsewhere.^{220–222} The bacteriophage Pf1 is a DNA phage composed of 7349 nucleotides and packed in a protein shell with a nucleotide: protein ratio of 1:1. This is a rod-like system with a length of $20\,000 \text{ \AA}$ and $60 \text{ \AA}$ in diameter, which is spontaneously oriented in a magnetic field; Pf1 has a negative surface charge. The orienting properties of the phage under various experimental conditions were considered in detail

using DNA and RNA as examples. Based on quadrupole splitting of deuterium, one can judge the degree of system alignment, which can be changed by varying the phage concentration and the temperature.²²⁰ The researchers recommended a medium pH of 6.5–8.0 and $[\text{NaCl}] < 100 \text{ mmol litre}^{-1}$.

Most biomolecules and orienting particles are charged and this should be taken into account when selecting the appropriate medium. Bacteriophages represent ideal media for the orientation of RNA and DNA molecules: negatively charged molecules of nucleic acids are aligned due to steric interactions with negatively charged phages Pfl, which produce a stable orientation over a broad range of conditions in a solution.

The use of negatively charged particles to align positively charged biomolecules is problematic, although in some cases, such media prove very convenient for investigations of proteins.²²⁰ Even when the bacteriophage concentration is abnormally low, these systems are effective.²²³ Presumably, in this case, a different orientation mechanism is involved associated with weak binding of the protein under study to the phage. The observed orientation is due to fast exchange between the bound and free states of the protein.

In the cholesteric phase of the bacteriophage fd, the degree of alignment of the dissolved protein and, what is especially important, the rhombicity, depend on the pH.²²⁴ The pH value can be varied over a broad range, from 2 to 8 (an erroneous opinion that working with phages is possible only at high pH values has been established).

The alignment of a phage-based LC system can be fixed and made independent of an external magnetic field. For this purpose, the system is placed in a polyacrylamide matrix. The polymer-stabilised system fully retains its specific orientation characteristics.²²⁵

b. Cellulose crystallites

Suspensions of cellulose crystallites are, probably, the cheapest, the most stable and the simplest media for the orientation of biomolecules.²²⁶ They are produced from natural cellulose fibres (for example, from filter paper) by careful hydrolysis by sulfuric acid, concentration and extensive dialysis. After some period, the system separates into an upper isotropic phase and a lower anisotropic phase. The latter is isolated, concentrated by evaporation and then used.

The cellulose crystallites are rods with dimensions $\sim 200 \times 10 \text{ nm}$. A separate crystallite has a large negative diamagnetic anisotropy; therefore it is oriented in a magnetic field with its long axis normal to the direction of the applied field. The orientation process is slow; to attain complete orientation, a freshly prepared specimen should be kept for several hours in a magnetic field. The surface negative charge of the crystallite caused by sulfate groups is smaller than the surface charge of bacteriophages; therefore, they orient biomolecules by a steric mechanism rather than an electrostatic one.

7. Stressed polymer gels

Polymer gels form promising media for the orientation of biomolecules. The effect of orientation of small molecules incorporated in rubber-like polymers has been known for a long time.²²⁷ Two groups of researchers working independently of each other proposed using this phenomenon for the orientation of biomolecules in polyacrylamide gels. The orientation is attained either upon mechanical treatment (stretching or straining)^{228, 229} or by means of aligned PM fragments or other particles embedded in the gel.²²⁹

The gel is prepared by polymerisation of an aqueous solution of a mixture of acrylamide and methylenebisacrylamide in a special tube whose diameter differs slightly from the diameter of an NMR ampoule. The polymerisation is initiated by a mixture of ammonium persulfate with tetramethylethylenediamine. After polymerisation, the gel is thoroughly washed, dried and placed in an NMR ampoule, and an aqueous solution of the studied

protein is added. The protein and water slowly diffuse into the gel, which swells. Subsequently the gel is subjected to mechanical treatment and, as a result, the macromolecules having penetrated into the gel are aligned. If the diameter of the tube used initially to prepare the gel is smaller than the diameter of the ampoule used in NMR experiments, the gel is compressed, while in the opposite case, the gel is stretched, and the axis of the alignment tensor of the biomolecules incorporated in the gel is oriented across or along the ampoule, respectively.

The pore sizes and the diffusion properties of the polyacrylamide gels can be changed by controlling the concentration of acrylamide and methylenebisacrylamide. Instead of the simple protein–water system, one can use protein–surfactant–water micellar systems.

Yet another option is to incorporate other particles into the gel during polymerisation, for example, PM fragments, phages and viruses able to orient protein molecules. Polymerisation is carried out in a magnetic field and, hence, the above particles are incorporated in the gel in the oriented state. The orientation of molecules of the protein introduced into the gel is due to the interaction with the oriented (orienting) particles.

The orientation of particles immobilised in the gel during polymerisation can be attained using other types of external macroscopic treatment, for example, electric or mechanical treatment.

A distinctive feature of polymer gels is that the direction of their orientation is determined by the preparation procedure and does not depend on a magnetic field. This allows one to change smoothly the gel orientation with respect to the direction of the magnetic field. This feature can also be used to produce a new, biaxial orientation of the system after completion of NMR measurements. In this axially asymmetrical system, one can determine the set of orientation-dependent parameters, which cannot be found in usual uniaxial LC media.²²⁸ The orientation in these systems is not violated when the specimen is rotated. This allows one to measure the spin–spin coupling constants during magic angle spinning of the specimen (to set the RDC to zero).²²⁵

By varying the pressure, polyacrylamide concentration or cross-linking density in the gel, one can change over wide limits the degree of alignment of biomolecules, whereas the direction and asymmetry of the alignment tensor remain virtually constant.²³⁰ Relatively large protein molecules can also be studied in gels because their relaxation times in the gel are rather long.

A simple funnel-like apparatus has been proposed for uniform squeezing of the polyacrylamide hydrogel.²³¹ The degree of alignment depends on the ratio of the diameters of a cylindrical hydrogel specimen before and after squeezing.

8. Mineral liquid crystals

The media for the orientation of biomolecules considered above are organic materials; therefore, the solvent signals predominate in the NMR spectra, because the number of molecules of the medium is much greater than the number of the biomolecules under study. This creates certain difficulties, especially in the studies of oligosaccharides or oligonucleotides for which the synthesis of isotopically enriched analogues is very complex and expensive.

Mineral liquid crystals devoid of ^1H or ^{13}C nuclei are very convenient in this respect. Systematic research into these crystals started not long ago. They are colloid systems consisting of highly anisotropic ribbon-, plate- and disc-shaped or column nanoparticles, which tend to form various types of LC phases. Systems oriented by a magnetic field are of special interest for NMR spectroscopy.

One system of this type is an aqueous suspension of vanadium pentoxide V_2O_5 , in which a nematic phase is formed within a certain range of concentrations and pH.²³² The particles of this phase are long (several hundreds of nanometers) 1 nm thick ribbons with a width of 25 nm. Due to the high negative charge of the particles, the mechanism of orientation of biomolecules is

similar to that effective in suspensions of viruses and phages. Yet another class of mineral liquid crystals well oriented in a magnetic field has also been proposed, namely, a series of swelling gels of salts of the solid acids generally described as $H_nM_nZ_2O_{3n+5}$ ($M = Sb, Nb, Ta$; $Z = P, As$; $n = 1, 3$), whose particles are plate-like.²³³

The ^{13}C – ^1H dipolar coupling constants of pentasaccharide Lewis X measured in these systems with a natural abundance of the ^{13}C isotope proved to be comparable in the order of magnitude with the RDC measured in organic LC, in particular, in a bicellar medium.

Advantages of inorganic systems over organic systems include high stability and inertness over a broad temperature range, the possibility of recovery of the substance under study by flocculation and the fact that at lower concentrations, they are oriented in the magnetic field much better and faster.

Unfortunately, none of the systems considered above is universal for structural research.¹⁷² The DMPC–DHPC bicellar system is susceptible to irreversible degradation due to hydrolysis at low pH values.¹⁸⁸ The DIODPC–CHAPSO system is more stable at low pH values but does not form an LC phase in a neutral medium.¹⁹⁴ The cetylpyridinium chloride–hexanol system is destabilised at high protein concentrations and, to increase its stability, high salt concentrations are required.¹⁷⁰ Conversely, the cetylpyridinium bromide–hexanol system is stable at low ionic strength of the solution.¹⁷¹ Phages are effective in neutral media, but at pH < 6, they tend to aggregate.²¹⁸ Purple membrane fragments and bicelles often bind proteins too strongly, which is manifested as line broadening in the NMR spectra and in perturbation of the alignment tensor; as a consequence, it is impossible to determine the real structure of the molecule in solution.^{214, 215}

V. Measurement of orientation-dependent parameters

1. Orientation-dependent parameters

Today, a number of NMR parameters containing diverse structural information concerning the molecules under study can be measured in experiments. Table 1 presents some of these NMR parameters. The most valuable and diverse structural information can be derived from orientation-dependent parameters such as RDC, the quadrupole coupling constants (QCC), and the chemical shift anisotropy.

The dipolar coupling constants proved to be more useful at any stage of structure determination for a biomolecule than the traditional parameters obtained mainly in NOE-based experiments. Comparison of the distances found in these experiments with those found using RDC showed that the use of the latter is preferred. The distances longer than 5–6 Å are inaccessible for NOE procedures, whereas the use of RDC allows determination of even longer distances.

Table 1. NMR parameters carrying structural information.

NMR parameter	Structural information
Chemical shifts ^1H , ^{13}C , ^{15}N , ^{31}P	signal assignment, secondary structure, torsion angles
Constants ^3J	torsion angles
NOE signals	proton–proton distances (< 5 Å)
Relaxation parameters	torsion angles, bond orientation, dynamics
RDC	bond orientation, internuclear distances, dynamics
CSA	bond or functional group orientation
QCC	distances, angles, bond orientation, dynamics

The fundamental difference between these methods is as follows: NOE signals permit one to estimate the length of the vector connecting the interacting nuclei, while RDC, in addition, provides information on the orientation of this vector with respect to the direction of the magnetic field; this allows one to determine the relative spatial orientation of the remote fragments of the molecule.

Another important difference is that the measured parameters depend in different ways on the distance. Dipolar couplings depend on the distance as $1/r^3$ and the NOE signals, as $1/r^6$. With a smoother dependence, one can distinguish sections corresponding to interactions between more remote nuclei.

Even when the number of NOE restraints is great, the use of RDC markedly increases the accuracy of structure determination. In those cases where NOE signals provide little information, as in the studies of nucleic acids or large, partially deuterated (to simplify the spectrum) proteins, RDC can play a crucial role.²³⁴

In order to determine orientation-dependent parameters, one must measure NMR spectra in both isotropic and oriented states. Two different patterns of these measurements are possible, each of them having advantages and shortcomings:

- separate measurements (isotropic and anisotropic parameters are determined in different experiments corresponding to isotropic and oriented states);

- simultaneous measurements (isotropic and anisotropic parameters are determined in one correlation experiment).

Up to the present day, separate measurements for the isotropic and oriented states have been carried out most often. In these experiments, it is possible to select the optimal conditions for recording the spectra for each of the states, in particular, the solvent, the concentration, the temperature, *etc.* However, the structure of a biomolecule may change depending on the experimental conditions. In addition, this type of measurement often requires large amounts of substances because a non-destructive transfer of biomolecules from one medium to another is very complicated. Yet another problem is the difficulty of signal assignment due to the dependence of chemical shifts and their anisotropies on the experimental conditions.

The techniques based on synchronous measurements of isotropic and anisotropic parameters are devoid of the above drawbacks. The measurements are carried out in multidimensional correlation experiments of various types, in one stage of which (evolution/recording), the orientation-dependent parameters are not averaged to zero.

This can be implemented in, for example, a COSY experiment in two ways. If the initial sample has anisotropic interactions, they can be temporarily removed at one stage of the correlation experiment by magic angle spinning (in the real or spin space). If the initial sample is isotropic, anisotropic interactions can be induced by some orienting factor.

This idea was proposed rather long ago; however, only experiments using magic angle spinning have been developed. Currently, experiments of a different type are quite topical, namely, those associated with fast controlled orientation/disorientation of the molecule. One of these experiments which uses orientation in an electric field^{165–167} was mentioned above.

It is noteworthy that NMR studies of oriented biomolecules were often preceded by traditional experiments in isotropic media. In many cases, this is a necessary phase because well-developed NMR procedures making use of orienting media are often missing. This is especially true for identification of the resonance signals of a primary sequence. However, another existing tendency is to make NMR spectroscopy of oriented molecules all-sufficient, *i.e.*, to develop a method which would allow determination of the structure of a biomolecule relying only on the measurements in an aligned phase.⁴⁶ However, we rather believe that both types of experiments, those in oriented and isotropic states, should supplement each other.

Below we discuss the experiments in which NMR spectra of weakly aligned molecules have been recorded; attention is focused

on methods specific to these molecules. In terms of the value to be measured, the experiments can be classified into those determining RDC, CSA and QCC.

2. Determination of the residual dipolar coupling constants

The possibility of measuring the RDC for biomolecules accounts for the interest in the NMR spectroscopy of weakly aligned systems.^{47,235}

The weak orientational contributions to the measured spin–spin coupling constants can be distinguished most easily for directly linked nuclei, which are located at the shortest distances and, hence, have the largest dipolar contribution. The pairs of nuclei encountered in biomolecules are H–C, H–N, C–C and C–N. However, due to low natural abundance of the required magnetic isotopes, one must use isotope-enriched specimens.

Almost any type of procedure for precise determination of spin–spin coupling constants developed to date is suitable for RDC determination. First of all, these are experiments based on E COSY (Exclusive COSY) or *J*-correlations and their modifications.

As a rule, RDC are determined in 2D or pseudo-2D experiments from the difference between the splittings of the scalar constant *J* in isotropic and aligned phases. In the case of large protein molecules where analysis of the results of 2D experiments is difficult (especially, if the protein contains predominantly α -helices), 3D NMR experiments are carried out.

In principle, dipolar constants can be measured between any pair of magnetic nuclei with a significant interaction but in practice, only several pairs are taken.

The first RDC between directly linked nuclei to be used were the ^1H – ^{13}C and ^1H – ^{15}N constants.^{45,141} Currently, the RDC between these nuclei constitute the major array of values measured in the NMR spectroscopy of weakly aligned biomolecules. Their interpretation in structural studies is simple because the distances between directly linked nuclei in biomolecules are well known and are virtually constant. This allows unambiguous determination of the orientation of the bond vector relative to the direction of the magnetic field. In $^{15}\text{N}/^{13}\text{C}$ -enriched proteins, one can determine the bond vector for any pair of interacting nuclei (except for oxygen). This information, which can be supplemented by the data from conventional isotropic experiments, is often sufficient for a considerable increase in the accuracy of structure calculations.

Although each of these RDC determines the orientation of the bond vector for one pair of nuclei, the total structure of the biomolecule still remains uncertain, no matter how many constants are known, because they do not contain translational information.

The next step was to use the ^1H – ^1H RDC.^{218,219} Unlike the RDC for heteronuclear pairs, ^1H – ^{13}C and ^1H – ^{15}N , which determine the orientation of vectors connecting these nuclei, the constants for the ^1H – ^1H pair simultaneously bear information on the distances between the nuclei (up to 7.4 Å).²¹⁹

In the presence of scalar and residual dipolar couplings, the efficiency of transfer in different types of homonuclear mixing (isotropic or dipolar) depends appreciably on the relative magnitudes of the constants.^{236–238} In the general case, efficient transfer for all possible relative values of the indirect and dipolar constants requires two different mixing sequences (Hartmann–Hahn and COSY).²³⁹

Today, in a typical study of a biomolecule by NMR spectroscopy, numerous experiments of different types are carried out to determine the RDC for both directly linked and remote nuclei. The procedures for RDC measurement are being further developed by adding new nuclei, for example, ^{19}F (see Ref. 240). The TROSY technique developed recently for increasing the resolution and sensitivity was immediately used in experiments for the determination of RDC,²⁴¹ in particular, in HSQC (Heteronuclear Single Quantum Coherence),²⁴² HNCO (3D ^1H , N, C' Heteronuclear Correlation Experiment),^{243,244} HN(CO)CA (3D ^1H , C',

C $^\alpha$ Heteronuclear Correlation Experiment)²⁴⁵ and other experiments.

Procedures for determining small scalar couplings and dipolar constants in purine or pyrimidine bases in nucleic acids^{246,247} and for detection of internucleotide dipolar couplings²⁴⁸ have been proposed.

a. Dipolar coupling constants between the nuclei separated by one bond

Numerous effective procedures for the measurement of RDC between nuclei separated by one bond have now been developed and used successfully for model proteins, most often, ubiquitin. Specific features of the application of these procedures to particular pairs of nuclei in biomolecules have been considered in detail in a number of publications. In proteins, these are RDC for N–H $^{\text{N}}$ (see studies^{140,241–243,249–257}), C $^\alpha$ –H $^\alpha$ (see studies^{177,251,253,258–261}), C $^\alpha$ –C' (see studies^{241–245,253,259,261,262}), C $^\alpha$ –N (see studies^{241,244,252,253,255,263}) and C'–N (see studies^{241,243,244,257}) pairs in the backbone and the C $^\beta$ –H $^\beta$ (see studies^{259,260,264}), C $^\alpha$ –C $^\beta$ (see studies^{244,245,259}), C $^{\text{Me}}$ –C and C $^{\text{Me}}$ –H pairs in the side chains.^{265,266} Many procedures are applicable to the determination of various types of constants and some allow one to measure simultaneously a number of constants.^{252,253} Special procedures for measuring the constants characterising particular groups, for example the side-chain NH $_2$ groups in asparagine and glutamine are being developed.²⁶⁷

The direct RDC in proteins are interpreted as values determining the direction of the vector of the corresponding bond, the bond length being considered constant. In particular, the C–H length is 1.095 Å, N–H is 1.02 Å, C $^\alpha$ –C' is 1.525 Å, C–C is 1.517 Å, N–C $^\alpha$ is 1.329 Å and N–C' is 1.45 Å.

In the case of ^{15}N -enriched RNA and DNA, one can determine only a limited number of ^1H – ^{15}N RDC, because imine-group protons usually undergo fast exchange. Therefore, it is more convenient to use ^1H – ^{13}C RDC for usual or ^{13}C -enriched specimens.²⁶⁸ Some C–H resonance signals of nucleic acids overlap appreciably even in 2D spectra, and special 3D experiments have been developed to resolve the signals.²⁶⁹

An elegant E COSY procedure of the S ^{3} E (Spin State Selective Excitation) type, which was called IPAP (In-Phase/Anti-Phase) procedure, has been proposed.²⁵¹ This procedure was successfully used in ^1H -coupled [^{15}N , ^1H]-HSQC and HN(CO) experiments, which made it possible to record in-phase and anti-phase *J*-coupled NMR spectra that supplement each other. The sum of and the difference between these spectra contain either only the high-field or only the low-field component of the doublet; therefore when they overlap, *J*-splittings can still be measured and the resolution does not deteriorate compared to that in the decoupled spectrum.

In most studies, different constants are found in different experiments. However, many specimens are unstable; moreover, the orientation of molecules in them can change. Therefore, 3D procedures have been developed; they allow one to measure several RDC of different types within a single experiment.²⁷⁰

Ottiger and Bax²⁵³ measured simultaneously four RDC between directly bonded nuclei in the backbone of the $^{13}\text{C}/^{15}\text{N}$ -enriched ubiquitin molecule. The results were in good agreement, especially with the N–C' and C $^\alpha$ –C' RDC. The distances found using these constants coincided with the corresponding X-ray diffraction data, while the N–H $^{\text{N}}$ and C $^\alpha$ –H $^\alpha$ distances proved to be somewhat longer. The researchers attributed this to vibrations whose amplitudes are much greater than the N–C' and C $^\alpha$ –C' vibration amplitudes.

The ^1H – ^1H coupling, resulting in line broadening in the spectra of oriented specimens, can be eliminated by using either adiabatic ^1H -selective homonuclear decoupling²⁵⁴ or partial deuteration.

The measurement of the C'–N RDC is faced with some difficulties due to low gyromagnetic ratios of the nitrogen and carbon nuclei and to the longer C'–N distance (1.33 Å). The

$D_{C'N}$ value is 8.3 times lower than D_{NH} . Therefore, the accuracy of determination of $D_{C'N}$ by this method can be considered to be critically low.²⁵³

The $D_{C'N}$ constant is usually determined from the difference between the $^1J_{C'N}$ splitting in isotropic and oriented phases, or from the in-phase splittings in HSQC (or TROSY) $^{13}C'$ -coupled spectra,^{252,253} or from the anti-phase splittings in TROSY–HNCO $^{13}C'$ -coupled spectra.²⁵⁵ However, due to the insufficient resolution of many of the ^{15}N – $\{^{13}C'\}$ doublets, their splitting cannot be measured with the required accuracy. To solve this problem, Permi and Annala²⁴¹ proposed that the doublet components should be displayed in two different sub-spectra (this is done in a similar way in the IPAP and S³E procedures described above).²⁵¹

A different, more facile method for solving the problem of precise measurement of splittings in poorly resolved multiplets based on J -correlation spectroscopy principles has been proposed.²⁶³ According to this method, the value of interaction is determined from the ratio of the amplitudes of two resonances rather than from the difference between the resonance frequencies. To this end, relative intensities of the signals in two 3D TROSY–HNCO spectra with different $^1J_{C'N}$ dephasing gaps, equal to $1/2^1J_{C'N}$ and $1/1^1J_{C'N}$, are found. The researchers also proposed a different, perhaps, more facile, way of recording two CT TROSY (Constant Time TROSY) ^{15}N – ^1H spectra, namely, with $^{13}C'$ -decoupling or with a 180-degree pulse at the $^{13}C'$ frequency applied simultaneously with the ^{15}N -pulse shifted by 180°.

Yet another modification of the HNCA–TROSY experiment allows the assignment of the signals of atoms along the biomolecular chain, together with the possibility of measuring the scalar and dipolar constants.²⁷¹

A procedure of spinning the specimen at different angles has been developed for fast determination of the sign of the ^1H – ^{13}C RDC.²⁷²

b. Dipolar coupling constants between the nuclei separated by several bonds

The above described experiments are suitable for determination of only RDC for directly linked atoms. The measurement of homonuclear and heteronuclear RDC through several bonds is hampered not only due to their lower values but also due to the lower values of spin–spin coupling constants.²⁷³ Nevertheless, in some studies, this is done using the procedures designed for the measurement of RDC of directly bonded nuclei. In particular, procedures for determination of C' – H^N (see studies^{241,243,252,257,274}), C^α – H^N (see studies^{241,243,244,274}), N – C^α (see studies^{241,244,274}), N – C' ^{243,252,274} and C^α – C' ^{243,274} RDC, the H^β – H^β and H^N – H^N RDC for side chains^{264,274,275} and H – H RDC for methyl groups²⁶⁵ have been developed.

Two-dimensional two- and zero-quantum experiments for the measurement of geminal spin–spin coupling constants and RDC in the NH_2 and CH_2 groups of proteins and for the determination of the signs of these constants have been described.²⁷⁴

Vicinal RDC in proteins were measured most often for the H^α – H^N , C^α – H^N , C' – H^N and C^δ – H^N pairs.^{244,276} Special J -correlated 2D spectroscopy techniques²⁷⁷ and a new CT COSY (Constant Time COSY) type experiment²⁷⁸ have been elaborated to measure the vicinal $^1H3'$ – ^{31}P RDC for nucleic acids.

Below, we describe in more detail the works devoted to measurement of vicinal ^1H – ^1H RDC.

The procedures described above designed for measuring the RDC of directly bonded atoms are poorly applicable to the ^1H – ^1H coupling due to low values of the corresponding J -constants. Nevertheless, numerous methods for determining these RDC in overlapping multiplets have been developed, because these constants allow one to determine longer distances than the methods based on NOE.²¹⁹ A special 2D experiment has been proposed on the basis of the TOCSY (Total Correlation Spectroscopy) pulse sequence and called DCOSY (Dipolar Coupling

Spectroscopy). The technique is based on the dependence of the direct cross-peak intensity on the RDC value. In this procedure, usual cross-peaks displayed in the spectra can be distinguished from the peaks of the relayed coherence transfer because they have different signs. A problem arises in the case of superposition of cross-peaks of these two types because signal deconvolution is impossible; this restricts the scope of the experiment.

The multiple relay cross-peaks are eliminated in another simple method for estimation of the ^1H – ^1H RDC based on analysis of the diagonal and cross-peak intensities in CT COSY experiments.²⁷⁹ However, since the cross-peaks in this experiment are anti-phase or out-of-phase, their integration is often faced with difficulties. Therefore, a 3D variant with additional ^{15}N -editing has been developed;²⁸⁰ the sensitivity of this method is not inferior to that of the NOE-based method. Another method for determining the ^1H – ^1H RDC in CT COSY experiments is based on the time dependence of the zeroing conditions for proton–proton cross-peaks.²⁸¹

Apart from methods based on estimation of the cross-peak intensities, special methods for direct determination of the sign and the magnitudes of the ^1H – ^1H RDC from the splittings measured in the spectra have also been developed.^{274,282}

An HNCA type experiment with observation of E COSY between the H^N and H^α protons has been developed.²⁸² Unfortunately, this method is applicable to the precise determination of the values and signs of RDC only between H^N and H^α .

Peti and Griesinger²⁸³ have further developed this method into a three-dimensional one by adding a NOESY (Nuclear Overhauser Enhancement Spectroscopy) stage. Their method, called JHH NOESY (J_{HH} -based NOESY), requires a minimum isotope enrichment and can be combined with elements of the S³E experiment for further spectral resolution enhancement.

An advantage of another 3D experiment (HNHA) developed for the measurement of unresolved RDC between the protons of amide groups and other protons in ^{15}N -enriched protein molecules is the possibility of using homonuclear decoupling and the TROSY procedure, which allows one to study large oriented proteins.²⁸⁴ Yet another simple and reliable method for the measurement of proton–proton RDC in the spectra with unresolved but not very large multiplets is based on iterative analysis of the shapes of multiplets in phase-sensitive COSY spectra.²⁸⁵

The signs of ^1H – ^1H RDC depend on the orientation of the proton–proton vector with respect to the external magnetic field, and their determination is often difficult, especially in the absence of scalar coupling between the protons or if the protons do not have a common partner through the bonds. Therefore, a very convenient JHH TOCSY (J_{HH} -based TOCSY) type experiment has been developed and called 'signed COSY'.²⁸⁶ This method determines the sign of the ^1H – ^1H RDC with respect to the sign of the ^1H – X direct coupling constants in linear X – ^1H – ^1H three-spin systems ($X = ^{13}C$ or ^{15}N). The advantages of this method include high sensitivity and the possibility of diagonal peak suppression, cross-peaks being observed only between the directly interacting protons.

Recently, it was found unexpectedly that the signs and magnitudes of the H^N – H^α RDC can be determined even in a usual homonuclear COSY experiment.²⁸⁷ It was found that only RDC with positive signs are manifested in the spectrum, while cross-peaks corresponding to negative RDC are either missing or greatly broadened and can be easily identified.

3. Measurement of the chemical shift anisotropy

The chemical shift is a tensor value. It is anisotropic, only the average value being observed for an isotropic liquid. In a study of a single crystal, all the six components of the symmetrical tensor can be found experimentally by measuring the values along the principal axes of the crystal. Only diagonal elements can be determined for a powdered specimen. However, due to the pronounced line broadening in the NMR spectra of solids, the accuracy of these measurements is low. Liquid crystals have some

advantage in this respect, although only a linear combination of diagonal elements can be determined.

The chemical shift anisotropy $\Delta\delta$ for each nucleus on passing from isotropic into an oriented state is determined using the relation

$$\Delta\delta = \sum_i \sum_j A_{ij} \delta_{ii} \cos^2 \theta_{ij},$$

where θ_{ij} is the angle between the principal axis of the chemical shift tensor δ_{ii} and the principal axis of the diagonalised molecular alignment tensor A_{ij} ; summation involves all i and j .

The $\Delta\delta$ value is a key parameter in investigations of biomolecular structures by solid-state NMR and in relaxation measurements to study chain dynamics. The correlation between the CSA and dipolar coupling provides important information about the angles⁶⁷ and is a key value in TROSY experiments.²⁶

The $\Delta\delta$ value for aligned biomolecules can be directly measured. In this case, the change in the chemical shift induced by transition of a biomolecule from the isotropic phase to the aligned phase provides information on the orientation of the CSA tensor of this nucleus with respect to the molecular alignment tensor.¹⁷⁵ In order to use this information, one has initially to find the components of the order parameter tensor of a biomolecule (which can be determined, for example, from RDC) and the principal components of the CSA tensor for the given nucleus (which can be determined from solid-state experiments or calculated if the structure of the protein under study is known). The measured differences between the chemical shifts of the isotropic and oriented molecule are converted into values describing the orientation of the vectors of a pair of bonds relative to the order parameter tensor. For example, for $^{13}\text{C}'$ nuclei of the carbonyl groups in the proteins, the vectors of the $\text{C}'-\text{O}$ and $\text{C}'-\text{N}$ bonds can serve as this pair;²⁸⁸ for phosphate ^{31}P atoms in nucleic acids, these are $\text{P}-\text{O}(1)$ and $\text{P}-\text{O}(2)$ bond vectors.²⁸⁹

The possibility of using the CSA parameter, together with RDC, in the structural studies of biomolecules was first indicated by Tjandra and Bax;⁴⁵ the same researchers confirmed this experimentally.¹⁴¹

According to Ottiger *et al.*,²⁹⁰ the average $\Delta\delta$ value for the ^{15}N nucleus in the amide group in protein molecules is -168 ± 20 ppm and the angle α between the $\text{N}-\text{H}$ bond vector and the principal axis of the ^{15}N CSA is $13 \pm 5^\circ$. A more thorough determination of the ^{15}N $\Delta\delta$ for the lysozyme molecule confirmed the legitimacy of using the average $\Delta\delta$ and α values in proteins:²⁹¹ values of -171.5 ± 2.2 and $18.3 \pm 0.8^\circ$, respectively, were found.

A correlation between the $^{13}\text{C}^\alpha$ CSA and elements of the secondary structure of the biomolecule has been established.²⁹² The $\Delta\delta$ value for C^α atoms in α -helices was found to be 6.1 ± 4.9 , that for β -sheets is 27.1 ± 4.3 ppm.

The procedure for involvement of CSA values in structure determination has been substantiated and developed taking the CSA of carbonyl groups (which can be easily measured) as examples.^{288, 293} The increase in the structure accuracy attained thereupon was estimated.

In a series of studies, Tjandra and Bax and co-workers justified the possibility of inclusion of this type of information, namely, the CSA of the amide nitrogen atoms,²⁹⁰ carbonyl C' atoms²⁹³ as well as C^α (see Ref. 292) and $^1\text{H}^\text{N}$ (see Ref. 294) atoms into standard procedures for structure determination of biomolecules.

Particular examples of using CSA can be found in subsequent publications. The $\Delta\delta$ value for the carbonyl-group C' atom was used as a restraint in the well-known XPLOR programme.²⁹⁵

In metal-containing proteins, so-called pseudocontact paramagnetic shifts appear due to the presence of a paramagnetic centre;²⁹⁶ these can be used as additional structure constraints. These constraints were taken into account in determining the structures of a number of protein biomolecules. Owing to the pseudocontact shifts, one can exactly determine the position of the

metal ion in a protein and to determine the components of the magnetic susceptibility tensor of a protein.^{158, 297}

4. Measurement of the quadrupole coupling constants

Nuclei with a spin of $> 1/2$ possess a nuclear electrical quadrupole moment and interact with an electric field gradient. This interaction is described by the second-range quadrupole coupling tensor $\mathbf{q}$. Its z -component, defined as

$$q_{izz} = \frac{eQ_i V_{izz}}{h},$$

where eQ_i is the quadrupole moment of an i th nucleus, V_{izz} is the element of the electric field gradient tensor at the i th nucleus, can be manifested in the NMR spectra.

The quadrupole coupling constant can be found from line splitting in the NMR spectrum and order parameters of the molecule in the nematic phase. Since a QCC depends only on the electronic properties of the ground state and the nuclear electric quadrupole moment, it bears information on the electronic structure around the nucleus under study. The QCC values found from the quadrupole splitting observed in the nematic phase can be used to determine the orientational and geometric parameters of the molecule.

The tensor $\mathbf{q}$ has a zero trace and, therefore, it has almost no influence on the NMR spectra in isotropic solutions, except for line broadening in some cases. Line broadening is also observed in anisotropic solutions, but simultaneously, additional splittings appear due to the non-zero average q_{izz} .

In practice, this splitting is not observed for most of the quadrupole nuclei due to fast relaxation. The iodine, bromine and chlorine nuclei, having very high eQ_i values, cannot furnish resolved NMR spectra unless the symmetry or alignment are such that they give relatively small V_{izz} . In the case of ^2H and ^{14}N nuclei, the eQ_i value is much smaller; therefore, quadrupole splitting can be observed in anisotropic solvents (however, the relaxation rate for ^{14}N is most often too great for observing a high-resolution spectrum).

The most convenient nucleus is deuterium with a much smaller nuclear quadrupole moment and moderate line broadening. Therefore, well resolved dipole–dipole interactions between protons and deuterons can be observed in a proton spectra of partially deuterated compounds. It should be noted that ^2H NMR spectra often do not display resolved dipole splittings, mainly due to the fact that deutron–deutron interactions are 36 times weaker than the corresponding proton–proton interactions.

Quadrupole couplings are much stronger than dipolar couplings under the same experimental conditions; therefore, they could be an alternative to the latter in the structural studies of weakly aligned biomolecules. In this case, deuterium is also the nucleus of choice. However, low sensitivity (100 times lower than the sensitivity of a proton), together with low natural abundance in biomolecules (667 times less than that of hydrogen) restrict its practical use.

The dependence of quadrupole couplings on the degree of alignment of molecules shows itself in the quadrupole splittings of signals. In NMR experiments with oriented molecules, these splittings are used only to confirm and measure the ordering of the lyotropic LC phase.

The quadrupole coupling constants of deuterium in $^{13}\text{C}/^{15}\text{N}$ -enriched proteins dissolved in D_2O , in which all the protons of amide groups are subject to exchange with solvent deuterons, can be used to describe $\text{N}-^2\text{H}\cdots\text{O}=\text{C}$ hydrogen bonds, moreover, in non-oriented specimens.²⁹⁸ This is done relying on the dependence of the relaxation time T_1 for deuterium on QCC, which, in turn, depends on the length of the hydrogen bond and the angle between the amide and carbonyl bonds.

The use of QCC for investigations of weakly aligned biomolecules became possible owing to the recently developed procedures for partial deuteration. However, line broadening caused by

quadrupole relaxation and non-resolved dipole splittings in the NMR spectra make QCC less promising than RDC. Nevertheless, using the procedure for measurement and interpretation of ^2H quadrupole splittings in the spectra of partially deuterated and oriented proteins reported by Mittermaier and Kay,²⁹⁹ one can observe the ^2H quadrupole splittings of the side-chain methyl groups in a protein molecule.

The possibility of using QCC for determining the structure and dynamics of weakly aligned deuterated carbohydrates has been demonstrated.³⁰⁰ A special pulse scheme of ^1H – ^2H 2D experiment was developed, and good prospects for this procedure for investigation of small carbohydrate molecules were shown. This requires, however, partial deuteration and ^{13}C -enrichment of the molecules. The applicability of this scheme to large biomolecules is also restricted by the ^2H relaxation times.

VI. Strategy of structure determination for weakly aligned biomolecules by NMR spectroscopy

1. Algorithms of structure calculation

Different types of information are used to determine the structure of a biomolecule. An algorithm for structure solution³⁰¹ implies minimisation of the system total energy function E_t

$$E_t = E_c + E_{vW} + E_{\text{NMR}},$$

where E_c determines the covalent geometry (bond lengths, angles, planarity, chirality); E_{vW} takes into account contacts without covalent bonding (for example, repulsion or some empirical functions including the Lennard–Jones, electrostatic and hydrogen bond potentials); E_{NMR} describes the experimental NMR restraints which are established during different NMR experiments carried out in different media.

The last term E_{NMR} consists (arbitrarily) of three terms

$$E_{\text{NMR}} = E_i + E_a + E_{\text{DB}},$$

where E_i includes the NMR parameters which do not depend on the orientation; E_a includes the orientation-dependent NMR parameters; E_{DB} corresponds to empirical information found in structural databases.

The term E_i involves the NMR parameters determined from isotropic spectra. In particular,

$$E_i = E_O + E_J + E_{J_{\text{CH}}} + E_{J_{\text{CC}}} + E_{C(\text{shift})} + E_{H(\text{shift})} + \\ + E_{\text{relax}} + E_{N(\text{relax})} + E_{\text{CCR}} + \dots$$

Here, E_O takes into account the NOE cross-peaks; E_J is for the vicinal ^3J constants; $E_{J_{\text{CH}}}$ corresponds to $^1J_{\text{CH}}$, $^2J_{\text{CH}}$ and $^3J_{\text{CH}}$ constants; $E_{J_{\text{CC}}}$ includes the $^1J_{\text{CC}}$, $^2J_{\text{CC}}$ and $^3J_{\text{CC}}$ constants; $E_{C(\text{shift})}$ includes the C^α and C^β chemical shifts; $E_{H(\text{shift})}$ is the term for proton chemical shifts; E_{relax} is the ratio of the ^{13}C and ^2H relaxation times; $E_{N(\text{relax})}$ is the ratio of the T_1/T_2 relaxation times for the ^{15}N atom; E_{CCR} takes into account cross-correlated relaxation data, etc.

For each term in the function, a potential is introduced. Usually, it has the form

$$E = k(\delta_{\text{calc}} - \delta_{\text{obs}})^2,$$

where k is the force constant, and δ_{calc} and δ_{obs} are the calculated and measured values of the corresponding energy, respectively.^{141, 302}

Now we consider the E_a term in more detail

$$E_a = E_d + E_{\text{CSA}} + E_{\text{QCC}} + \dots,$$

where E_d represents the RDC for the ^{15}N – ^1H , ^{13}C – ^1H , ^1H – ^1H and ^{15}N – ^{13}C pairs; E_{CSA} is the chemical shift anisotropy; E_{QCC} are the quadrupole couplings.

A set of so-called distance and angle restraints for the molecule under study is formed from the different-type data obtained in NMR experiments; these restraints are used in the iteration procedure for minimisation of the total energy of the biomolecule

in order to find the global energy minimum. This procedure, called adjustment, may use various methods developed in molecular dynamics. The ‘simulated annealing’ technique is the most popular.

The result of adjustment is evaluated using numerical performance criterion.³⁰³ In crystallography, the R -factor — a quantitative estimate of the degree of agreement between the measured and calculated reflections — is a key criterion of the quality of structure determination. It is defined as

$$R = \sum \frac{|A_{\text{exp}} - A_{\text{calc}}|}{|A_{\text{exp}}|},$$

where A_{exp} and A_{calc} are the experimental and calculated values, respectively. A similar criterion can also be defined for the set of RDC. However, introduction of the R -factor in the same form is impossible for RDC, because the dipolar coupling tensor is unitary; hence, the average $|A_{\text{exp}}|$ value will be zero.

It has been proposed²⁹³ to define the Q -factor for CSA in the form

$$Q = \frac{\text{rms}(\Delta\delta_1 - \Delta\delta_2)}{\text{rms}(\Delta\delta_1)},$$

where the numerator is the root-mean-square difference between the measured ($\Delta\delta_1$) and predicted ($\Delta\delta_2$) values.

This criterion is also applicable for RDC and for other orientation-dependent values. However, for these, it is not quite convenient for interpretation. Although in the case of full fitting, its value is 0, the value for completely random structure is $\sqrt{2}$. Therefore, the following R -factor was proposed for RDC:³⁰³

$$R_{\text{dip}} = \left[\frac{\langle (D_1 - D_2)^2 \rangle}{2\langle D_1 \rangle^2} \right]^{1/2},$$

where D_1 and D_2 are the predicted and calculated RDC values.

This fitting criterion is smaller than the previous one by a factor of $\sqrt{2}$. Theoretically, this quality criterion corresponds to the case where the distribution of bond vectors is completely random, while their number is infinite. In reality, the vector distribution is not entirely random, the number of measured values is small and the $(2\langle D_1 \rangle^2)^{1/2}$ value determined experimentally is not equal to the expected root-mean-square difference between the measured and predicted values. Therefore, in the same publication,³⁰³ a different quality criterion was proposed to take into account the pattern of distribution of the vectors

$$R_{\text{dip}} = \left[\frac{5\langle (D_1 - D_2)^2 \rangle}{2A_a^2(4 + 3\eta^2)} \right]^{1/2},$$

where A_a is the axial component of the order parameter tensor and $\eta = A_r/A_a$ is its rhombicity.

The success of using NMR spectroscopy techniques for determination of the structures of biomolecules is largely determined by the possibility of automation. With the development of multidimensional methods and triple resonance experiments, signal assignment procedures and 3D structure determination were consecutively automated. This process is currently in progress and there are grounds to believe that in the near future, NMR would be competitive with X-ray in the determination of the 3D structure of biomolecules regarding not only the accuracy but also the duration and cost.³⁰⁴

Now we consider a typical procedure used to analyse the spectra taking protein structure determination as an example.

First, automated processing of the multidimensional spectrum is carried out in order to identify, describe and catalogue all the observed signals and also to verify them (distinguish real signals from possible artifacts).

The next stage is to assign the identified signals to particular members of the primary sequence; this is accompanied by identification of secondary structure elements in the biomolecule. This is

done using information for homologous molecules with a known structure. The secondary structure elements are recognised or confirmed using known chemical shifts, J -constants, specific NOE signals and hydrogen bonds. The use of $^1\text{H} - ^1\text{H}$ RDC in standard calculation programmes is faced with some problems, because the corresponding distances and angles with the magnetic field are unknown for most protons, unlike the constants through one or two bonds. Therefore, the procedure for the calculation of a biomolecular structure should envisage the possibility of varying both the length and orientation of the internuclear vector. In particular, it was shown for ubiquitin that inclusion of the $^1\text{H} - ^1\text{H}$ RDC in the calculation markedly increases the accuracy of the structure determination.³⁰⁵

Finally, the last stage is determination of the 3D structure of the protein. Of prime importance in this stage is the problem of folding. Homologous structures for folding are found by searching through databases (see below).

An algorithm for fast packing of the already known elements of the secondary structure of the protein molecule to form a protein fold using the residual RDC has been developed:³⁰⁶ first, the relative orientations of the secondary structure elements with respect to one another are determined, then, using data on the elements located at short distances, the packing of secondary structure elements is completed.

The inclusion of the option of RDC analysis into the Rosetta *ab initio* programme allows one to solve the protein folding problem relying only on these constants, without using additional information.³⁰⁷

Tian *et al.*³⁰⁸ developed a strategy of simultaneous resonance assignment and folding of the protein molecule based on RDC measurements. This strategy allows rather quick and reliable identification of most signals in the NMR spectrum and provides a good initial approximation for the structure of a biomolecule on the basis of brief information on the chemical shifts and vicinal constants. This sharply accelerates the NMR structure determination procedure for proteins. Another similar strategy³⁰⁹ is based on a single 3D triple-resonance experiment (HA)CANH.

In the general case, information of different types can be used as the initial data:

- distance restraints found in the analysis of multidimensional NOESY spectra;
- torsion angle restraints determined from experimental and/or statistical data including data from relaxation experiments, NOESY, chemical shifts, and spin – spin coupling constants;
- residual dipolar couplings, CSA and QCC;
- distance restraints from the data on disulfide bridges and hydrogen bonds.

There exist several algorithms for structure determination using this set of data embodied in different computer programmes.^{141, 301} Most of the conventional programmes were developed before the experiments with oriented biomolecules were carried out. As spectroscopic information on oriented molecules was accumulated, these programmes were upgraded. In particular, the XPLOR programme was modified,^{302, 305} the algorithms for inclusion of RDC information into the CNS programme were developed,³¹⁰ and the DYANA programme was supplemented by the PSEUDYANA module designed to take into account the pseudo-contact shifts.^{154, 158, 297} New versions of these programmes contain all the parameters determined from the NMR spectra of oriented biomolecules.

An important component of the structure determination for a biomolecule is graphical visualisation of molecular structures. This is done, most often, using the graphical viewers MOLMOL, GRASP, RASMOL, WHATIF and MIDAS. For the computation and visualisation of the structures of biomolecules from different-type NMR data, the combined VMD–XPLOR programme package was developed;³¹¹ The special IVM module, which allows use of the intrinsic coordinates instead of Cartesian ones, was designed to accelerate the adjustment procedure.³¹²

The interactive MODULE programme,³¹³ which permits one to determine order parameters for macromolecules and for multi-domain systems and complexes on the basis of RDC, is an excellent add-in to the existing programme packages used in the molecular simulation.

The achievements and prospects for the development of research into the theory and calculation of the structures of biomacromolecules using NMR data have been covered in detail in reviews.^{304, 314}

2. Dipolar coupling and the order parameter tensor

Dipolar coupling is a unique feature of matter which provides information on molecular structure and dynamics. The dipolar coupling between the spins of nuclei i and j situated in a magnetic field is characterised by the dependence on the distance r_{ij} between them and on the angle θ between the internuclear vector $\mathbf{r}_{ij}$ and the magnetic field (Fig. 3)

$$D_{ij} = \frac{K(3 \cos^2 \theta - 1)}{2r_{ij}^3},$$

where $K = (h\gamma_i \gamma_j / 4\pi^2)$ is the constant depending on the gyromagnetic ratios γ_i , γ_j of nuclei i and j , respectively.

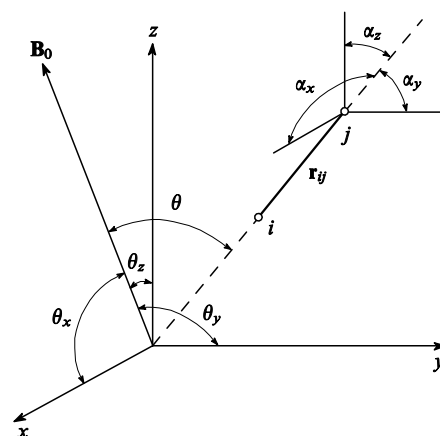


Figure 3. Scheme representation of the parameters used for determination of the dipolar coupling and elements of the Saupe order matrix; i and j are nuclei located in magnetic field $\mathbf{B}_0$; θ is the angle between the internuclear vector $\mathbf{r}_{ij}$ and the magnetic field direction; (x, y, z) is a molecular-fixed system of coordinates; θ_x , θ_y , θ_z are the angles between the corresponding molecular axes and the magnetic field direction; α_x , α_y , α_z are the angles between the vector connecting the nuclei i and j and the molecular axes x , y , z .

Dipolar couplings occur both between the nuclei of one molecule and between the nuclei of neighbouring molecules. In an isotropic medium, rigid molecules are arranged chaotically and execute chaotic translational and reorientation motion; therefore, dipolar coupling is averaged over the whole molecular ensemble and over the observation time, *i.e.*,

$$D_{ij} = K \left\langle \frac{3 \cos^2 \theta - 1}{2r_{ij}^3} \right\rangle$$

(the angled brackets mean averaging over time and over all the possible orientations and distances).

Apart from participation in the molecular motion as a whole, the nuclei are involved in the intramolecular motion; the RDC are averaged over these motions, too. Since the characteristic frequencies of these types of motion are substantially different, they are supposed to be not correlated, and these two averaging operations are considered to be independent, *i.e.*,

$$D_{ij} = K \left\langle \frac{3 \cos^2 \theta - 1}{2} \right\rangle \langle r_{ij}^3 \rangle^{-1}.$$

If the magnetic field is uniform (as is normally the case for NMR spectrometers), the translational motions do not influence the averaged constant and it depends only on the reorientation motion and the instantaneous distribution of the molecular axes in the magnetic field.

In an isotropic medium in the absence of aligning factors, the spatial distribution of molecular axes is spherically symmetrical and the times of molecular reorientation are markedly shorter than the characteristic times of an NMR experiment; therefore, in this medium, the dipolar couplings are completely averaged and are not manifested in the spectra because the average $\langle (3 \cos^2 \theta - 1)/2 \rangle$ is zero.

Under the action of aligning factors or when the molecules are placed in an aligned medium, the molecular motion in the specimen becomes anisotropic, the direction along the orientation axis, which is called the director, being the predominant one. The molecules of the compound under study are compelled to move anisotropically even if they do not tend to be oriented along the director. This anisotropic motion, together with the partial alignment along the director is responsible for the fact that magnetic dipole–dipole interactions are observable, because in this case, the average $\langle (3 \cos^2 \theta - 1)/2 \rangle$ value is no longer equal to zero.

Saupe³¹⁵ proposed describing the degree of ordering of a molecule by the value $\langle (3 \cos^2 \theta - 1)/2 \rangle$, which he called the order parameter tensor. This value can range from -0.5 to 1 . Zero corresponds to the absence of orientation and the values 1 and -0.5 correspond to the maximum degrees of alignment along and normal to the direction of the orienting factor, respectively.

Since the magnetic field in a spectrometer has spatially fixed axes, it is convenient to express the components of coupling tensors in this laboratory system of coordinates, which can be converted into a molecular-fixed system of coordinates in different ways, namely, using the order matrix, the formalism of the motion constants or averaged Wigner rotation matrix. In the Saupe scheme, the alignment of molecules is described by a symmetrical order matrix S having a zero trace, whose elements are determined by the expression

$$S = \frac{1}{2} (3 \cos \theta_p \cos \theta_q - \delta_{pq}),$$

where p, q mean one of the Cartesian axes ($p, q = x, y, z$) of a molecular-fixed system of coordinates; θ_x, θ_y and θ_z are the angles between the corresponding molecular axes and the direction of the magnetic field (see Fig. 3); δ_{pq} is the Kronecker symbol ($\delta_{pq} = 1$ for $p = q$ and $\delta_{pq} = 0$ for other cases).

The degree of order along the axis containing two nuclei i and j and having the angles α_x, α_y and α_z with molecular axes x, y and z is determined by the relation

$$S_{ij} = \sum \cos \alpha_p \cos \alpha_q S_{pq}.$$

The 3×3 order matrix is characterised by only five independent elements (because it is symmetrical and has a zero trace, *i.e.*, $S_{xx} + S_{yy} + S_{zz} = 0$). With appropriately chosen molecular axes, the matrix can be reduced to a form in which its elements are independent and their number varies from 1 to 5, depending on the symmetry of the molecule or, more precisely, the symmetry of the system of interacting nuclei. For example, the degree of alignment of highly symmetrical molecules having a threefold (or higher-fold) axis of symmetry can be described by only one independent element of the matrix. The degrees of alignment of molecules having two perpendicular symmetry planes, can be described by two independent elements. When the molecule has only one plane of symmetry, knowledge of the three independent elements of the order parameter matrix is required. In the general case, where the molecule is asymmetric, three elements determine the direction of the principal axis of the tensor with respect to the magnetic field

and the other two describe the degree of orientation along this direction and the degree of orientation in the plane normal to the principal axis. In the system of x, y, z principal axes, the order parameter tensor is diagonal and only two independent values determine the above degrees of orientation: S_{zz} and the asymmetry parameter

$$\eta = \frac{S_{xx} - S_{yy}}{S_{zz}}.$$

Since the symmetry of biomacromolecules is low, as a rule, all five elements of the order parameter tensor need to be known to describe their orientation.³¹⁶ In these molecules, the distances between the directly bonded nuclei virtually do not change and only two independent values determine the orientation, namely, the order parameter and the angle between the bond vector and the magnetic field direction; therefore, these parameters are often called orientational constraints.

For clarity, the orientation of biomolecules is commonly described, instead of S_{ij} tensor components of the order matrix, as is usually done in NMR spectroscopy of small molecules,¹³¹ by the axial A_a and rhombic A_r components of the diagonalised molecular orientation tensor $\mathbf{A}$, *i.e.*, in the system of the principal axes of the tensor of the magnetic susceptibility anisotropy of the molecule and three Euler angles determining the position of the principal axis of this tensor relative to the direction of the magnetic field. In this system, the expression for the RDC between the nuclei P and Q has the form

$$D_{PQ}(\theta, \varphi) = S \frac{\mu_0}{4\pi} \gamma_P \gamma_Q h \frac{A_a (3 \cos^2 \theta - 1) + (3/2) A_r \sin^2 \theta \cos 2\varphi}{4\pi^2 r_{PQ}^3},$$

where θ and φ are the angles for the vectors of the nuclei P and Q in the coordinate system of tensor $\mathbf{A}$, h is the Planck constant, γ_P and γ_Q are the gyromagnetic ratios of these nuclei, r_{PQ} is the distance between them, S is the main order parameter, μ_0 is the magnetic susceptibility of a vacuum.

If the magnetic susceptibility tensor is axially symmetric, then η (or A_r) is equal to 0, and only one parameter S_{zz} (or A_a) determines the RDC, which, in turn, determine the direction of vectors connecting the pairs of nuclei relative to the principal orientation axis. This allows easy interpretation of the dipolar constants, for example, for the DNA molecule or some DNA–protein complexes.¹⁴¹ For the case where the aligned molecules have a nearly axial symmetry, a simple algorithm for including the information on dipolar couplings has been developed using the CNS computation programme as an example.³¹⁷

However, most often, the molecule is not axially symmetrical; therefore, for data interpretation, one should also determine the second component of the tensor, which measures the degree of its deviation from the axial symmetry, *i.e.*, its rhombicity and asymmetry. This is a difficult task for molecules with a small number of magnetic nuclei.

For biomolecules containing a large number of identical pairs of nuclei whose vectors are approximately uniformly distributed in space, this task is markedly easier.³¹⁸ In this case, by analysing the column diagram for the distribution of dipolar couplings (corresponding to the spectrum of a powdered specimen), one can determine unambiguously the axial and rhombic components of the diagonalised tensor (Fig. 4). No preliminary structural information on the biomolecule is required; in this stage, there is even no need to determine the main direction of the tensor.

The same principle underlies a method used to determine components of the diffusion tensor from the T_1/T_2 distribution for ¹⁵N nuclei of the amide groups in the protein molecules.³¹⁹ It should be noted that diffusion and orientation tensors for proteins in bicelles are unidirectional,³²⁰ which can also be used in determining the orientation of a biomolecule.

To evaluate the possibility of determining the tensor components from the set of measurable orientation-dependent param-

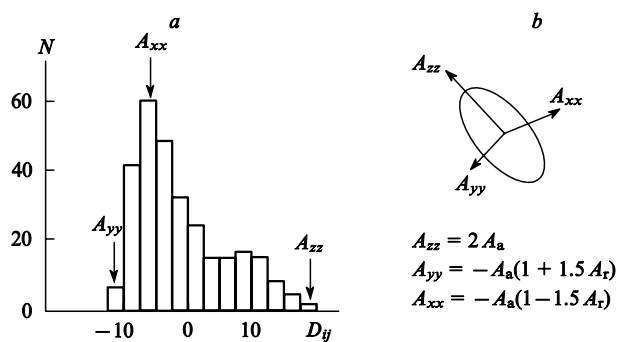


Figure 4. Column diagram for the distribution of dipolar couplings (a) and the component of the diagonalised molecular alignment tensor A (b).³¹⁸

ters, a method for analysing the pattern of filling of the orientational space by internuclear vectors has been proposed.³²¹

If only few RDC have been determined for a biomolecule, or they are non-uniformly distributed in space, or they contain several domains with different orientations, the column diagram analysis mentioned above is inapplicable. Therefore, a more advanced procedure for the analysis of the whole set of RDC and determination of the axial and rhombic components of the order parameter has been developed on the basis of the maximum likelihood method.³²²

Determining the orientation of the order parameter tensor relative to the molecule-fixed system of coordinates is a rather complicated problem, which can be solved unambiguously if the structure of the biomolecule is already known. This results in multiple possible orientations of the vectors of each pair of nuclei, corresponding to the mirror reflections relative to each axis of the order tensor (altogether 8). This appreciably complicates the energy hypersurface in searching for the minimum. Finally, the convergence of the iteration is very slow.

Attempts at estimating the order parameter tensor of the biomolecule on the basis of calculation results or specific experiments have been undertaken in a number of studies. The most trivial approach implies a network search among the possible pairs of the parameters A_a and A_r .³⁰²

If data on the biomolecule structure have been derived preliminarily from other experiments, they can be used for more precise determination of the axial and rhombic components of the tensor.^{323,324} Finally, one can do without the preliminary determination of the values of this tensor by including them as variable parameters into programmes for calculation of the biomolecule geometry.³²⁵ In particular, such a modification of the XPLOR algorithm has substantially facilitated the calculation and accelerated its convergence; the obtained results are very close to those found with the conventional algorithm.³²⁶

To simplify the analysis of RDC, a method for predicting the orientational order has been proposed, based on a model taking into account the steric repulsion between the protein molecule and the aligning particles of the LC medium.¹⁹⁷

A more advanced method for predicting the order parameter taking into account only steric effects has been reported;³²⁷ in this method, the protein molecule under study is modelled by an ellipsoid. The principal axes of the orientation tensor and the moment of inertia tensor of the molecule coincide. The other components of the orientation tensor are determined using the standard algorithm for minimisation of the difference between the predicted and experimental RDC. The order parameter tensor differs from the moment of inertia tensor because it has a zero trace. Therefore, when information about the other two axes of the moment of inertia tensor is used to predict the other elements of the order parameter tensor, the eigenvectors of these tensors are taken to be parallel if there are no electrostatic effects.³²⁸ An analytical solution to the problem of alignment of ellipsoidal

particles by planar obstacles has been obtained. If the 3D structure of the protein molecule is known, the order parameters of both the protein molecules incorporated in membranes and the molecules aligned under the action of a magnetic field or an LC medium can be predicted using simple expressions.

In a more convenient algorithm for predicting the order parameter tensor from the moment of inertia tensor, the eigenvalues of the order tensor are proportional to the molecular asymmetry in the planes determined by the corresponding pair of eigenvectors of the moment of inertia.³²⁹ This method, which the authors called TRAMITE (Tracking Alignment from Moment of Inertia Tensors), proved to be very convenient in investigating not only protein molecules but also non-rigid or small molecules.

The relative orientation of the order parameter tensors can be determined without knowing the protein structure on the basis of correlation analysis of two sets of RDC by conducting experiments in two media that orient in different directions.³³⁰ The graphical representation of the correlation map of such sets depends appreciably on the relative orientation of the tensors; therefore, it allows one to obtain a good initial approximation for further analysis of RDC.

A new strategy for the calculation of the 3D structure based on the transformation of a set of RDC into a set of angles between vectors has been developed.^{331,332} The values comprised in this set no longer depend on the direction of the orientation tensor with respect to the molecular axes; they can be used in calculations instead of RDC.

Skrynnikov and Kay³³³ also proposed that a set of pairwise angular restraints independent of the chosen system of coordinates be used instead of RDC. This set proved to be very convenient for evaluating the compliance of the set of RDC with the next structure generated in adjustment programmes. Using n vectors of dipole couplings, $n(n-1)/2$ new values determining the angles between each pair of vectors are composed. In addition, the maximum and minimum values are determined for each angle between the vectors proceeding from the current generated structure. If the vector angle does not fall in the range between these values, it is considered as a mismatch. The total number of these mismatches can serve as a quality criterion for a given structure and can be used in calculations. The compliance of RDC with the structure is visualised by the 'RDC compliance map'. Using this map, it is convenient to evaluate the quality of each generated structural element or domain and its compliance with experimental data.

The procedures considered are based on the strategy of a generalised, model-free order parameter, developed previously for analysing the diffusion tensor in the interpretation of relaxation data.^{334,335}

Yet another method which allows one to solve the problem of ambiguity and to obtain an exact solution for the set of equations with RDC is to convert these equations to elliptical equations in the principal alignment frame.³³⁶

The effects caused by molecular motions of different types that influence the resultant RDC values of a globular protein have been studied by molecular dynamics methods.³³⁷ The structures of biomolecules calculated by virtue of these constants for different models of globule reorientation proved to be model-dependent. It was found, however, that the application of the developed self-coordination procedure to the sets of RDC measured for several (in the ideal case, five) different oriented LC media allows one to determine the structure without making suggestions concerning the pattern of the reorientation motion of the globule. This procedure does not require the simulation of these motions.

Taking rubredoxin as an example, it was shown that two or more different alignment media can be used to remove the degeneracy of orientation parameters when determining the structure of protein molecules (in order to obtain a larger number of parameters).^{338,339}

Actually, the dependence of dipolar couplings on the degree of alignment of the protein molecules and the globule orientation in

the spectrometer magnetic field can be used for obtaining numerous sets of parameters for different directions and magnitudes of the order parameter tensor, for example, in experiments with various aligning factors and also with a change in the conditions affecting the orientation (temperature, relative concentrations of components and additives). However, the sets of parameters determined are often linearly related and do not provide new information.

The precision of NMR determination of the structure of a biomolecule is still inferior to that of X-ray determination. One of the reasons for this is the lack of perfection of the computation algorithms used, which mainly copy the X-ray algorithms. With the progress in NMR techniques, specific computation algorithms that reflect the specific character of NMR experimental data are developed.³⁴⁰

3. The effect of vibrational motions

When the set of RDC is interpreted, the bond lengths are usually assumed to be constant and known for each type of bond. Therefore, the measured RDC describe either the variation in the angle orientation of the mean position of the bond or fluctuations around this mean position. However, RDC-based studies of the structures of small molecules have shown that the effect of the molecular vibrations may be appreciable in some cases.³⁴¹

The influence of vibrational motions on the averaging of RDC has been studied by quantum chemistry methods for direct N–H^N, C^α–H^α, C'–N and C^α–C' RDC and also the RDC between C'–H nuclei separated by two bonds.³⁴² The vibrational averaging was shown to influence the constants and to entail a resultant elongation of the effective bond lengths by 0.5%–3%, the effect of bending or torsion vibrations being more pronounced than the effect of stretching vibrations. The hydrogen bond formed by an amide group also increases the effective N–H bond length. The changes in the effective bond length are fairly small but, nevertheless, they can be used, especially in those cases where RDC from different types of bonds (nuclear pairs) are used to determine the structure of a biomolecule.

4. Databases for energy minimisation and for the search for homology and motifs

The use of homologous sequences with a known structure to generate structural models for a biomolecule is helpful for structural studies.

The most labour-consuming and prolonged stage in NMR investigations of the protein structure is the assignment of signals in the spectra to particular amino acid residues of a known primary sequence. This is especially true for NOESY spectra.

In protein databases, information on the spatial structure of a large number of proteins has been accumulated and the results of processing of numerous NMR spectra are presented. This information can be used for recognising separate structural elements and motifs often repeated in proteins. This is especially useful at the preliminary stage.

Apparently, RDC are the most convenient values that can be measured and used to search for similar images in protein databases. A trivial method is based on comparing the whole set of the N–H RDC measured for a biomolecule with the sets of these constants calculated from known structures deposited with protein databases.³⁴³ Thus in the search for homologies in the PDB, Meiler *et al.*³⁴⁴ created the DipoCoup programme taking into account all types of RDC and even pseudocontact shifts.

Delaglio *et al.*³⁴⁵ have developed a method for the construction of a 3D structure of a protein molecule by means of the search for similar fragments in a specially composed sample from the PDB. The fragment should contain 7 amino acid residues. Comparison is carried out against not only RDC but also chemical shifts taken from a special database for each fragment.

Instead of comparing the whole set of N–H RDC, one can search through databases for structural motifs (fragments) con-

taining, for example, ~20 amino acid residues using image recognition techniques. Andrec *et al.*³⁴⁶ intend to compose a library of structural motifs on the basis of available protein databases for use in RDC-based studies. By applying special fitting criteria (for example, self-consistency of overlapping fragments) for each set of experimental data, one can restrict consecutively the fragment retrieval.³⁴⁷

It is possible to compose a large number of such protocols for the design of a protein structure based on homologies and RDC. However, the information contained in protein and nucleic acid databases can also be used in a different procedure for determining the structures of biomolecules.

The crystal structures of many proteins and nucleic acids have now been established with high accuracy. Analysis has shown that only a few dihedral angles determining the molecular conformation are possible in these structures for energy reasons. This conformational information accumulated as a database can be used for determining the structures of new biomolecules.

In order to select the conformations that are physically realised and described in databases from amongst the possible conformations proposed by the procedure of structure adjustment in experimental results, an additional pseudo-potential is introduced into the energy function in the following form:

$$E_{DB}(i) = -k_{DB}(\ln P_i),$$

where k_{DB} is a scale coefficient or a force constant and P_i is the partial probability that this parameter falls in the allowed range of values.

The introduction of this pseudo-potential into the energy function restricts the possible range of dihedral angles and accelerates the convergence during the iteration procedure.

Similar potentials with one-, two-, three- and four-dimensional potential surfaces describing the degree of likelihood of various combinations of torsion angles have been reported.^{348–355}

The use of such potentials for minimisation is especially efficient for the adjustment of parameters determined from the spectra of oriented specimens, for example, dipolar couplings. In particular, the introduction of this type of potential for describing the positional coupling between pairs of bases in nucleic acids has sharply increased the accuracy of DNA structures determined in NOE-based experiments and using RDC.³⁵⁶

5. De novo structure determination using only residual dipolar couplings

At present, the 3D structure of a biomolecule is commonly determined using NOE. The new NMR techniques developed in recent years are usually considered as auxiliary and are used in those cases where the number of NOE signals is too small. However, the new methods are gradually becoming self-sufficient (without using the NOE data) methods for structure determination.

The method for determining the structure of a biomolecule with the use of only RDC may have been all-sufficient if it was not for the ambiguity of RDC interpretation caused by the fourfold degeneracy and the ambiguity of determination of the order tensor orientation.

An attempt at using only orientation parameters in structural studies was undertaken by Tjandra.³⁵⁷ Subsequently, in a study of cytochrome *c'* (although using several methods), Hus *et al.*³⁵⁸ developed an algorithm that allows the structures of any paramagnetic proteins and complexes to be determined without resorting to NOE data. The algorithm employs the geometric information contained in paramagnetic pseudocontact shifts¹⁵⁸ and cross-correlated Cuire spin–dipole electron–nuclear relaxation^{153,359} as well as the information contained in RDC (only N–H RDC were used). This algorithm underlies the SCULPTOR programme (Structure Calculation using Long-Range, Paramagnetic, Tensorial and Orientational Restraints) meant for determining the structures of biomolecules using only orientation-

dependent data. This algorithm is also applicable to many metal-containing molecules.¹⁴³

An algorithm for determining protein backbone structure on the basis of only RDC has been proposed.⁴⁶ The authors have defined it as MECCANO (Molecular Engineering Calculations using Coherent Association of Nonaveraged Orientations). This is a key study which demonstrates the real possibility of determining the structure of a biomolecule using the set of RDC alone. To solve the ambiguity problem, two sets of RDC were determined for the molecule in the LC media with different orientations and the self-coordination procedure was carried out for all RDC and each peptide plane.

The ambiguity of interpretation of the RDC determined in one experiment has been eliminated by invoking additional information.³⁴⁵ In particular, a new algorithm for the protein folding was proposed, which can be used to attain self-consistency of all sorts of protein fragments during the search and screening of the structures of protein fragments in the database.³⁴⁷

Yet another algorithm using only RDC and the changes in the chemical shifts of carbonyl carbon atoms has been proposed.²⁸⁸

The all-sufficiency of RDC for the structural studies of biological macromolecules by NMR spectroscopy has been proven.³⁶⁰

VII. The use of NMR spectroscopy for the study of the structures of biomolecules

As has been noted in the Introduction, the X-ray and NMR techniques are based on different kinds of physical phenomena and the structural data obtained by these methods supplement each other. X-Ray diffraction analysis produces a three-dimensional map of the electron density of the molecule, which is used to identify the relative positions of atoms (each experimental point on the map bears information on all atoms). An NMR study gives the distances and the angles between some pairs of atoms, which are used to reproduce a set of non-contradictory three-dimensional structures, and each experimental point bears information on the distance between some pair of atoms, or the size of some angle, or on the orientation of some bond vector with respect to a specified direction. In X-ray diffraction studies, hydrogen atoms almost cannot be seen, whereas in the case of NMR, they provide the main bulk of information. In turn, NMR spectroscopy virtually does not determine oxygen and sulfur. Whereas solution of the phase problem by X-ray requires the presence of a heavy atom in the molecule, in the case of NMR, isotope enrichment is needed to replace the non-magnetic ¹²C and quadrupole ¹⁴N nuclei by magnetic isotopes, ¹³C and ¹⁵N, respectively. An X-ray study gives rise to a static (frozen) structure of a biomolecule containing no mobile groups, while NMR allows one to study biochemical processes and the behaviour of flexible groups.

The main achievements and the potential of NMR spectroscopy of weakly aligned molecules in the research into various classes of biomolecules are briefly considered below.

1. Proteins

An advantage of NMR procedures for aligned specimens is the fact that information on the long-range order can be derived from dipolar coupling parameters. This provides a substantial increase in the accuracy of determination of the molecular structures of proteins and protein complexes determined by other NMR techniques.

The number of measured RDC characterising the polypeptide chain is great. It can be markedly increased by replacing non-magnetic nuclei by magnetic isotopes. The efficiency and simplicity of including RDC into the standard set of parameters for determining the 3D structures of not only biomolecules but also their complexes have been convincingly demonstrated in many publications.^{361–367} For example, Gronwald *et al.*³⁶⁸ could determine the structure of the protein kinase Byr2 only after adding RDC to NOE data.

The structure of a very important anti-HIV protein, cyano-virin-N, which binds to the glucoproteins of the viral shell and inhibits their activity, has been studied.³⁶⁹ This protein can become a key point in the development of a new anti-AIDS strategy. The ¹H, ¹³C, ¹⁵N NMR signals were assigned and a twisted folding was confirmed using RDC analysis;³⁷⁰ this is significant for further research into the structure–activity relationship for this protein.

The structure of the signalling human G α interacting protein (GAIP) in solution was determined in two different LC media.³⁷¹ Comparison with the crystal structure of the homologous rat RGS4 protein complexed to the α -subunit of the G protein showed the presence of equally aligned fragments which do not change after binding to G α , indicating that these fragments are not involved in the G α interaction. Comparative analysis of the structures of the bound and free proteins allowed the researchers to represent the binding geometry and the GTPase activation mechanism.

The structure of the DinI protein inhibiting the activity of the RecA protein from *Escherichia coli*, which initiates the repair or mutagenesis of DNA, was also determined in two different LC media (bicelles and phages).³⁶⁶ This made it possible to identify the role of the C-terminal α -helix, which forms a negatively charged ridge on the globule; this mimics electrostatically the DNA phosphodiester backbone and thus it can compete with DNA for binding to RecA.

The structure of hen lysozyme was studied in particular detail in two bicellar LC phases with different orientations;³⁷² comparative analysis with and without RCD data was performed and the importance of RDC restraints has been demonstrated. The protein structure was determined more precisely in this study than this had been done by X-ray crystallography.

Using RDC, it was possible to study the thermal stability of the protein aporubredoxin in the native (metal-containing) and metal-free forms.³⁷³ The native form of the protein proved to be fairly stable over a broad temperature range, while the metal-free form is susceptible to reversible thermal denaturation.

Analysis of the RDC for molecules of denatured proteins in a strained polyacrylamide gel showed that the topology of the native state of some structure elements is retained^{374,375} and is insensitive to the replacement of hydrophobic residues in the amino acid sequence by polar residues of a similar size.³⁷⁶

2. Domain orientation in proteins

The molecules of many proteins consist of two or more packed independent domains. The type of biological process executed by multidomain proteins, for example, enzymic catalysis, often depends on the relative orientation of the domains. Therefore, one of the goals of structural studies is to determine the relative orientation of the domains. The crystal structures of these proteins may differ from the structures occurring in liquids, because the forces acting during crystal packing may change the relative orientation of the domains. By investigating multidomain proteins by liquid-state NMR, one can determine the domain orientation and its changes induced by different factors (*e.g.*, ligand binding or covalent interactions). However, usually, the number of observable domain–domain contacts is small. Therefore, only measurement of the orientation-dependent NMR parameters offers new opportunities for determining the orientation of domains or secondary structure elements for the molecules of non-rigid proteins.

The foregoing can be illustrated by the results of the investigation of a two-domain protein barley lectin.³⁷⁷ First, it was demonstrated that the ¹⁵N–¹H RDC are applicable for determination of the relative domain orientation in the fragment of this protein and the use of the SVD method (Singular Value Decomposition) was theoretically substantiated.³⁷⁸ The orientation of each domain can be determined with a few RDC (five is plenty). The domain orientation and dynamics were studied in different LC media.³⁷⁹ The domain orientation was found to differ from

that determined for a highly homologous protein in the crystal. Furthermore, differences in the order tensor values suggest that the two domains have different reorientational dynamics and can be considered as independently reoriented.

In a study³⁸⁰ dealing with determination of the relative orientation of Zn-finger domains of the TFIIIA protein in the protein–DNA complex, RDC were also shown to be highly sensitive and reliable parameters. After inclusion of RDC, the spread in interdomain angles (thoroughly studied by X-ray, NMR and computer simulation) is reduced from 24 to 9°. However, in this case, too, the local structure of the domains should be known before; moreover its accuracy influences also the accuracy of RDC-based determination of the orientation.

The relative orientation of the monomer subunits in the cyanovirin-N domain-swapped dimer³⁸¹ and the full structure of its monomeric mutant³⁸² were established. This was done using a combination of SVD techniques³⁷⁸ and calculations based on the molecular shape;¹⁹⁷ less than one-third of the total number of RDC was involved. A combination of 'simulated annealing', torsion angle dynamics and rigid-body minimisation proved to be even more successful for determining the full structure of this protein.³⁸³ The combinations of these methods open up good prospects for fast determination of the full structure of homologous or chimeric proteins and structural analysis of mutations if the structure of the main protein is known.

The different orientation of domains in the ribosomal protein S4 Δ41 in the crystalline and liquid states has been demonstrated³⁸⁴ using RDC measured in two different uniaxial LC phases formed by DMPC/DHPC bicelles and bacteriophage Pf1. It was shown that domain orientations determined in the isotropic medium using NOE and in two anisotropic media are identical and the helical subdomain is twisted by 45° around the long axis of the molecule with respect to the subdomain in the crystalline phase.

Orientation of paramagnetic protein metal complexes in the magnetic field has also been used to establish the relative orientation of domains.¹⁴⁴ For this purpose, it is possible, for example, to replace the diamagnetic Ca²⁺ ion in calcium-containing proteins by a paramagnetic Tb³⁺ ion. This replacement virtually does not influence the protein structure as a whole. It was shown that Tb³⁺ is bound in only one of the domains and induces a substantial protein orientation. It is possible to measure not only domain–domain long-range pseudocontact shifts but also RDC.

If the crystal structure of a multidomain protein is known, the relative orientation of its domains in a liquid can be easily determined by measuring the RDC for only some easily identifiable residues incorporated in different domains.³⁸⁵ In particular, this procedure was used to determine the conformation of the complex formed by the maltodextrin-binding MBP protein with β-cyclodextrin containing 370 residues; it was also demonstrated that the relative orientation of its domains in the crystal structure differs substantially (by ~ 11°) from that in the liquid, although the structure of each domain corresponds to that in the crystal. Full structure determination for this protein using RDC, NOE and vicinal constants³¹⁰ confirmed the domain orientation determined by a fast assay.³⁸⁵ Measurements of the diffusion tensor anisotropy³⁸⁶ also confirmed the relative orientation of the domains established using RDC and showed substantial deviations from X-ray data. Finally, the RDC procedure was used to carry out a systematic study of the relative orientation of the domains of free and β-cyclodextrin- and maltotriose-bound MBP proteins.³⁸⁷ The domain orientations for apo-MBP and the MBP complex with maltotriose were found to coincide with the orientation in the crystalline phase, whereas in the case of the MBP–β-cyclodextrin complex, they were found to be different. The authors attributed this to the crystal packing effect.

The discrepancy of the conformations of multidomain proteins determined in the crystal phase and in solution appears to be the rule rather than an exception. Therefore, NMR spectroscopy of oriented biomolecules can be considered to be a unique method

for investigating their conformations in solution. This is especially important in the studies of enzymes and in the search for new drugs.

The ¹³C^α–¹³C^β RDC in ¹⁵N-, ¹³C- and ²H-enriched proteins can also be used to determine domain orientation.²⁴⁵ It should be noted that both intra- and interdomain structures of one of the studied proteins, namely, the maltose-bound protein in the liquid and crystalline states were found to be similar.

The RDC method was used to demonstrate the unique possibility of fast identification of medium- and large-scale interdomain motions in modular proteins.³⁸⁸ Actually, RDC provide information on the relative motions of domains. By using these data, together with structural and relaxation data, one can calculate the amplitudes and time scales of these motions.

In a study of relative orientation of Bacteriophage lysozyme T4 domains using RDC, the averaged conformation of this protein in solution was determined.³⁸⁹ The lysozyme T4 hydrolyses the β(1-4)-glycoside bond in the peptidoglycan substrate, which is bound to the protein in a gap between two domains. The crystal structures of various mutants of this enzyme are characterised by different opening angles, which implies a substantial mobility of the domains. In the native enzyme structure in solution, the opening angle was found to be 17° greater than that in the crystal phase.

A significant deviation (25°) from the crystal structure was found for Ca²⁺-calmodulin.³⁹⁰

The applicability of RDC to investigations of the dependence of functional properties on minor structural differences in homologous series of proteins was demonstrated in relation to the variation of the calmodulin-binding geometry for five different calmodulin-regulated kinases.³⁹¹

Yet another example is determination of the relative orientation of the subdomains of the heparin-binding domain of the vascular endothelium growth factor VEGF₁₆₅; this became possible only after RDC had been included in the analysis.³⁹²

Using RDC, it is also possible to study the dynamics of flexible fragments in non-rigid proteins; the RDC values averaged over various modes of motion are collated with the experimental values. For example, the mutual arrangement and the mobility of three helices in the p8^{MTCP1} protein molecule were determined in this way.³⁹³

The MODULE graphical interactive programme³¹³ mentioned above is convenient for the simulation of multidomain macromolecules. This programme allows each domain to be described by its own set of RDC. By varying domain orientations, one finds the best agreement of the sets of RDC with experimental data.

The methods developed for investigating the relative orientation and the dynamics of separate protein domains can also be used to study the structure and dynamics of individual rigid fragments of various molecular systems, for example, in non-rigid proteins, oligosaccharides and molecular complexes. Evidently, they would also be useful in the study of non-rigid organic molecules and liquid crystals.³⁹⁴

3. Protein–ligand complexes

Determination of the geometry of protein binding to the ligand is important as regards elucidation of the structure–biological activity relationships for proteins.³⁹⁵ The spatial structure of the protein–ligand complex needs to be known for the development of new pharmaceuticals, because this allows the search for a new drug to be target-directed, *i.e.*, aimed at providing the structural and charge complementarity of the required ligand to the active cavity of the protein.

The NMR spectrum of the ligand is usually rather simple and the signals can be readily identified even without isotope enrichment. This is taken into account in the most widely used scheme of investigation of protein complexes which implies the use of ¹⁵N/¹³C-enriched proteins and ligands with natural isotope abundance. Hence, it is possible to use special heteronuclear filtration

and editing methods in experiments for resonance correlations of only the protein, only the ligand, or only through-space protein–ligand couplings.^{24, 396}

Study of the change in the ligand conformation upon binding in protein complexes is often difficult, especially in the complexes with low affinity. In this case, the ligand cannot be observed separately in the free and bound states in the spectrum due to fast exchange. Therefore, it was proposed to use the dipolar couplings of the ligand in the oriented complex. Using the protein complex of a trisaccharide as an example, the possibility of measuring the orientation parameters of a free and bound ligand and determining its conformation has been demonstrated.³⁹⁷

The isotope enrichment of proteins, unlike that of small organic molecules, is currently a relatively easy task. In the development of new drugs, the use of traditional NMR procedures is complicated by the fact that the ligand becomes a kind of invisible. The structure of a non-enriched ligand complexed with an enriched protein can be determined by measuring the RDC of the ligand in an oriented complex.³⁹⁸ The structure of the whole complex can be determined with the highest accuracy if RDC are also used in determining the protein structure.

Algorithms for determination of the geometry of complexes making use of orientation parameters of both the ligand and the protein and taking into account the molecular symmetry have been developed.³⁹⁹ The geometry of the α -methyl-D-mannoside and its complex with a 53 kDa protein has been found using this type of algorithm.⁴⁰⁰

The orientation of a ligand (a transducin peptide fragment) weakly bound to light-activated membrane rhodopsin has been studied.^{401, 402} The rhodopsin-containing discs are oriented similarly to membrane fragments. The possibility of investigating the binding dynamics and ligand orientation was shown.

The measurements of the RDC for a ^{13}C -enriched Gb₃-oligosaccharide⁴⁰³ made it possible to locate its binding site to the protein verotoxin 1. The exchange between the bound and free states of the trisaccharide was fast on the NMR time scale and the measured RDC values were weight-averaged over these states. One of the three possible binding sites was reliably identified on the basis of simulation results (X-ray). The structural changes induced by the ligand have been observed for MBP binding to β -cyclodextrin.³⁸⁷

4. Protein–protein complexes

In recent years, NMR studies of multiprotein complexes and protein–protein interactions, like the studies of multidomain proteins, have become nearly routine. These studies make use of intermolecular NOE, cross-saturation, paramagnetic methods, analysis of chemical shift perturbations, analysis of relaxation parameters and so on. It is obvious that combination of RDC-based procedures with TROSY is the most promising for relative positioning of the proteins in the complex.⁴⁰⁴

Most of the above methods for determining the relative orientation of domains are also applicable to studies of various types of complexes (protein–protein, protein–ligand, protein–nucleic acid).

If the structure of each protein forming the complex is known, one can determine rapidly and accurately the structure of the whole complex using RDC and intermolecular NOE signals. This was demonstrated⁴⁰⁵ in relation to a protein–protein 40 kDa complex. In the algorithm described, dockings of the proteins incorporated in the complex are considered rigid. The use of this method markedly accelerates determination of the structures of complexes by NMR. The same method was used to determine the structures of two protein–protein complexes from the phosphotransferase system of *E. coli* sugars.^{406, 407}

McCoy and Wyss⁴⁰⁸ were able to solve the problem of protein docking using only the information contained in the RDC and chemical shift perturbations.

To determine the relative orientation of domains or molecules in calcium-containing proteins and complexes, one can use a facile

procedure which does not require aligning solvents,¹⁴³ orientation being induced by replacement of the Ca^{2+} ions by lanthanide ions having a similar ionic radius.

The presence of a paramagnetic label in one monomer in symmetric complexes, for example, in homodimers, eliminates the symmetry-related degeneracy and the overlap in the spectra and allows one to determine the RDC and pseudocontact shifts specific for each of the monomers.⁴⁰⁹

5. Protein side chain conformations

For the present moment, the attention of researchers focuses on the 3D structure of the protein backbone. However, significant items are determined by the side chain conformation; in some cases, they play a crucial role in the functioning of a biomolecule.

The assignment of signals corresponding to the side chain nuclei to particular members of the protein sequence is the most difficult and lengthy phase in determination of the protein structures by traditional methods based on NOE.

The dipolar coupling constants proved to be very convenient for investigating the side chain conformations and dynamic behaviour. The RDC values for side chains can also be useful for determining the backbone structure as additional structure constraints. A lot of various RDC can be measured (homonuclear or heteronuclear, between either directly linked or remote nuclei). The $\text{C}^\beta\text{--H}^\beta$ (see studies^{259, 260, 264}) and $\text{C}^\alpha\text{--C}^\beta$ (see studies^{244, 245, 259}) RDC as well as C--C ,^{265, 410} C--H ^{266, 410} and H--H ^{264, 265} RDC for methyl groups are used most often.

Even the earliest measurements of RDC in side chains showed good agreement with the values predicted on the basis of the 3D structure of the protein backbone.⁴¹¹ The subsequent studies confirmed the high information content of these constants not only in protein structure determination but also in a study of side chain dynamics.

In particular, the torsion angles χ_1 and their dynamic behaviour in ^{13}C -enriched partially deuterated proteins were determined with high accuracy using the direct $^1\text{H}^\beta\text{--}^{13}\text{C}^\beta$ RDC in CH and CH_2 groups²⁶⁰ (which can be interpreted rather easily, especially using the force potential of torsion angle databases).³⁵⁵

The possibility of precise determination of the orientation of functional groups in asparagine and glutamine in the protein side chains was shown.²⁷⁶ Determination of the arrangement of these groups is especially important because they are involved in specific hydrogen bonds.

The information concerning the positions of the methylene and methyl groups is important in determining the positions of the hydrophobic side chains in the protein.

A simple and efficient method for the measurement of RDC in methyl and methylene groups has been developed based on the 3D version of the well-known [$^1\text{H}\text{--}^{13}\text{C}$] CT HSQC experiment.⁴¹¹ The only drawback of this method is the fact that the sum of only two C–H RDC in the methylene group is determined.

Another method specially developed on the basis of the S^3E type HSQC experiment is more convenient for investigating the methylene groups of ^{13}C -enriched proteins.²⁶⁴ A new pulse sequence, SPITZE–HSQC (Spin State Selective Zero Overlap HSQC), made it possible to measure simultaneously the C–H and H–H RDC. The glycine methylene groups in ubiquitin were used as an example to demonstrate the unique possibilities of this method for fast determination of the magnitudes and signs for all three RDC in the methylene group, $D(\text{H1}, \text{H2})$, $D(\text{C}, \text{H1})$ and $D(\text{C}, \text{H2})$, in the spectra with minimal spectral overlap and a better signal-to-noise ratio compared to that in the HSQC experiment.

The first RDC-based systematic study of the methyl groups in the proteins showed a similarity in their geometry; the average value for the C–C–H angle (110.9°) proved to be greater than 109.5° (see Ref. 410).

Study of the methyl groups is complicated by two circumstances. First, a fourfold increase in the number of resonance signals after switching-off the ^1H decoupling may result in peak superposition and deteriorate the resolution. The specially devel-

oped IPAP–CT HSQC type protocol permits one to separate the multiplet components and markedly facilitates the measurement of RDC in the methyl groups.²⁶⁶ Second, the rotation of the methyl groups around a threefold symmetry axis decreases RDC by a factor of $(3\cos^2\theta - 1)$ (θ is the angle between the symmetry axis of the group and the C–H bond), *i.e.*, by almost 70%. The geminal H–H constants for which both the magnitude and the sign can be measured in a single experiment are more advantageous in this respect.²⁶⁵ The measurements of these constants are especially reasonable if deuterium substitution is used, *i.e.*, the protein molecule is perdeuterated except for the methyl groups.

The measurement of the quadrupole splittings in the spectra of aligned proteins with partially deuterated and ^{13}C -enriched methyl groups ($^{13}\text{CH}_2\text{D}$) is yet another promising line of investigations of these groups. The high correlation observed between quadrupole splittings and the $^{13}\text{C}^{\text{Me}} - ^{13}\text{C}$ RDC has been interpreted²⁹⁹ as being indicative of the similarity of all the methyl groups in proteins. The researchers cited calculated the average QCC for the methyl groups in the free rotation approximation taking the angle between the rotation axis and the axis of the electric field gradient tensor to be 109.5° . They proposed that the resulting value (167 ± 1 kHz) should be used subsequently in interpreting the ^2H relaxation data in the protein methyl groups.

An isotope effect was observed on deuterium substitution at the methyl groups. The spin–spin coupling constants for directly linked C–H and C–C nuclei decreased with an increase in the number of deuterium atoms in the group.⁴¹² The very weak isotope effect also had an influence on the methyl group geometry: the C–C–H angle slightly changed (by fractions of a degree).

6. Carbohydrates

Oligosaccharides are important compounds participating in many processes that take place in a cell. They occur in biological systems either in the free state in solution or as parts of proteins (glycoproteins) or lipids (glycolipids) on the cell surface. They are used more and more often in the development of drugs.

The cell functions of oligosaccharides are directly related to their structures, conformations and dynamic behaviour. Knowing these structures both in the free state in solution and in the bound state is an important prerequisite for understanding of the major factors that control the recognition of oligosaccharides by specific cell receptors.

At present, multidimensional high-resolution NMR spectroscopy in combination with molecular simulation is the major method used to determine the structures of carbohydrates. The advent of the procedures based on the measurement of RDC gave a renewed impetus to these studies.

The use of RDC for structure determination and conformational analysis of oligosaccharides was started in 1998 simultaneously by three research groups, headed by Prestegard,⁴¹³ Widmalm⁴¹⁴ and Homans^{415,416} and, later, by a group headed by Bush.⁴¹⁷ Actually, by that time, the methods based on the measurements of RDC and CSA have already been used to determine the structures of oriented glycosides, glycolipids and other carbohydrates,^{418–427} but this line of research has been generally recognised only after successful use of these methods in the studies of biomolecules.

Bolon and Prestegard⁴¹³ proposed a simple COSY experiment for measurement of the $^1\text{H} - ^1\text{H}$ RDC in oriented oligosaccharides and demonstrated its efficiency in relation to a trisaccharide. The high information content of these new data for the conformational analysis of oligosaccharides was used by Kiddle and Homans⁴¹⁵ to refine the conformation of another trisaccharide, studied previously using NOE and $^{13}\text{C} - ^1\text{H}$ and $^1\text{H} - ^1\text{H}$ vicinal constants. The $^{13}\text{C} - ^1\text{H}$ RDC were measured for a ^{13}C -enriched trisaccharide dissolved in a bicellar LC medium.

Rundlof *et al.*⁴¹⁴ used C–H dipolar coupling to study the conformation of a tetrasaccharide, lacto-N-neotetrose (LNnT), from human milk with natural ^{13}C abundance. By using energy minimisation, experimental data were adjusted to the molecular

model generated by the molecular dynamics method. Good correspondence was observed for a conformation in which the linear tetrasaccharide was described as a uniaxial cylinder. To confirm this model, LNnT was also studied in two other lyotropic LC media with conformation averaging.⁴²⁸ Using the Monte Carlo and molecular dynamics methods, various molecular structures were generated, the orientation parameters and RDC were calculated for them and compared with experimental values. It was shown that, apart from the expected difference between the orientational characteristics of the tetrasaccharide LNnT in two different media, a slight difference between the conformations was found.

Martin-Pastor and Bush⁴¹⁷ studied the conformations of six other natural oligosaccharides isolated from human milk; they used molecular dynamics and NMR spectroscopy based on NOE and RDC measurements for molecules oriented in bicelles. The inclusion of information contained in RDC markedly increased the reliability and the accuracy of results. The conformational study of these oligosaccharides and the pentasaccharides LNF-2 and LNF-3 (LNF is lacto-N-fucopentose) was continued on the basis of analysis of C–H RDC.^{418,429} (It should be noted that the conformations of these complex oligosaccharides were studied without isotope enrichment.) To this end, a strategy was developed for fast comparison and calculation of the difference between the experimental and calculated RDC for a large number of structures generated during computer simulation.⁴²⁹ Two different consecutive algorithms were used to analyse thousands of generated structures in the space of dihedral angles corresponding to the high and low values of the energy to be minimised. This two-stage strategy proved to be very efficient for a conformational study of the carbohydrate antigens of blood groups Lewis X and Lewis A trisaccharide⁴²⁹ and two synthetic trisaccharides of blood groups A and B and tetrasaccharide alditol of blood group A.⁴³⁰

These studies demonstrated the possibility of measuring the heteronuclear C–H RDC in oligosaccharides with a natural ^{13}C abundance. The 2D *J*-modulation HSQC procedures developed recently allow one to measure them with a higher accuracy.⁴³¹

The paramount importance of the $^1\text{H} - ^1\text{H}$ RDC for determination of the 3D structures of oligosaccharides was noted in another study.⁴³² The authors developed a new procedure for the measurement of RDC and determined the structure of a partially deuterated decasaccharide also using traditional NMR methods. The decasaccharide structure could be determined only when direct ($^1D_{\text{CH}}$) and long-range (D_{HH}) dipolar couplings have been included in the analysis. A method for determination of the conformation distribution function for disaccharides in the LC medium has been proposed.⁴³³

A new strategy for conformational analysis of flexible oligosaccharides based on the use of RDC has been reported.⁴³⁴ This strategy implies analysis of order matrices for each of the sugar rings. The resultant RDC values averaged over internal motions are used to estimate the amplitude of these motions. These data are well combined with the results of conventional relaxation methods.

The $^{13}\text{C} - ^1\text{H}$ and $^1\text{H} - ^1\text{H}$ dipolar coupling constants were used successfully to determine the structure and dynamics of simple sugars in solution.⁴³⁵ The structures of saccharose (disaccharide) and raffinose (trisaccharide) in solution were found to differ substantially from their structures in the crystal phase. For example, the disaccharide can exist with four different orientations of monosaccharides with respect to each other (for example, like protein domains³⁹⁹). However, only one orientation was observed, possibly due to the short bridging unit. Meanwhile, in the case of the galactose fragment of raffinose, clear-cut dynamic behaviour was found, which markedly decreased the degree of orientation of this fragment compared to the other two fragments.

The quadrupole couplings in deuterated carbohydrates were used to determine the structure and dynamic behaviour of $^{13}\text{C}/^2\text{H}$ -

enriched methyl- β -D-glucopyranoside.³⁰⁰ The quadrupole constants of endocyclic deuterons proved to be very uniform; therefore, a single average value of this constant can be used in relaxation studies of glycan fragments in glycoproteins and glycopeptides.

Comparison of the results of structure calculations of the pentasaccharide constructed from D-mannose residues by molecular dynamics methods with the structures obtained using relaxation data and RDC has shown³²⁸ that, although the results obtained using RDC are in good agreement with both the model of averaging over the whole possible ensemble of conformations and with one structure of this ensemble, it is still more legitimate to take into account all the conformational motions of the molecule. The relaxation data can be interpreted only in the ensemble model. The researchers also carried out quantitative conformational analysis of the core region of N-glycans in water using RDC and molecular dynamics methods.⁴³⁶

In determining the structure of a flexible heptasaccharide,⁴³⁷ success was achieved owing to the combination of traditional NMR experiments with the measurement of direct ($^1D_{CH}$) and long-range (D_{HH}) dipolar couplings.

The 3D structure of the enterobacterial cyclic antigen containing four repeating trisaccharide units was also determined by combined use of RDC, data of NOE experiments and vicinal $^3J_{CH}$ constants.⁴³⁸

Using only RDC, Freedberg was able to study rather easily the deformation of the fructofuranosyl ring of sucrose.⁴³⁹

Thus, the NMR spectroscopy techniques for aligned molecules open up new, unique opportunities for research into the structures and for conformational analysis of both simple sugars and complex oligosaccharides and their protein complexes in solution.⁴⁴⁰

7. Nucleic acids

Study of the structure of nucleic acids by conventional NMR spectroscopy methods is much more difficult than the study of protein structures, due to a number of specific features of biomolecules of this class. First, there is a relatively low density of protons in nucleic acids, and, correspondingly, small number of NOE constraints. Second, due to the non-globular structure of the DNA molecule, the spectra contain no NOE signals between different sections of the chain but contain only signals due to nucleotides that adjoin each other in the sequence. Even in the RNA molecule, which is less linear and has a clear-cut tertiary structure, the number of internucleotide contacts is very little. Third, the dispersion of nuclear chemical shifts is insignificant; therefore, only a relatively small number of resonance signals can be resolved. Finally, it is necessary to determine five (rather than two as in proteins) backbone angles per structural unit.

The foregoing implies that global characteristics of nucleic acid structures such as helical twisting, helix step and torsion angles in the chain are difficult to determine, although a number of local conformation parameters (for example, the conformations of carbohydrate chains and the torsion angles of the glycoside bonds) can be established rather accurately. The RDC and CSA measurements in weakly aligned nucleic acids provide new, in principle, opportunities for structural studies.^{218, 441–444}

Almost any of the alignment methods mentioned above is applicable to nucleic acids; the use of filamentous phages is considered to be the method of choice.²²⁰

The attempts to measure the RDC for nucleic acids have been undertaken even in the first experiments with weakly aligned biomolecules in bicellar systems⁴⁵ and in LC suspensions of phages;²¹⁹ however, Bayer *et al.*,⁴⁴⁵ who used the ^1H – ^{13}C and ^1H – ^{15}N RDC in the protein–RNA complex, were able to considerably improve the resolution in the determination of the structure of a nucleic acid.

The structure of the DNA dodecamer d(CGCGAATTCGCG)₂ has been studied in a bicellar medium.⁴⁴⁶ In addition to the 162 NOE responses, 198 ^{13}C – ^1H ,

10 ^{15}N – ^1H and 200 ^1H – ^1H RDC were determined. It was shown that the dodecamer structure could in principle be determined using only RDC.

The same dodecamer was used to demonstrate a procedure of direct determination of the parameters of nucleic acid helices using only RDC⁴⁴⁷ based on the analysis of their order matrix. An advantage of this method is that it does not require the knowledge of the refined molecular structure.

A method for fast determination of a stoichiometry in homomultimeric nucleic acid complexes by analysis of RDC induced by a magnetic field has been proposed.⁴⁴⁸ Depending on the number of monomer units in the multimer, the components of its diamagnetic susceptibility vary. Having found or calculated the diamagnetic susceptibility of the monomer, one can determine the diamagnetic susceptibility of the multimer from the RDC values and, hence, the number of monomer units in the multimer. This does not require the knowledge of any structural information or even assignment of the resonance signals.

Using RDC, it is possible to determine the relative lengths of hydrogen bonds²⁴⁸ and their orientation in DNA.⁴⁴⁹ A systematic study of two DNA duplexes has shown⁴⁵⁰ that inclusion of RDC into the set of NMR parameters used in structural studies substantially increases the accuracy of determination of both the local and global structures of duplexes.

The use of RDC allows fast determination of the relative positions of known elements of RNA secondary structure.⁴⁴¹ For example, a few additional ^{15}N – ^1H RDC proved sufficient for determining the global structure of transport RNA⁴⁵¹ and a hammerhead ribozyme,⁴⁵² in which the local structures of helical regions had already been known.

The spatial packing of nucleic acid homodimers with C_2 symmetry has been established unambiguously using two sets of RDC measured independently.⁴⁵³ In this case, two independently oriented states of DNA quadruplexes were obtained using a bacteriophage solution as an orienting medium and on exposure to a strong magnetic field of the NMR spectrometer (800 MHz). The developed procedure was tested in relation to a $^{15}N/^{13}C$ -enriched deoxynucleotide sequence d(GGGTTCAGG), which dimerises in solution to give a quadruplex and forms a pair of G(CA) triads and GGGG tetrads.

The measurement of RDC is a rather fast and facile method for detecting the specific conformational changes taking place in RNA upon binding to drugs. This was demonstrated using the conformational changes induced by binding of an aminoglycoside antibiotic to the RNA chain.⁴⁵⁴

Measurement of the ^1H – ^{31}P RDC has been proposed for determining the geometry of binding of nucleic acids to the phosphodiester backbone.^{455, 456} The efficiency of measurement of the vicinal $H3'$ – P RDC (NOESY version of the CT COSY experiment) was demonstrated in the study of the d(CGCGAATTCGCG)₂ dodecamer mentioned above.⁴⁵⁶ The scalar and dipolar $H3'$ – P constants were measured in isotropic and LC states both without and with ^{31}P decoupling. Yet another variant of using through-space ^1H – ^{31}P RDC has been developed on the basis of the TOCSY experiment.⁴⁵⁵ In this case, one should measure the ^{31}P – ^1H RDC with base protons H6 and H8. The efficiency of this procedure was demonstrated by determining the structure of HIV-2 TAR 30-mer RNA in a solution of bacteriophage Pf1.

Wu *et al.*²⁸⁹ demonstrated that the great ^{31}P CSA values observed in aligned samples of nucleic acids can be efficiently used to determine the orientation of the phosphodiester groups relative to the molecular alignment tensor.

When in the NMR spectrum many proton resonances overlap, and, moreover, protons have many coupling partners (as, for example, the protons of the RNA ribose), it can be difficult to measure the ^1H – ^1H constants. In these cases, one can use selectively fluorinated compounds. In particular, an E COSY-based procedure with X-filtration has been developed for these measurements. The resulting ^1H – ^{19}F RDC were used successfully

to determine the structure of 2'-fluorolabelled 21-mer RNA hair-pin.⁴⁵⁷

The use of RDC simplifies the study of the structures of protein–DNA^{380, 458–460} and protein–RNA complexes.⁴⁴⁵ In particular, combined use of the measured J_{NN} constants through a hydrogen bond and the RDC induced due to alignment of the RNA molecule by the magnetic field made it possible to determine the geometry of binding of the 16-mer HTLV-I Rex peptide to the 30-mer RNA aptamer.⁴⁶¹

A new algorithm for fast assignment of NMR signals and simultaneous determination of the tertiary RNA structure has been developed;⁴⁶² in this case, the time-consuming NOE-based sequential assignment step is completely excluded.

Determination of components of the alignment tensor is much more complicated in the case of nucleic acids because the column diagram approach (see Ref. 318) based on the rather uniform distribution in space of the directions of internuclear vectors in proteins is inapplicable in this case. The mapping strategy developed by Warren and Moore³²² may be a good substitute for nucleic acids. The authors used this strategy to determine the structure of the sarcin-ricin RNA loop.⁴⁶³

Thus, the use of RDC markedly extends the scope of modern NMR techniques as applied to structure determination for any type of nucleic acids and their complexes.^{463–466}

8. Internal dynamics

The study of dynamic processes in macromolecules represents yet another promising application of NMR spectroscopy of aligned biomolecules. Unlike the spin relaxation or chemical exchange methods used conventionally, this method provides information on the dynamic behaviour on a time scale typical of biologically significant motions (picoseconds to seconds).^{467, 468}

We have already mentioned studies in which RDC have been used to examine the dynamics of protein side chains,²⁶⁰ domain orientation^{379, 385} and the conformational mobility in carbohydrates.^{328, 434, 436} It is usually assumed that internal motions in the biomolecules are either missing or negligible or that they are similar and have an axial symmetry.

However, in reality, internal motions of various types always occur in biomolecules and neglecting them should undoubtedly influence the accuracy of structure determination based on RDC. Indeed, when the biomolecule contains non-rigid fragments, RDC are determined by averaging not only over reorientations of a biomolecule as a rigid particle but also over internal motion. The additional averaging gives rise to deviation of the RDC values of flexible fragments from the values expected for the given degree of orientation of the biomolecule as a whole and deteriorates the accuracy of the determined structure. These deviations can serve as a measure of mobility of the given fragment and a criterion for choosing a particular model of motion.

For separating the structural information in RDC from dynamic information, a special strategy based on analysis of the order matrix was developed; this strategy allows one to distinguish the most flexible fragments of a biomolecule. The internal motions are especially pronounced in carbohydrates; naturally, RDC were first used to study their dynamics.^{434, 435} The potential of this method was also demonstrated for proteins in analysis of the internal dynamics of ubiquitin⁴⁶⁹ and the functional dynamics of the active state of ribonucleotide binase.⁴⁷⁰ The most extensive prospects are opened for investigations of the RNA internal dynamics and the dynamics of RNA binding to proteins.⁴⁷¹

Another strategy for extracting dynamic information from RDC^{337, 472} is based on a large number (at least five) of independent measurements in different orienting media.

VIII. Conclusion

The information considered in this review demonstrates the vigorous development of the application of NMR spectroscopy to biomolecules.[‡]

An advantage of NMR spectroscopy for weakly aligned biomolecules is the fact that, along with structure determination, it allows one to determine rather promptly the relative arrangement of individual groups during functioning of the biomolecule without the necessity of repeated labour-consuming determination of the structures of all current states of the dynamic system.[§] Therefore, this method can be regarded as most promising in the studies of the structure–biological function relationship for biomolecules.

The development of NMR spectroscopy of weakly aligned biomolecules is especially topical for biology and medicine. Apart from the possibility of determining the tertiary and quaternary structures and the dynamics of biomolecules and their complexes, this technique is suitable for: quick diagnostics of molecules in solutions and investigation of their functions; screening of drugs; fast elucidation of structure–property relationships for mutant or modified biomolecules; spectroscopic studies of the biomolecules of various tissues and organs *in vivo* either in the oriented state or in exchange between oriented and non-oriented states; visualisation of the structures of various biological objects using the degree of alignment of biomolecules or their fragments as the contrast factor.^{473–477}

The combination of this method with other methods (for example, with small-angle X-ray scattering in solution,⁴⁷⁸ diffraction methods and advanced structural analysis using synchrotron radiation⁴⁷⁹) opens up new opportunities for research into biomolecules.

The Tables presented in the Supplement summarise characteristics of the systems used for weak alignment of biomolecules and the results of studies using NMR of weakly aligned molecules for compounds deposited with the PDB and the BMRB (Biological Magnetic Resonance Bank).⁴⁸⁰

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IX. Supplement

Table S.1 presents brief characteristics of the systems used for weak alignment of biomolecules. Table S.2 lists the structures of biomolecules deposited with the PDB and the BMRB which were determined using dipolar coupling parameters. Note that the term 'structure' is used to mean both a set (ensemble) of structures with close values of minimisation criteria in the adjustment programmes used and a single (the most probable) of these structures. Some identical biomolecules are recorded in the databases under different numbers. The structures of these biomolecules were determined by different groups of researchers or by the same group but based on different assumptions.

[‡] K Wütrich (Switzerland) was awarded a Nobel Prize in 2002 for a series of studies dealing with NMR spectroscopy of biomolecules.

[§] For the series of fundamental research dealing with the development of the procedures for the measurement of residual dipolar couplings of weakly aligned molecules, three outstanding scientists, A Bax, A Bothner-By and J H Prestegard, were awarded the Laukien Prize at the 43rd Experimental NMR Conference, Pacific Grove, CA, 2002.

Table S.1. Media used for weak alignment of biomolecules (the alignment direction is indicated relative to the magnetic field direction).

System				Biomolecule	Aligning factor	Alignment direction	Ref.
composition	description	advantages	drawbacks				
Without orienting medium	isotropic solution of biomolecules	no special orienting media are required	very weak alignment	nucleic acids, paramagnetic proteins	magnetic field of the spectrometer		42, 43, 140, 142–147, 149, 150, 152, 161
DMPC/DHPC, DMPC/CHAPSO	isotropic solution of discs with encapsulated protein	the same	—	membrane proteins	the same	⊥	183, 184
DMPC/DHPC	bicellar LC, flat discs, 4–5 nm thick	easily modifiable	hydrolysis at low pH	proteins, nucleic acids, carbohydrates	bicelles with negative $\Delta\chi$	⊥	174, 175, 179, 180, 182, 185–190, 196, 200
DMPC/DHPC/CTAB	the same	stable, positively charged	—	proteins	the same	⊥	192, 196, 200
DMPC/DHPC/SDS	"	stable, negatively charged	—	proteins, nucleic acids	"	⊥	192, 196
Dialkyl phospholipids	"	broad pH range, stable against hydrolysis	—	proteins, nucleic acids, carbohydrates	"	⊥	196
DMPC/CHAPSO	"	—	—	proteins, glycolipids	"	⊥	175, 179, 203
DLPC/CHAPSO	"	stable over a broad temperature range	—	proteins	"	⊥	193, 203
DIODPC/CHAPSO	"	stable against hydrolysis, stable at low pH	—	"	"	⊥	194, 203
Acid bicelles DMPG/DHPC, DMPS/DHPC, DMPC/DHPC/DMPX	"	negatively charged, analogue of natural membranes	—	membrane proteins		⊥	182, 195
Bicelles doped with lanthanide ions DMPC/DHPC + Ln ³⁺	"	—	—	proteins	bicelles with positive $\Delta\chi$		204–207
DMPC/DHPC/DMPG + DMPE–DTPA (doped with Yb ³⁺)	"	—	—	"	the same		206
DBPC/DHPC	bicellar LC, one lipid chain contains a biphenyl group	—	—	carbohydrates	"		211, 212
DBBPC/DHPC	the same	—	—	"	"		212
DMPC/CHAPSO + aromatic amphiphiles	"	—	—	proteins	"		191
Bacteriophage Pf1	LC medium, negatively charged, 2 μ m long cylindrical particles 6.5 nm in diameter	broad range of concentrations and temperatures; easy sample recovery by centrifugation	aggregated at low pH, binds to some proteins	proteins, nucleic acids, carbohydrates	filamentous phages, viruses		218, 220–222, 441

Table S.1 (continued).

System				Biomolecule	Aligning factor	Alignment direction	Ref.
composition	description	advantages	drawbacks				
Bacteriophage fd	negatively charged, 2 μm long cylindrical particles 6.5 nm in diameter	broad range of concentrations and temperatures; easy sample recovery by centrifugation	aggregated at low pH, binds to some proteins	proteins, nucleic acids, carbohydrates	filamentous phages, viruses		202, 224
Tobacco mosaic virus	the same	the same	the same	the same	the same		202, 234
CTAB–pentanol, disc-like micelles	forms a nematic LC phase	stable	strong orienting effect	proteins	lamellae		160
CTAB–rod-like particles	the same	"	unstable	"	"		160
Cetylpyridinium chloride–hexanol	positively charged, forms a lamellar LC phase	"	sensitive to salts	proteins, carbohydrates	"		170
Cetylpyridinium bromide–hexanol	the same	"	—	the same	"		171, 200
C8E5–n-octanol, C12E6–n-hexanol	non-charged, forms a lamellar LC phase	inert, stable; easy to make, easy sample recovery by dialysis	—	proteins, nucleic acids	coaxial cylindrical lamellae		172, 200
Polyacrylamide gel: acrylamide–methyne-bis(acrylamide) copolymer	hydrogels containing anisotropic cavities, non-charged, oriented under mechanical impact (compression, stretching)	inert, orientation can be changed, biaxial orientation is possible, easy sample recovery by elution	non-homogeneous, low rates of rotational diffusion	proteins	deformed pores of the gel	depends on the type of mechanical treatment	228–231
Natural cellulose fibres	LC medium, negatively charged rods, 200 $\times$ 10 nm	stable, inert	slow alignment	"	cellulose crystallites	$\perp$	226
Purple membrane fragments of halobacteria containing bacteriorhodopsin	non-liquid crystal, negatively charged, particles, aligned by magnetic field	low concentrations, stabilised by acrylamide gel	interacts with proteins, aggregated at high ion strength	proteins, peptides	electrostatic interaction with aligned membrane fragments		214, 215, 229
The same doped with lanthanide ions	the same	—	the same	the same	the same	$\perp$	216
Vanadium pentoxide	aqueous LC suspension, negatively charged units up to 600 nm long	stable, inert, absence of ^1H and ^{13}C nuclei, easy sample recovery by flocculation	low pH	carbohydrates	LC medium of ribbons		232

Note. The following abbreviations are used: C8E5, C12E6 are n-alkylpoly(ethylene glycols) C_mE_n , where m is the number of carbon atoms in the alkyl group, n is the number of ethylene glycol units; DBPC is 1-dodecanoyl-2-(biphenyl-4-acetyl)-*sn-glycero*-3-phosphocholine; DBBPC is 1-dodecanoyl-2-[4-(4-biphenyl)butanol]-*sn-glycero*-3-phosphocholine; DMPE–DTPA is 1,2-dimyristoyl-*sn-glycero*-3-phosphoethanolammonium diethylenetriaminepentaacetate.

Table S.2. Examples of biomolecules whose structures were determined using RDC.

PDB code	BMRB number	Description	The number of calculated structures	The number of residues	The number of RDC	Ref.
1B4C		rat apo-S100B ($\beta\beta$) metal binding protein	21	184	521	362
1C05	4577	ribosomal protein S4 Δ 41	see ^a	159	101	384
1C06	4577	the same	16	159	101	384
1C7U		DNA binding core domain of the transcription factor Mef2A with a 20-mer oligonucleotide	—	210	368	458
1CMZ	4407	human G α interacting protein GAIP	20	152	291	371
1D2B	4327	N-terminal domain of human tissue inhibitor of metalloproteinases-1	29	126	159	365
1D3Z		ubiquitin	10	76	945	293
1D8V	4522	antitumour protein MAP30	see ^a	263	387	364
1DUF		DNA dodecamer d(CGCGAATTCGCG) ₂	5	24	408	446
1E8L	4831	Hen lysozyme	50	129	209	372
1EKY		cytochrome c' from <i>Rhodobacter capsulatus</i>	32	129	68	358
1EZX		maltodextrin binding protein complexed with β -cyclodextrin	10	370	970	310
1F0A		DNA-damage-inducible protein I (DinI)	20	81	534	366
1F16	4632	pro-apoptosis protein Bax	20	192	575	481
1F3Y		nudix enzyme diadenosine tetraphosphate hydrolase from <i>Lupinus angustifolius</i> L.	25	165	94	482
1F70		calmodulin N-terminal domain	10	76	72	483
1F71		calmodulin C-terminal domain	10	67	65	483
1FH1		lipid binding nodulation protein Nodf	see ^a	92	41	306
1FZX		DNA dodecamer d(GGCAAAAAACGG)/d(CCGTTTTTTGCC)	10	24	85	484
1G03	4649	N-terminal domain of human T-cell leukemia virus type I HTLV-I CA ₁₋₁₃₄	20	134	193	485
1G14		DNA dodecamer d(GGCAAGAAACGG)/d(CCGTTTCTTGCC)	10	24	80	484
1GE9		ribosome recycling factor	15	184	108	
1GGR		complex of enzyme IIA ^{Glc} and the histidine-containing phosphocarrier protein HPr from <i>E. coli</i>	see ^a	253	77/118	407
1GHH		DNA-damage-inducible protein I (DinI)	20	81	534	366
1GIP		DNA dodecamer d(CGCGAATTCGCG) ₂	2	24	408	356
1GJJ		N-terminal constant region of the nuclear envelope protein LAP2	see ^a	50	123	486
1HJ7		LDL receptor EGF-AB Ca ²⁺ -binding epidermal growth factor-like domains	20	80	45	487
1H9C	4955	cysteinyI-phosphorylated enzyme IIB of the <i>N,N'</i> -diacetylchitobiose specific phosphoenolpyruvate-dependent phosphotransferase system of <i>E. coli</i>	9	106	73	488
1H92		SH3 domain of human Lck tyrosine kinase	30	63	44	489
1I35	4463	Ras-binding domain of the protein kinase Byr2	10	95	28	368, 490
1I42		Ubx domain from P47	10	89	56	
1IB8		conserved protein SP14.3 encoded by an essential <i>Streptococcus Pneumoniae</i> gene	see ^a	164	153	491
1IUUF		two DNA-binding domains in <i>Schizosaccharomices pombe</i> Abp1 protein	"	144	47	459
1J46		wild type HMG-Box domain of the human male sex determining factor SRY complexed to DNA	"	113	274/197, 101/96	492
1J47		M9I mutant of HMG-Box domain of the human male sex determining factor SRY complexed to DNA	"	113	274/197, 101/96	492
1J4V		domain-swapped dimer of the HIV-inactivating protein cyanovirin-N	"	202	136	383
1J4W		complex of the KH3 and KH4 domains of human FBP with single-stranded 29-mer DNA	"	203	140/154	460
1J5K		complex of the KH3 domain of hnRNP K with a single-stranded 10-mer DNA	"	99	147/140	493
1J6T		complex of the enzyme IIA ^{Mtl} and histidine-containing phosphocarrier protein HPr from <i>E. coli</i>	"	233	528	494
1J7O		calcium calmodulin N-terminal domain	3	71	323	390
1J7P		calcium calmodulin C-terminal domain	3	67	305	390
1JO7		influenza A virus promoter RNA	32	31	22	464
1JOX		LP5.1 hairpin from <i>Bacillus</i> RNase P RNA	24	21	56	495

Table S.2 (continued).

PDB code	BMRB number	Description	The number of calculated structures	The number of residues	The number of RDC	Ref.
1JWE	4297	N-terminal domain of <i>E. coli</i> DnaB helicase	20	114	84	496
1K31, 1KQV		Ca Ln calbindin D _{9k}	30	79	64	497
1KSM		the same	see ^a	79	64	497
1KAT	5185, 5198	phage-derived peptide antagonist complexed with vascular endothelial growth factor	24	118	146	498
1KHM	4405	C-terminal KH domain of hnRNP K (KH3)	20	89	209	361
1KMX	5238	heparin-binding domain of vascular endothelial growth factor	20	55	38	392
1KQQ		dead ringer ARID-DNA complex	20	169	94	499
1KR8		d(GCGAAGC) hairpin	14	7	38	466
1KVN	4935	protein SRP19 of <i>Archaeoglobus fulgidus</i>	10	104	66	500
1KVV	4935	the same	see ^a	104	66	500
1L4S	5315	ribosome associated factor Y	20	112	80	501
1L5E		the domain-swapped dimer of cyanovirin-N in a metastable folded state	see ^a	202	80	502
1LUD	5396	dihydrofolate reductase complexed with trimethoprim and NADPH	24	162	229	
1LVZ	5376	metarhodopsin II bound C-terminal peptide of transducin α -subunit	20	11	38	402
1M2Y		mutant <i>Pyrococcus furiosus</i> rubredoxin	see ^a	54	400	308
1MAG		gramicidin A	"	34	141	95
1MPE		tetrameric mutant of the B1 domain of streptococcal protein G	21	224	33	
1UD7	4493	ubiquitin core mutant 1D7	20	76	63	504
2EZM		HIV-inactivating protein cyanovirin-N	see ^a	101	380	369
2EZN		the same	40	101	380	369
1QCK		human barrier-to-autointegration factor Baf	20 + see ^a	178	259	503
2EZX		the same	20	178	496	505
2EZY, 2EZZ		"	20	178	496	505
2GAT		C-terminal domain of chicken transcription factor GATA-1 bound to DNA	see ^a	98	48	141
3GAT		the same	34	98	48	141
3EZA		complex of the N-terminal domain of enzyme I and the histidine-containing phosphocarrier protein HPr from <i>E. coli</i>	see ^a	334	238	406
3EZB		the same	40	334	238	406
3GB1		immunoglobulin binding protein B1 domain of streptococcal protein G	—	56	300	503
4GAT		wild type DNA-binding domain of area complexed to a 13-mer DNA containing a CGATA site	see ^a	92	48	141
6GAT		L22V mutant DNA-binding domain of area complexed to a 13-mer DNA containing a TGATA site	"	92	49	141
	4319	oxidised rubredoxin	—	54	53	506
	4320	reduced rubredoxin	—	54	53	506
	4335	calerythrin (EF-hand calcium-binding protein)	—	176	172	363
	4822	regulatory domain of human cardiac troponin C (apo form)	—	89	53	507
	4823	regulatory domain of human cardiac troponin C (holo-form)	—	89	53	507
	4824	regulatory domain of human cardiac troponin C (complex with peptide)	—	89	52	507
	4927	circular permuted variant of the potent HIV-inactivating protein cyanovirin-N	—	202	75	370
	4986	maltodextrin-binding protein (MBP) (ligand free)	—	370	903	387
	4987	maltodextrin-binding protein (MBP) (maltotriose bound state)	—	370	908	387
	5368	human ADP ribosylation factor 1 (ARF1)	—	360	—	508

^a Average structure.

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Methods for the synthesis of oligonucleotides containing reactive electrophilic groups

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Abstract. The published data on the methods of chemical synthesis of oligonucleotides containing 5'- and 3'-terminal or internal carboxy or aldehyde functional groups are considered. The known methods are systematised and their advantages and disadvantages are discussed. The bibliography includes 65 references.

I. Introduction

At present, modified oligonucleotides are widely employed in molecular biology for the study of regularities of nucleic–protein recognition, in antisense biotechnology as well as in the design of therapeutic drugs for the treatment of viral and hereditary diseases. Successful solution of these tasks requires the synthesis of oligonucleotide conjugates with various compounds, *e.g.*, reporter molecules, intercalators, biologically active peptides and enzymes possessing unique properties. In this context, the preparation of single- or double-stranded DNA molecules containing functional groups differing from those of natural DNA in reactivity is of special importance. The introduction of new reactive groups into the oligonucleotide chain allows successful synthesis of hybrid molecules.

Numerous methods for the synthesis of oligonucleotides containing nucleophilic groups (*e.g.*, amino or thio groups) are known;¹ their incorporation is usually achieved using commercially available reagents. In contrast, the preparation of oligonucleotides containing reactive electrophilic groups (*e.g.*, carboxy or aldehyde groups) is rather problematic. The body of literature on this subject is rather scarce.[†] We believe that the analysis and systematisation of the available data can give an impetus to the development of methods for the synthesis of oligonucleotides with electrophilic groups.

Carboxy or aldehyde functional groups can be introduced at any predetermined position of a synthetic DNA fragment, *viz.*, as the 5'- or 3'-end group or within the oligonucleotide chain. It is the

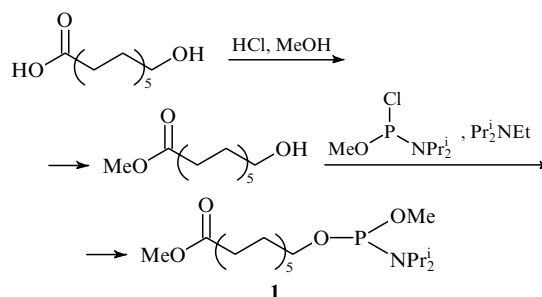
position that has been chosen as the basis for the classification of methods for the synthesis of modified oligonucleotides.

In all the studies reviewed herein, oligonucleotides were prepared by the automated solid-phase phosphoramidite method using a standard protocol.^{1,2} The synthesis of oligonucleotides containing a dialdehyde group is not considered here, being detailed in another review.³ Standard procedures for the isolation of modified oligonucleotides (reversed-phase, ion-exchange HPLC, polyacrylamide gel electrophoresis, *etc.*) and the methods used to confirm the structures of intermediate and target products also fall beyond the scope of this review, since in the vast majority of studies the correct analysis using NMR spectroscopy and mass spectrometry has been carried out.

II. Synthesis of oligonucleotides containing a 5'-terminal carboxy or aldehyde group

The carboxy group is commonly incorporated at the 5'-end of the oligonucleotide using a modified non-nucleoside unit attached to the oligonucleotide chain in the final step of the automated synthesis. It is desirable to protect the carboxy group in the course of solid-phase synthesis by esterification.

A method for the synthesis of carboxy-containing oligonucleotides using a phosphoramidite derivative of methyl 12-hydroxydodecanoate **1** synthesised as shown in the scheme below has been described.⁴



The attachment of phosphoramidite **1** to the oligonucleotide chain was carried out in accordance with a standard protocol of

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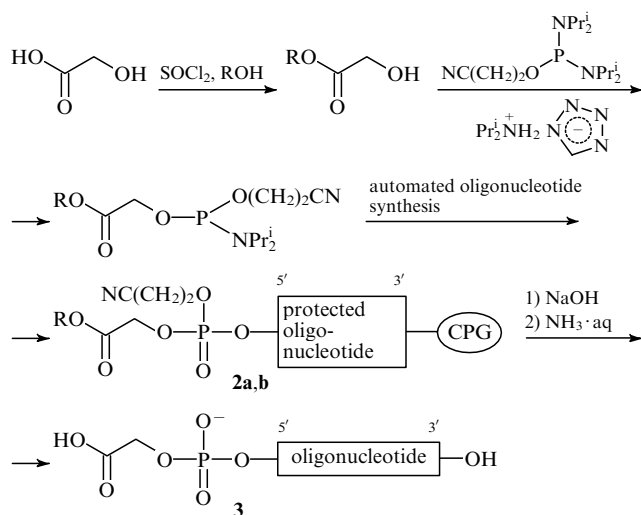
Uspekhi Khimii 71 (12) 1173–1192 (2002); translated by R L Birnova

[†] Several papers describing the preparation of 5'-carboxy- and 5'-aldehyde-containing oligonucleotides have recently been surveyed in brief in a review¹ devoted to the synthesis of various derivatives of nucleic acid fragments.

automated oligonucleotide synthesis. The 5'-ester group was hydrolysed with aqueous trimethylamine ($\text{Me}_3\text{N}:\text{H}_2\text{O} = 3:1$, 37°C , 48 h) with subsequent deprotection with ammonia to yield the target oligonucleotide. This reaction sequence was used because treatment of an ester with a concentrated aqueous solution of ammonia yields the corresponding amide.

The reactivity of the carboxy group incorporated was confirmed in the reaction with amines in the presence of 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide (DEC).⁴ At the concentration of the amine of 5×10^{-3} mol litre⁻¹ and pH 4.0, *N*-acylurea is formed. One possible reason is the protonation of the free amino group of the nucleophile in acidic media. Attempts to avoid the formation of a side product by increasing the concentration of the amine up to 0.1–0.5 mol litre⁻¹ or by increasing the pH to 5.5–6.7 failed. This problem was overcome by adding imidazole to the reaction mixture: this reacts with *O*-acylisourea to give an active intermediate, *viz.*, acid imidazolid, which reacts with the amine. The rapid formation of imidazolid prevents *O* → *N*-acyl migration. This approach allowed the preparation of conjugates of 5'-carboxy-containing oligonucleotides with amines in quantitative yields.⁴

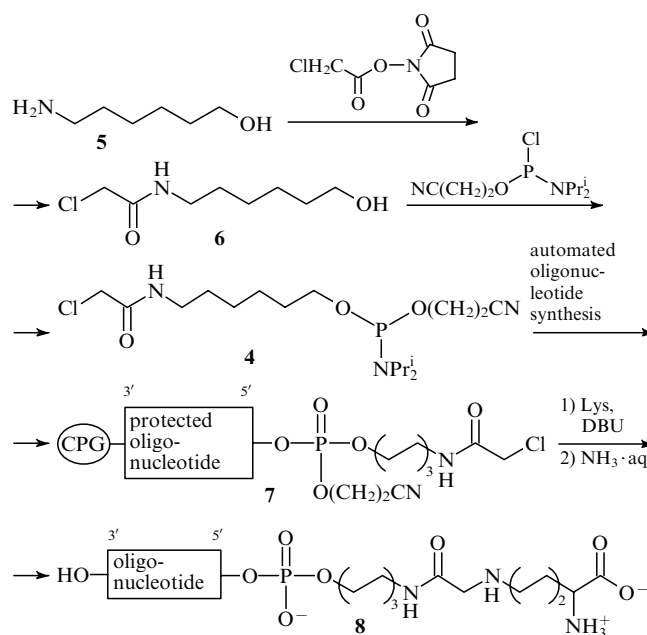
A method for the synthesis of modified oligonucleotides **2a,b** containing ester groups at the 5'-termini has been described.⁵ Post-synthetic treatment of these compounds successively with 0.1 M NaOH (4 h, 20°C) and concentrated aqueous ammonia (7 h, 55°C) afforded the 5'-carboxy-containing oligomer **3**.



R = $\text{Cl}(\text{CH}_2)_2$ (**2a**), CF_3CH_2 (**2b**); CPG is controlled pore glass.

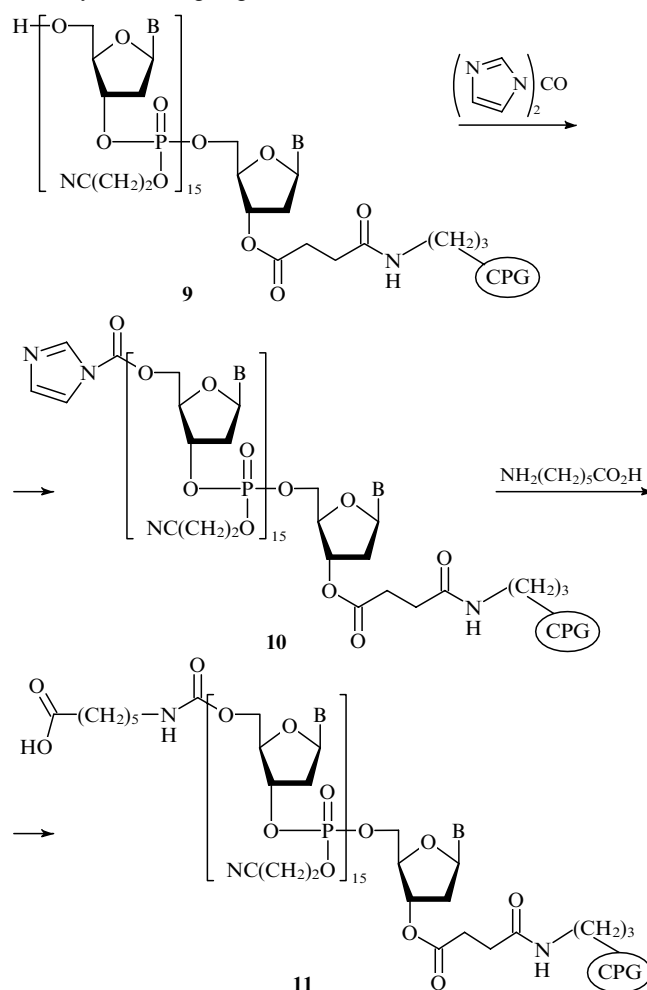
A similar procedure was proposed by Guzaev *et al.*⁶ for the synthesis of 5'-carboxy-containing oligonucleotides. In this case, automated oligonucleotide synthesis included incorporation of a non-nucleoside phosphoramidite **4** prepared by treatment of 6-aminohexanol (**5**) with *N*-chloroacetoxy succinimide with subsequent phosphitylation of compound **6**. It was found⁶ that an attempt to synthesise a bromoacetamide analogue of phosphoramidite **4** gave products of the Michaelis–Arbuzov reaction as deduced from ^{31}P NMR spectra. The presence of both nucleophilic and electrophilic reaction centres in the target phosphoramidite **4** makes the latter storage-unstable; therefore, compound **4** was introduced into an automated oligonucleotide synthesis immediately after its preparation.

Postsynthetic treatment of model oligonucleotides **7** with lysine in the presence of a base, 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), and then with concentrated aqueous ammonia gave oligomers **8** with 5'-terminal carboxy groups. It is noteworthy that the derivatives **7** can be used in the synthesis of oligonucleotides containing various functional groups.



A method for the synthesis of oligonucleotides with 5'-terminal carboxy groups involving introduction of the carboxy groups after completion of the automated oligonucleotide synthesis has been described.⁷

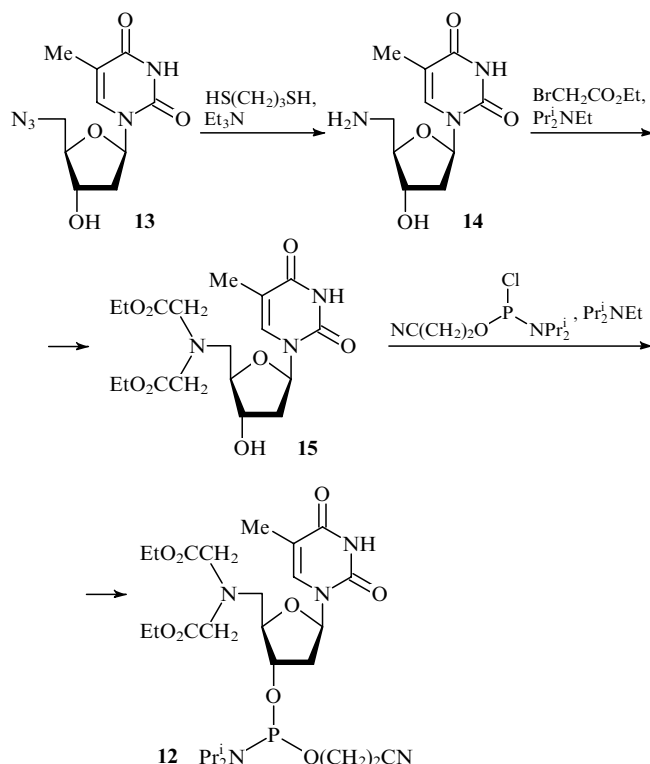
In this case, the 5'-terminal hydroxy group in the oligonucleotide **9** was activated with 1,1'-carbonyldiimidazole and the derivative **10** reacted with 6-aminohexanoic acid in pyridine to yield the carboxy-containing oligonucleotide **11**.



B is a heterocyclic base.

After detachment of compound **11** from the solid phase and deprotection of the functional groups, an intercalator (daunomycin) was attached.⁷

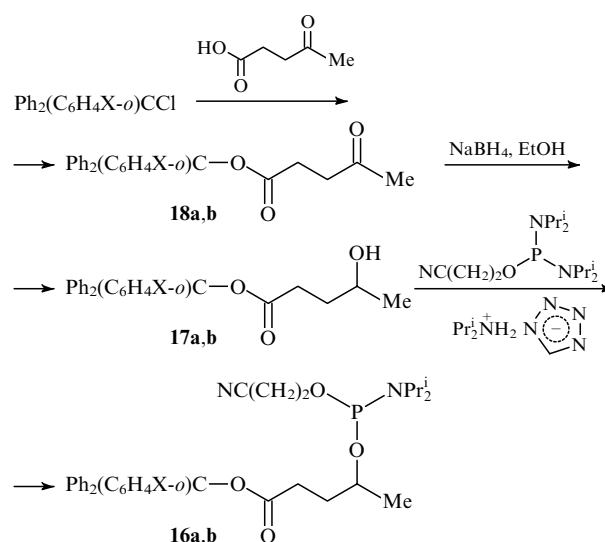
An original approach to the synthesis of modified oligonucleotides containing an iminodicarboxylic acid residue at the 5'-end has been developed.⁸ The phosphoramidite derivative **12** was synthesised starting from 5'-azido-5'-deoxythymidine (**13**). Reduction of the azide with propane-1,3-dithiol gave nucleoside **14** with a 5'-group; alkylation of the latter with ethyl bromoacetate and subsequent phosphitylation of the derivative **15** afforded 5'-modified phosphoramidite **12**. The resulting compound was introduced into a standard automated oligonucleotide synthesis; after its completion, the ester was hydrolysed with aqueous sodium hydroxide.



The method for the synthesis of oligonucleotides with 5'-terminal carboxy groups described in study⁹ is based on the use of the modified phosphoramidite derivative **16a** which was introduced into the automated oligonucleotide synthesis in the final step. The 2-chlorotrityl and trityl groups commonly employed in peptide synthesis, which can easily be eliminated by mild acid treatment,¹⁰ were used for the carboxy protection.

The starting phosphoramidites **16a,b** were obtained by phosphitylation of 2-chlorotrityl (**17a**) and trityl (**17b**) esters of 4-hydroxyvaleric acid (formed upon reduction of the corresponding oxo derivatives **18a,b** with sodium borohydride) with 2-cyanoethyl-*N,N,N',N'*-tetraisopropylphosphorodiamidite. Since the total yield of compound **16a** markedly exceeded that of compound **16b** and taking into account the higher stability of the 2-chlorotrityl group under the conditions used in the automated procedure, modified oligonucleotides **19** containing 5'-terminal carboxy groups were prepared from the phosphoramidite derivative **16a**.

The 5'-terminal 2-chlorotrityl protective group was removed under standard conditions. The carboxy group in the oligonucleotide **19** formed was activated using 1-hydroxybenzotriazole (HOBt) and *O*-(benzotriazol-1-yl)-*N,N,N',N'*-tetramethyluronium (HBTU) hexafluorophosphate (40 min, 35 °C). The activated oligonucleotide was used⁹ in solid-phase syntheses of a series of conjugates of modified oligonucleotides containing various nucleophilic components including fluorescent labels and short-chain peptides (Scheme 1).



X = Cl (**a**), H (**b**).

The introduction of an aldehyde group at the 5'-end of an oligonucleotide has been described.⁴ The 5'-terminal ester group of a synthetic oligomer **20** was deprotected with aqueous trimethylamine, and the resulting compound **21** was introduced into a reaction with 3-aminopropane-1,2-diol in the presence of DEC and imidazole to give the vicinal diol **22**. The latter is a precursor of the aldehyde which can be formed upon oxidation of the diol **22** with sodium periodate (Scheme 2).

It was recommended⁴ that the oxidation of the vicinal diol **22** should be performed immediately before further modification of the oligonucleotide **23**, since the aldehyde group reacts with the amino groups of the heterocyclic bases. The reactivity of the aldehyde function was demonstrated by the reaction of the oligonucleotide **23** with biotin hydrazide with subsequent reduction of the acylhydrazone formed with sodium cyanoborohydride.

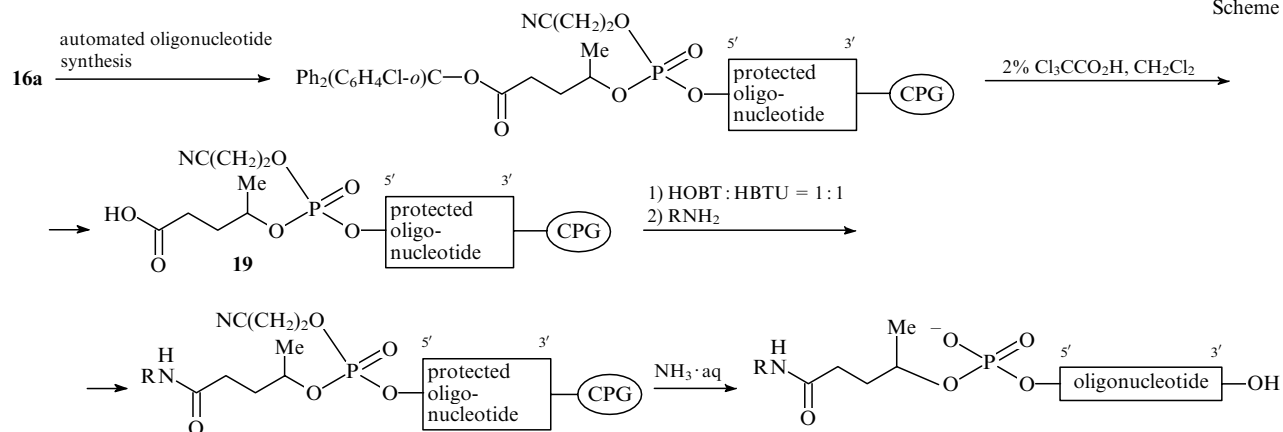
The introduction of the aldehyde group into the 5'-end of the oligonucleotide can be effected using an alternative approach which does not require any preliminary synthesis of a carboxy-containing oligomer. For this purpose, a phosphoramidite derivative of an aldehyde-containing nucleoside (or a non-nucleoside unit) or its precursor is incorporated inside the oligonucleotide chain in the final step of the automated synthesis. Obviously, in the former case, the carbonyl group must be protected. Such protection is necessary in order to avoid side reactions during the synthesis and postsynthetic treatments. Only one protective group, *viz.*, the 1,3-bis(*m*-chlorophenyl)imidazolidine group, meets all the requirements for protective groups in automated oligonucleotide synthesis,¹¹ however, this group is not used very often.

The problems related to the side reactions of aldehyde groups can be overcome by introducing a precursor of an aldehyde-containing fragment, *e.g.*, vicinal diol, instead of an aldehyde-containing fragment, into the oligonucleotide chain. The phosphoramidite derivative **24** was synthesised¹² in order to obtain oligonucleotides with 5'-terminal aldehyde groups.

Phosphoramidite **24** was synthesised from the alcohol **25** as the starting compound. The latter was converted into *tert*-butyldimethylsilyl ether **26** which was further oxidised into the vicinal diol **27** using catalytic amounts of osmium tetroxide in the presence of *N*-methylmorpholine *N*-oxide. After benzylation of the diol **27**, *tert*-butyldimethylsilyl protection was removed with tetrabutylammonium fluoride followed by phosphitylation of compound **28**.

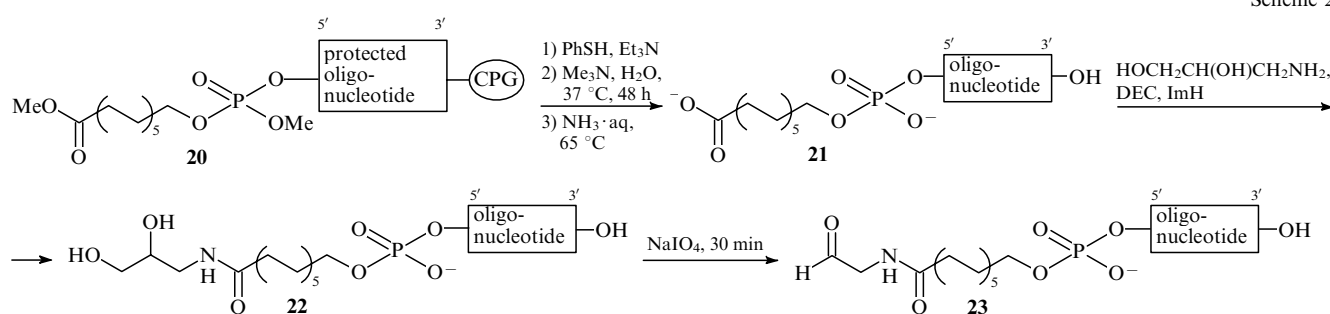
The resulting phosphoramidite derivative **24** was introduced into an automated oligonucleotide synthesis; after its completion, protective groups were removed with concentrated aqueous ammonia. The oxidation of the *vic*-diol groups in the resulting

Scheme 1



R is amine, amino acid, peptide residue

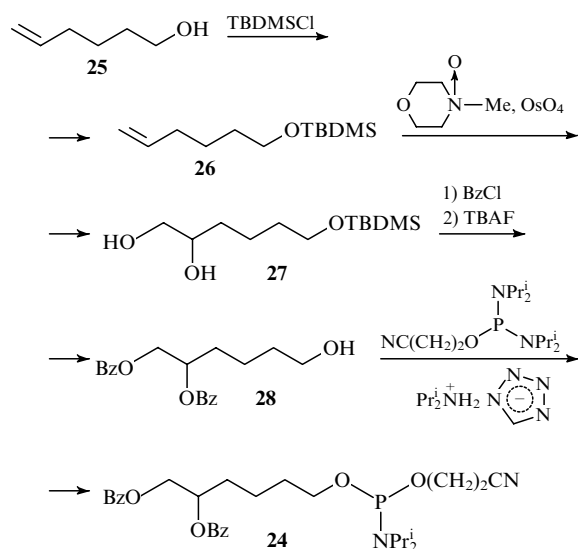
Scheme 2



ImH is imidazole.

oligomers with sodium periodate was carried out as described previously,⁴ *i.e.*, immediately before further transformation of the aldehyde function.¹²

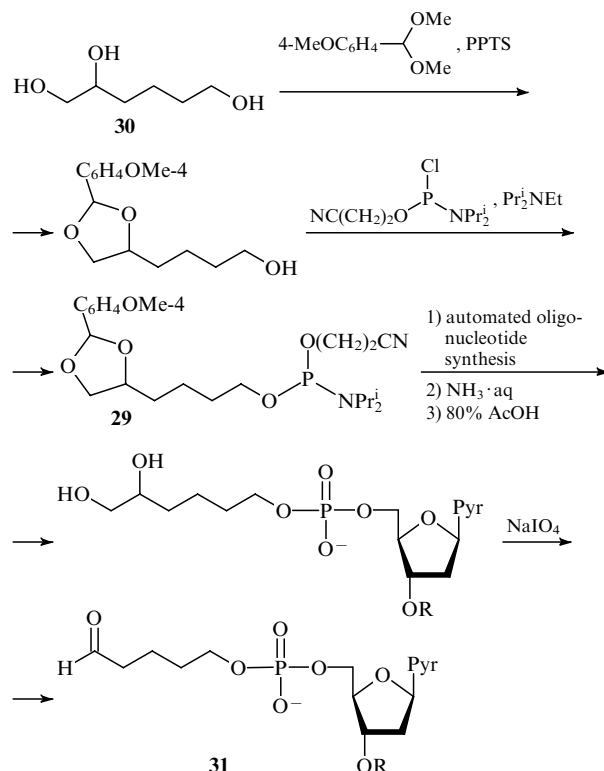
p-toluenesulfonate (PPTS). This protective group is stable under conditions of the automated oligonucleotide synthesis and is deblocked with 80% aqueous acetic acid in 1 h. In addition, the



TBDMS = $\text{Bu}^t\text{Me}_2\text{Si}$, TBAF = $\text{Bu}_4\text{N}^+\text{F}^-$.

The method for the synthesis of oligonucleotides with 5'-terminal aldehyde groups proposed by Forget *et al.*¹³ also entails the introduction of modified phosphoramidite **29** in the final step of the automated synthesis. It is noted that the two-step synthesis of compound **29** is a simpler and more convenient procedure than that described elsewhere.¹²

The *vic*-diol fragment of commercially available hexane-1,2,6-triol (**30**) was selectively blocked with the 4-methoxybenzylidene protective group under the action of 4-methoxybenzaldehyde dimethylacetal in the presence of catalytic amounts of pyridinium

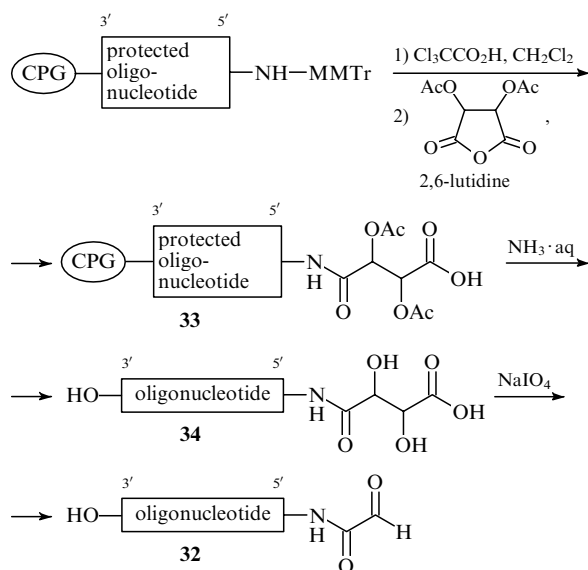


Pyr is pyrimidine heterocyclic base,
R is a fragment of the oligonucleotide chain.

hydrophobic nature of this protective group allows one to use it as an analogue of the dimethoxytrityl group in the isolation of target oligomers by reversed-phase HPLC. In the final step, treatment of deprotected oligonucleotides with a 50-fold excess of sodium periodate (30 min, 20 °C) gave the modified oligonucleotides **31** containing an aldehyde group at the 5'-end. A series of conjugates of oligonucleotides **31** with peptides¹³ and sugars¹⁴ containing aminoxy groups have been synthesised.

An original procedure for the synthesis of oligonucleotides **32** containing 5'-terminal glyoxylic amide has been developed.¹⁵ This functional group reacts with hydrazines, hydroxylamines and ω -aminothiols without any activation, but unlike the aldehyde group, it is storage-stable.

In the synthesis of modified oligonucleotides **32**, a commercially available phosphoramidite with a linker containing a protected amino group was incorporated into the oligomeric chain in the final step of the automated synthesis. Monomethoxytrityl protection was removed with trichloroacetic acid in dichloromethane; the free amino group was acylated with diacetyltartaric anhydride in the presence of lutidine. The acetyl groups in the modified oligonucleotide **33** formed were removed by treatment with concentrated aqueous ammonia; the amide bond was resistant to ammonolysis. The oxidative cleavage of the vicinal diol **34** with sodium periodate (1.7 equiv. of NaIO₄, pH 6.6) yielded modified oligomers **32** with 5'-terminal glyoxylamide groups which were further used in the synthesis of oligonucleotide-peptide conjugates.



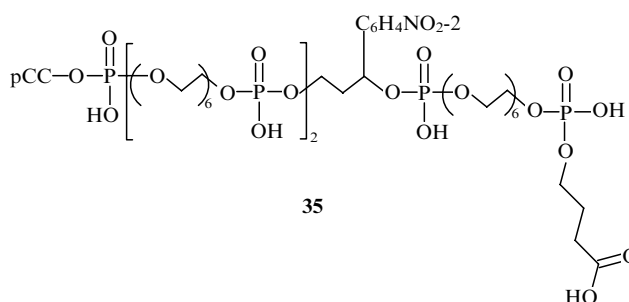
MMTr = (4-MeOC₆H₄)Ph₂C.

III. Synthesis of oligonucleotides containing a 3'-terminal carboxy or aldehyde group

At present, the synthesis of oligonucleotides with a 3'-terminal carboxy or aldehyde group usually entails incorporation of an additional non-nucleoside unit. Two different approaches to the synthesis of oligonucleotides modified at the 3'-end are known. In one of them, a fragment containing a protected hydroxy group is immobilised on a polymeric support. After completion of oligonucleotide synthesis, a reactive electrophilic group is formed at the 3'-end of the oligonucleotide as a result of chemical or photolytic cleavage of the covalent bond between the polymer and the linker. An alternative approach consists in the introduction of a carboxy or a carbonyl group after detachment of the synthesised oligonucleotide from the polymeric support. On the whole, the methods for the synthesis of oligonucleotides with 3'-terminal reactive electrophilic groups have a significant disadvantage, *viz.*, in both cases, the principle of incorporation of the functional group

excludes further solid-phase reactions with the nucleophilic components.

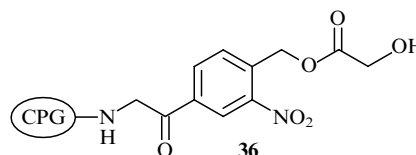
The dinucleotide **35** containing a photolabile *o*-nitrophenyl group and a carboxy group at the 3'-end, which was further used for the attachment of amines, has been synthesised.¹⁶



After termination of the solid-phase synthesis, the dinucleotide immobilised on the polymer through an ester bond was treated with a 33% aqueous solution of triethylamine (60 °C, 12 h) to detach it from the support and then with concentrated aqueous ammonia to remove the protective groups. The terminal carboxy group can be used for the attachment of reporter molecules to the oligonucleotide; these can selectively be removed from the support owing to the presence of a photolabile fragment.

In many cases, selective cleavage of the oligonucleotide from the polymeric support without removal of all protective groups acquires special importance in the synthesis of nucleotide-peptide conjugates. To this end, Greenberg *et al.*¹⁷⁻¹⁹ used polymeric supports modified with photolabile groups.

Initially, in the synthesis of carboxy-containing oligonucleotides, a method was applied in which the first nucleoside fragment was attached to the polymer **36** through a photolabile *o*-nitrobenzyl linker. In the final step of the synthesis, the oligonucleotides were split from the polymer by irradiation with light with the wavelength ~ 400 nm. The yields of the modified oligomers did not exceed 62%, which can be attributed to the destruction of the target product upon irradiation.¹⁷

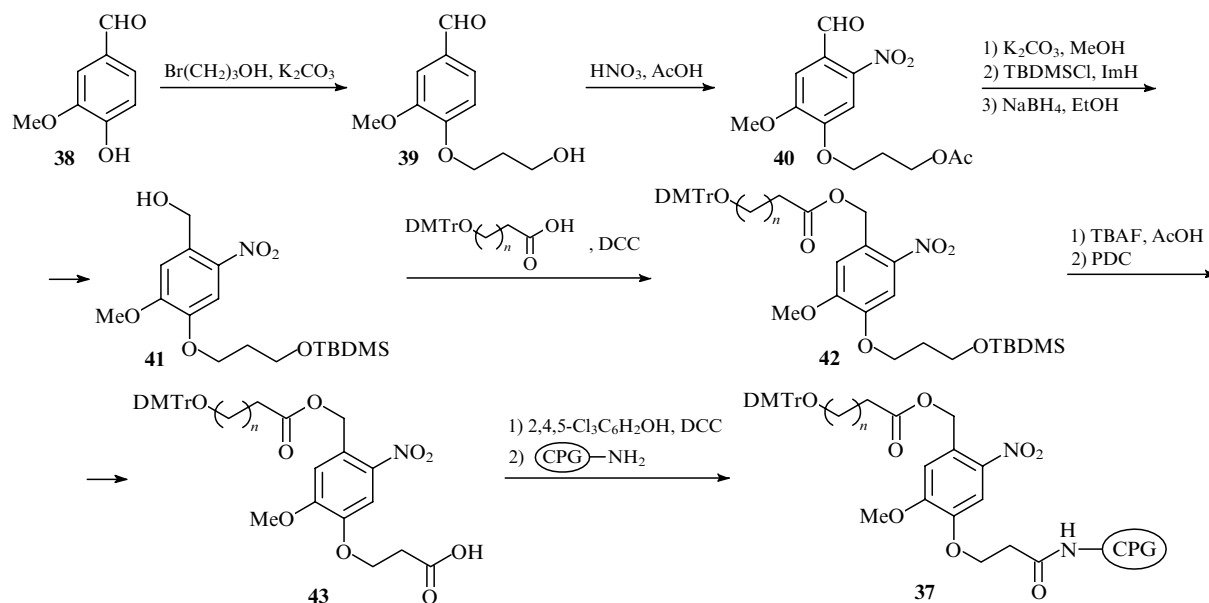


Polymers **37** with linkers of variable lengths between the first nucleoside fragment and the photolabile group were used for the synthesis of oligonucleotides, the time of photolysis was thereby reduced.¹⁸ Vaniline (**38**) was used as a starting compound in the synthesis of the polymeric support **37** (Scheme 3). In the first step, vaniline was alkylated with 3-bromopropanol after which the intermediate **39** was subjected to nitration in glacial acetic acid accompanied by simultaneous *O*-acetylation to form the derivative **40**. Removal of the acetyl and introduction of the *tert*-butyldimethylsilyl protective group and further reduction of the formyl group to the hydroxymethyl group gave substituted benzyl alcohol **41**. Condensation of compound **41** with the corresponding protected hydroxycarboxylic acid in the presence of dicyclohexylcarbodiimide yielded the derivative **42**, one of the protected hydroxy groups in which was converted into a carboxy group as a result of selective deprotection and subsequent oxidation with pyridinium dichromate.

Immobilisation of the resulting compound **43** on a polymeric support was carried out using activated trichlorophenyl esters in the final step of the synthesis. To minimise the formation of side products, the remaining amino groups of the polymer were acetylated.

The use of the polymeric support **37** made it possible to obtain the target oligonucleotides with 3'-terminal carboxy groups in quantitative yields. The yield of a modified oligonucleotide was

Scheme 3

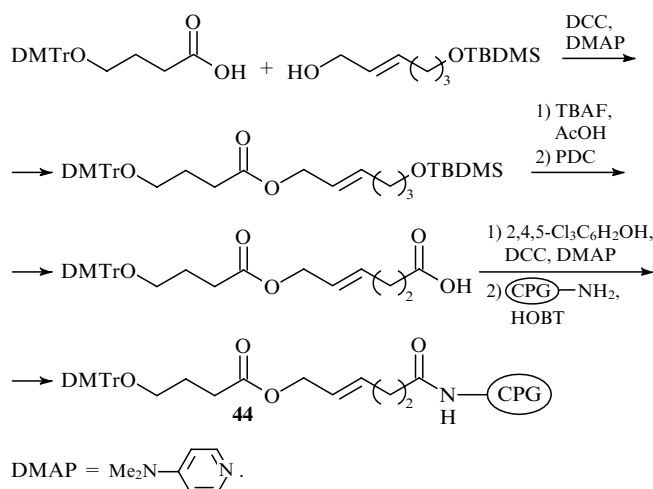


defined as the ratio of the amount of the modified oligomer obtained upon photolysis and deprotection with concentrated aqueous ammonia to the amount of the oligomer prepared by treatment with ammonia without preliminary irradiation.

The oligonucleotides prepared were further employed in the synthesis of conjugates with peptides and fluorescent labels without removal of protective groups.¹⁹ The reactions were carried out in organic media; the carboxy groups were activated with a HOBT–HBTU mixture (HBTU:HOBT:peptide = 1:1:5) in the presence of diisopropylethylamine. The yields of the conjugates were 85%–100%.

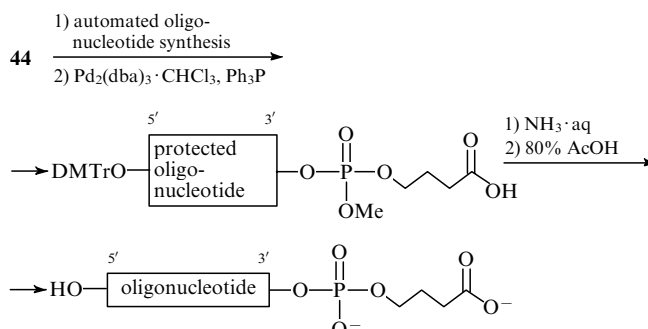
It was proposed²⁰ that polymeric support **44** with a linker containing an allylic-type ester selectively cleavable under the action of a palladium catalyst²¹ would be used in the synthesis of oligonucleotides with 3'-terminal carboxy groups. This allows the removal of the modified oligonucleotide from the polymeric support without deprotection of the functional groups.

The synthesis of the modified polymer **44** was carried out as shown in the scheme below.



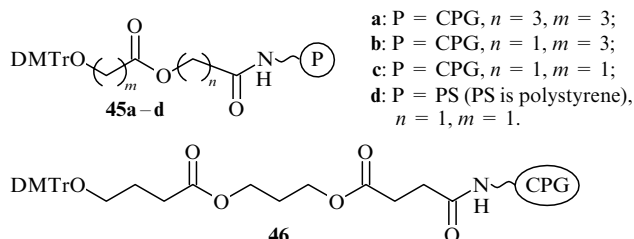
The use of the polymeric support **44** requires a change in the standard protocol of the automated synthesis. Thus *tert*-butyl peroxide was used instead of iodine in a pyridine–water mixture, since this results in iodination of the double bond in the oxidation of internucleotide phosphite groups.²⁰ Moreover, the methyl

group was used instead of the β-cyanoethyl group to protect the internucleotide phosphate groups. The reason is that during the cleavage of an ester bond between the oligonucleotide and the polymeric support under the action of tris(dibenzylideneacetone)-dipalladium(0) and triphenylphosphine in a *n*-butylamine–1.2 M formic acid mixture, the β-cyanoethyl protective group is cleaved completely at 55 °C in 1 h, whereas removal of the methyl group was less significant under identical conditions (10% in 7 h). The same method was used for the synthesis of a series of modified oligonucleotides.²⁰

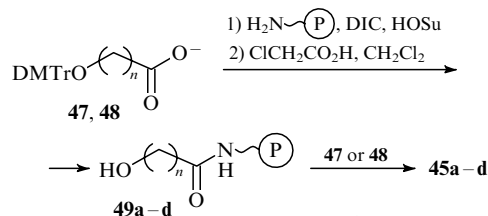


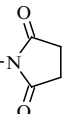
dba is dibenzylideneacetone.

Since functional groups are introduced at the 3'-end of the oligonucleotide owing to the cleavage of the ester bond between the solid phase and the oligomer, the requirements of the polymeric supports are very strict as regards the stabilities and reactivities of the ester fragments. A series of homologous polymers **45a–d** and **46** have been designed in a search for a polymeric support which meets better these requirements.^{22,23}

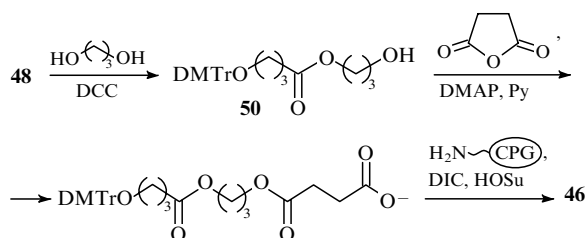


The polymeric supports **45a–d** were prepared by the reaction of glycolic (**47**) and 4-hydroxybutyric acids (**48**) containing a dimethoxytrityl protective group with the amino groups of the polymer in the presence of *N,N'*-diisopropylcarbodiimide and *N*-hydroxysuccinimide. After detritylation, the polymers **49a–c** were introduced into a reaction with protected acids **47** and **48** in the presence of 2,4,6-triisopropylbenzenesulfonyl chloride and catalytic amounts of *N*-methylimidazole. When polystyrene was used as a starting support, the activation of the carboxy group in compound **47** was carried out in the presence of carbodiimide and *N*-hydroxysuccinimide.

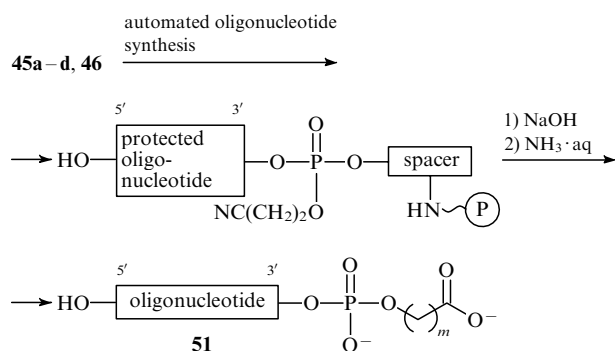


DIC = $\text{Pr}^i\text{N}=\text{C}=\text{NPr}^i$, HOSu = ;
P = CPG (**49a–c**), PS (**49d**);
 $n = 1$ (**47, 49b–d**), 3 (**48, 49a**).

The modified polymeric support **46** was prepared by esterification of the protected 4-hydroxybutyric acid **48** with propane-1,3-diol in the presence of DCC resulting in compound **50** which was further acylated with succinic anhydride and immobilised on a solid phase using the carbodiimide method.



The polymeric supports **45a–d** and **46** were used in the synthesis of oligonucleotides **51** containing a 3'-terminal carboxy group using the phosphoramidite approach. Cleavage of the oligomers from the solid phase and deprotection of internucleotide phosphates were performed by treatment with a 0.1 M aqueous solution of sodium hydroxide or 0.5 M DBU in H_2O ; deprotection of heterocyclic bases was achieved by subsequent treatment with concentrated aqueous ammonia.

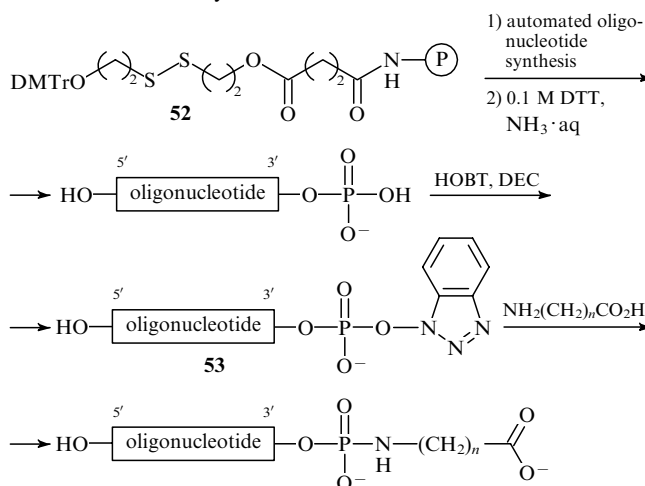


$m = 1, 3$.

Conjugates of modified oligonucleotides **51** with α,ω -diaminoalkanes were prepared by treatment of oligomers immobilised on modified supports with the corresponding amino component. However, the action of these reagents on oligodeoxyribonucleotides is accompanied by transamination of *N*-protected cytidine residues. Therefore, prior to the synthesis²³ benzoyl protective groups of the heterocyclic bases (cytosine and adenine) were

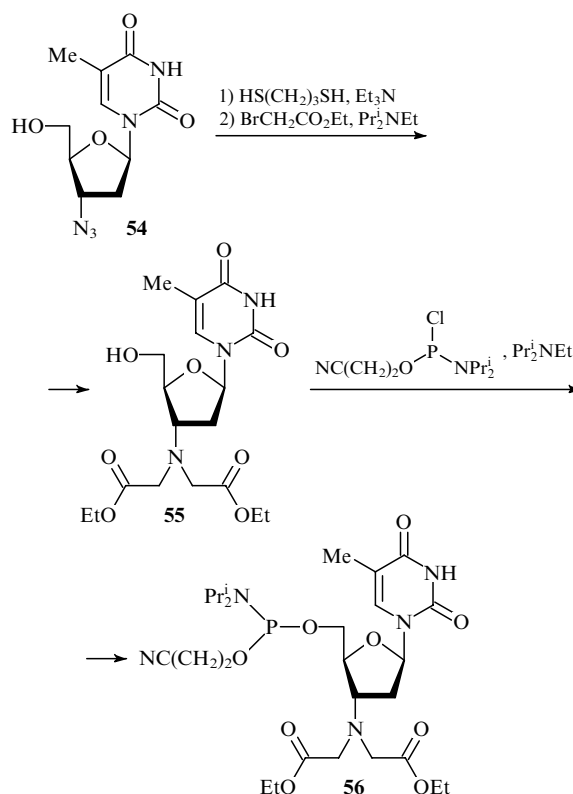
selectively removed with hydrazine in acetic acid. Under these conditions, oligonucleotides remained bound to the polymeric supports.

The 3'-terminal carboxy group was introduced into the oligonucleotide following termination of the automated synthesis.⁷ The cleavage of the target product containing a 3'-terminal phosphate group from the modified polymer **52** occurred under the action of 0.1 M dithiothreitol (DTT) in concentrated aqueous ammonia as a result of cleavage of the disulfide bond and subsequent intramolecular attack of the sulfide ion formed at the carbon atom. The carboxy group was introduced by treatment of the activated deprotected 3'-phosphorylated oligonucleotide **53** with ω -aminocarboxylic acid.

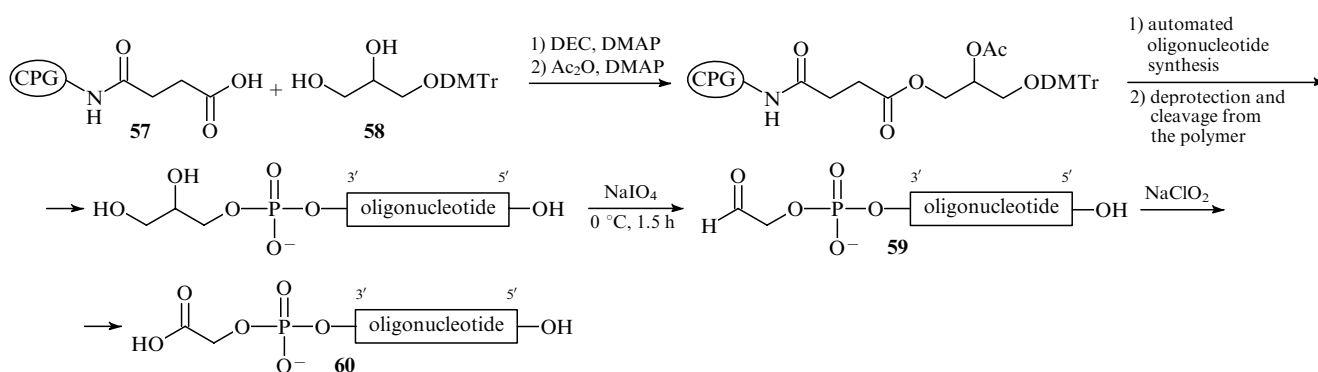


(P)—NH—aminopropylfructosyl-500, $n = 5, 10$.

The synthesis of modified oligonucleotides containing a 3'-terminal iminodiacetic acid residue has been described.⁸ These compounds can bind metal ions which stabilise the function of certain proteins. 3'-Azido-3'-deoxythymidine (**54**) as a starting nucleoside component was further converted into 3'-amino-3'-deoxythymidine and alkylated with two equivalents of ethyl



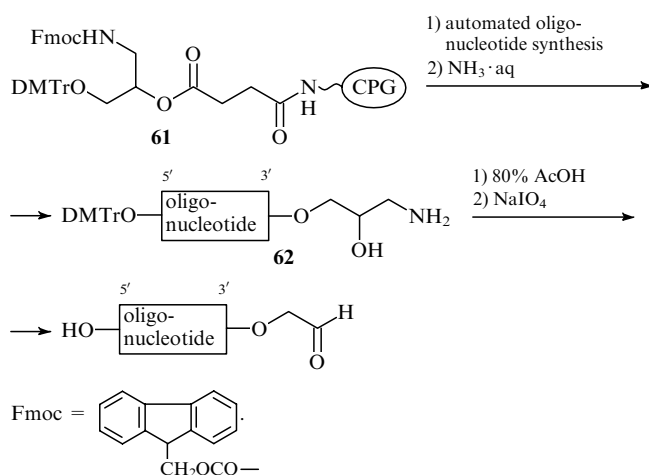
Scheme 4



bromoacetate. The resulting product **55** was converted into a modified phosphoramidite derivative **56** which was introduced into the oligonucleotide synthesis in the final step. The elongation of the chain was performed from the 5'-end of the oligomer to its 3'-end. On termination of the synthesis, the carboxy groups of the target oligonucleotides were deblocked with an aqueous solution of sodium hydroxide.

The synthesis of oligonucleotides containing 3'-terminal aldehyde groups has been described.²⁴ The polymeric support **57** was treated with monosubstituted glycerol **58** and the modified polymeric support with a linker was introduced into the automated oligonucleotide synthesis. After deprotection and cleavage from the polymer, the oligonucleotide containing a fragment with a vicinal diol group was oxidised with sodium periodate to yield modified oligomers **59**. Treatment of oligonucleotides **59** with sodium chlorite gave oligonucleotides **60** with 3'-terminal carboxy groups (Scheme 4).

An original approach²⁵ to the introduction of aldehyde groups into the 3'-termini of oligonucleotides based on the use of a commercially available polymeric support **61** in an automated synthesis²⁶ has been proposed.



Ammonolysis of the ester bond between the polymer and the synthetic oligonucleotide yields the oligomer **62** containing a 3'-terminal α -aminoalcohol fragment. Subsequent removal of the dimethoxytrityl group and oxidative cleavage with sodium periodate results in oligonucleotides with 3'-terminal aldehyde groups.

Conjugates of synthetic oligonucleotides with aminoxy derivatives of some peptides have been prepared.²⁵ The reactions were carried out in aqueous solutions in the presence of a threefold excess of aminoxy components (pH 4.5, 2 h). The yields of the conjugates were $\sim 50\%$.

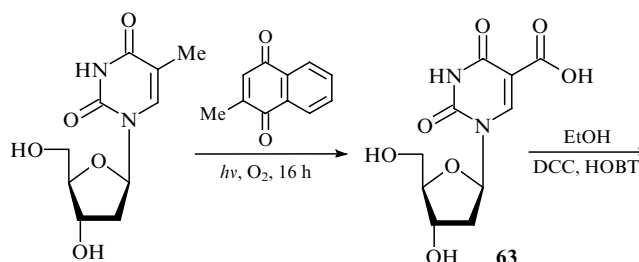
IV. Synthesis of oligonucleotides containing an internal carboxy or aldehyde group

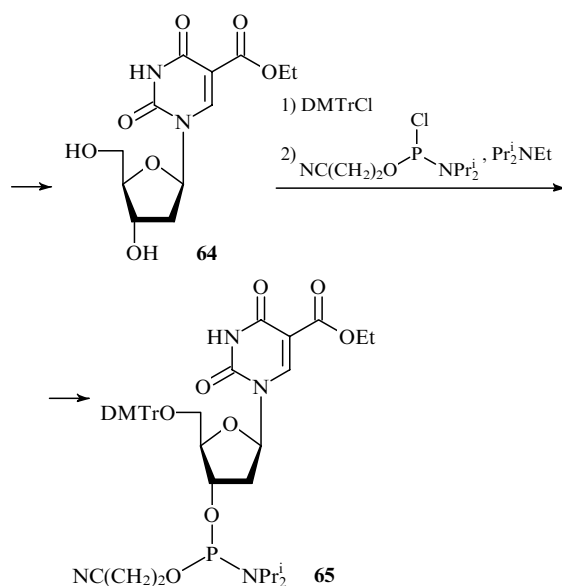
Oligonucleotides with electrophilic groups within the chain are especially preferred in molecular biology studies. This type of modification seems to hold great promise, since it leaves the ends of the oligomeric chain free, which allows incorporation of a radioactive or fluorescent label at the 5'-end and further transformations of the functional group on the polymeric support provided this can selectively be deprotected. A reactive group can be introduced at any predetermined position of the oligonucleotide chain, *viz.*, at a heterocyclic base, at the 2'-position of the carbohydrate fragment or the internucleotide phosphate group. The presence of a reactive functional group in the oligomeric chain influences the stability of DNA duplexes formed by modified oligomers and complementary NA matrices as can be judged from the change in the melting temperatures of such duplexes in comparison with the melting temperatures of non-modified analogues.

1. Oligonucleotides containing a carboxy or aldehyde group in the heterocyclic base

The preparation of oligonucleotides containing a reactive electrophilic group in the heterocyclic base entails the introduction of a modified phosphoramidite derivative, with a carboxy or aldehyde group either blocked or formed upon postsynthetic treatment of the oligomer, into the automated oligonucleotide synthesis. The methyl group of thymidine is modified especially easily. Modified oligonucleotides containing 5-carboxy-2'-deoxyuridine **63** have been synthesised.²⁷

Substitution of the carboxy group for the methyl group of thymidine was carried out by oxidation with 2-methyl-1,4-naphthoquinone (menadione) in the air under irradiation (350 nm, 16 h). Esterification of the carboxy group in compound **63** was carried out in dry ethanol in the presence of carbodiimide and 1-hydroxybenzotriazole without preliminary protection of the hydroxy groups of the carbohydrate residue. The resulting compound **64** was converted into the phosphoramidite derivative **65**, which was further incorporated into the oligonucleotide chain in the automated synthesis. The hydrolysis of the ethyl ester of 5-carboxy-2'-deoxyuridine with simultaneous removal of the remaining protective groups and cleavage of the target product

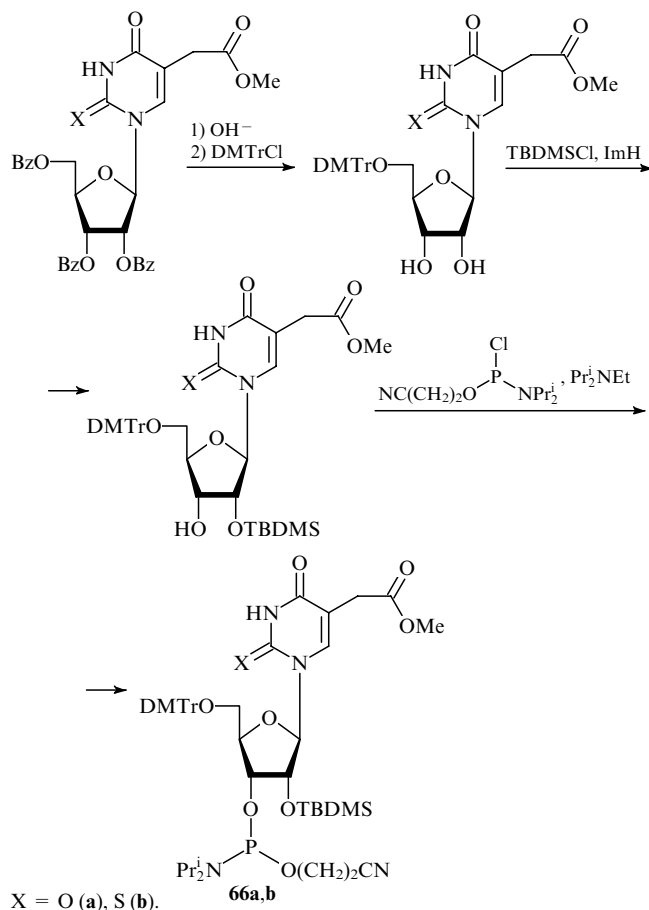




from the solid phase were performed by treatment with 0.2 M sodium hydroxide in methanol.

To investigate the relationship between the structure and biological properties of the anticodon domain of *E. coli* tRNA^{Lys}, Davis *et al.*^{28,29} synthesised modified RNA fragments containing substituents with carboxy groups in position 5 of uridine or N⁶ of adenosine.

The synthesis of modified oligoribonucleotides containing 5-methoxycarbonylmethyluridine or 2-thio-5-methoxycarbonylmethyluridine has been described.²⁸ The starting nucleosides for the synthesis of phosphoramidites **66a,b** were prepared by the Vorbruggen glycosylation³⁰ of the corresponding disilylated 5-methoxycarbonyluracil and 5-methoxycarbonylmethyl-2-thio-



uracil derivatives with 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribofuranose. Subsequent transformations were carried out by standard procedures used in the synthesis of ribonucleoside phosphoramidite derivatives.

Compounds **66a,b** were incorporated into the oligoribonucleotide chain. The oligomers synthesised were deprotected with 10% DBU in methanol (12 h, 25 °C) and Et₃N·3 HF; interestingly, treatment with DBU was accompanied by deprotection of the carboxy group. The structures of the modified oligoribonucleotides were confirmed by mass spectrometry and ¹H NMR spectroscopy. The authors²⁸ call special attention to the fact that incorporation of the 5-methoxycarbonylmethyluridine and 2-thio-5-methoxycarbonylmethyluridine residues into the RNA fragment did not virtually affect the thermal stability of the RNA hairpin.

The same group of American investigators reported the synthesis of oligoribonucleotides containing a modified nucleoside **67**.²⁹ The target phosphoramidite derivative **68** containing protected hydroxy and carboxy groups was synthesised starting from adenosine (**69**) (Scheme 5). Acetylated adenosine reacted with ethyl chlorocarbonate to give the nucleoside **70**. Simultaneous introduction of carboxy and secondary hydroxy groups into compound **70** was effected by treatment with L-threonine. Trimethylsilyl ethyl and *tert*-butyldimethylsilyl protective groups, which can be removed with Et₃N·3 HF after termination of the automated synthesis, were selected for the protection of the incorporated functional groups.

The phosphoramidite derivative **68** was used²⁹ for the synthesis of the modified oligoribonucleotide sequence of the *E. coli* tRNA^{Lys} fragment.

An interesting procedure for the synthesis of oligodeoxyribonucleotides containing 5-methoxycarbonylmethyluridine residues has been described.^{31,32} Condensation of dimethyl-2-bromomethyl fumarate (**72**) and arabinoaminooxazoline **73** synthesised from D-arabinose under the action of cyanamide and 6 M aqueous ammonia (Scheme 6) is the key step in the synthesis of the modified phosphoramidite derivative of 5-methoxycarbonylmethyl-2-deoxyuridine **71**. Treatment of *O*²,2'-anhydro-5-methoxycarbonylmethyluridine formed (**74**) with acetic anhydride in boiling acetic acid results in the opening of the anhydrocycle. Acetyl protective groups are removed by treatment with methanolic ammonia. The resulting modified nucleoside **75** can be used as a starting compound in the oligoribonucleotide synthesis.

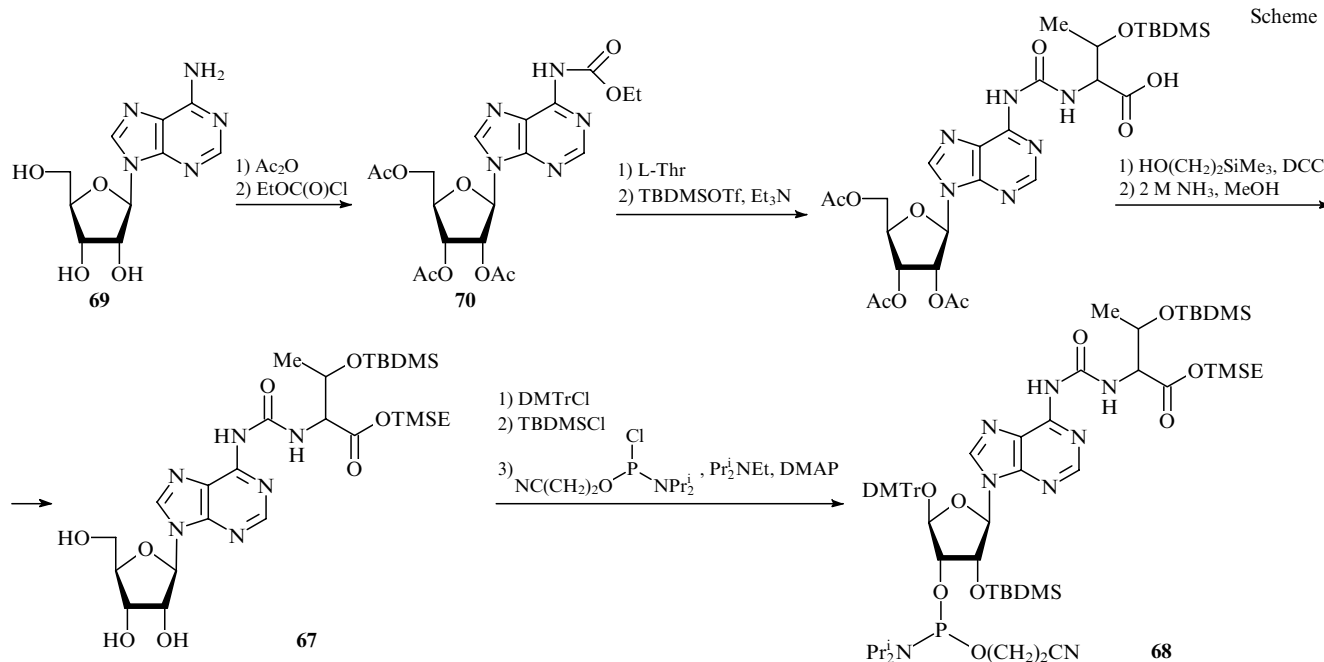
The opening of the anhydrocycle in compound **74** under the action of hydrogen bromide in trifluoroacetic acid or of acetyl bromide in acetonitrile results in 2'-bromo-2'-deoxy-3',5'-di-*O*-acetyl-5-methoxycarbonylmethyluridine (**76**); reduction of the latter with hydrogen over palladium or with tributyltin hydride in the presence of azoisobutyronitrile affords compound **77**. Further transformations of nucleoside **77** into phosphoramidite **71** were carried out using standard methods.

The phosphoramidite derivative **71** was used³² in the synthesis of oligonucleotides containing substituents with protected carboxy groups in position 5 of the heterocyclic base. The presence of a modified fragment in the oligonucleotide chain was confirmed by HPLC of products of enzymatic hydrolysis by snake venom phosphodiesterase and alkaline phosphatase.

These oligonucleotides immobilised on a solid phase were treated with 50% solutions of diamines in ethanol at room temperature to give the corresponding amides. However, it was shown³² that the 5-methoxycarbonylmethyl group (methyl ester) in position 5 is not very reactive: the reaction time with diamines is 12 h.

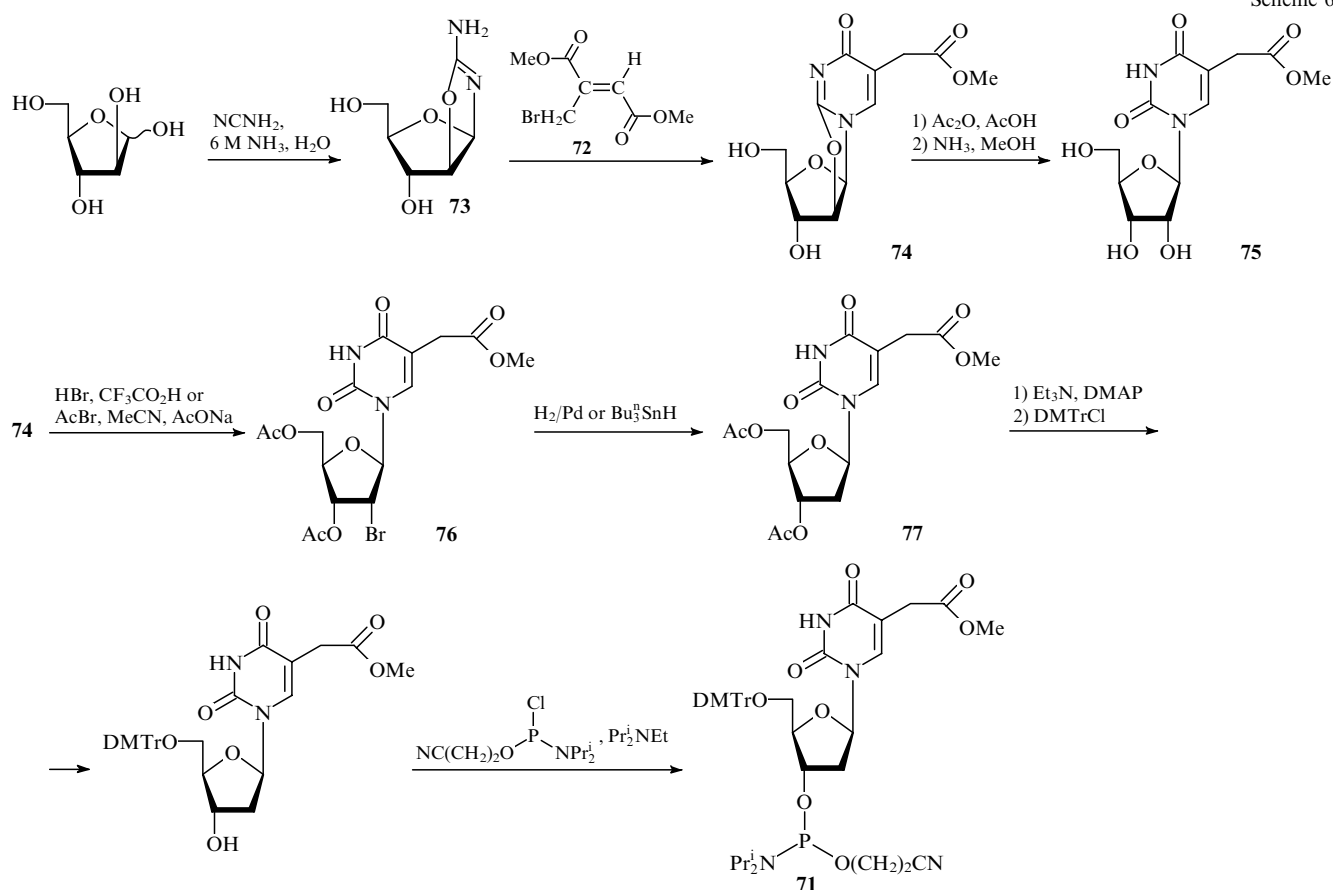
In order to reduce the reaction time with diamines, the same group of Japanese investigators used modified oligonucleotides in which the carboxy group of the substituent at C(5) of the heterocyclic base was protected as a cyanomethyl ester.³³ The target phosphoramidite **78** was prepared from the diacetyl derivative **77**. The key stage in this synthesis is esterification of the free carboxy group of nucleoside **79** with bromoacetonitrile in the

Scheme 5



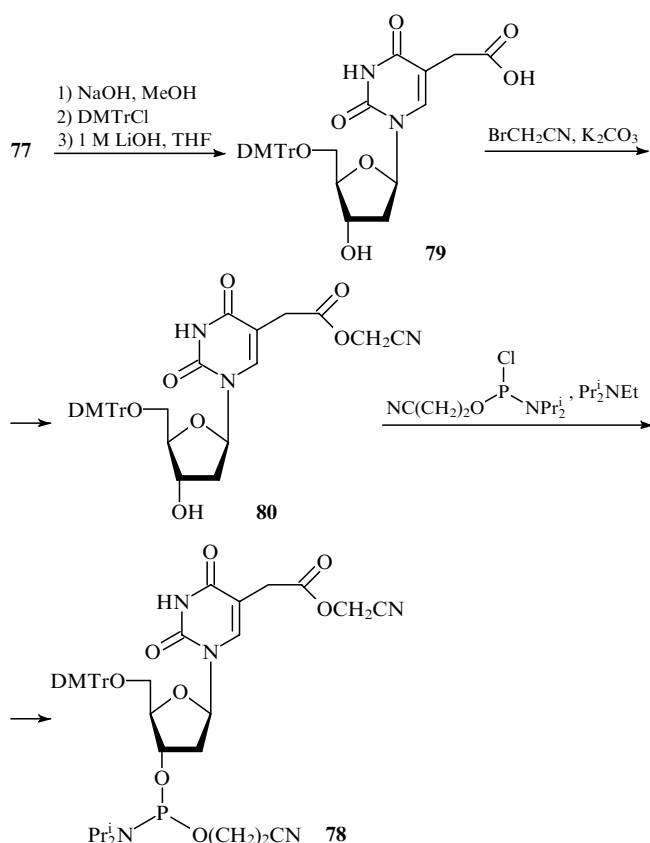
Thr = NH₂CH(CO₂H)CH(OH)Me, Tf = CF₃SO₂, TMSE = Me₃Si(CH₂)₂.

Scheme 6



presence of potassium carbonate in hexamethylphosphoric triamide (HMPA). The yield of the product **80** was 70%. The increase in the reaction time and the use of chloroacetonitrile and triethyl-

amine decreased the yield of the ester **80** to 30% due to the formation of the *N*³-cyanomethyl derivative.

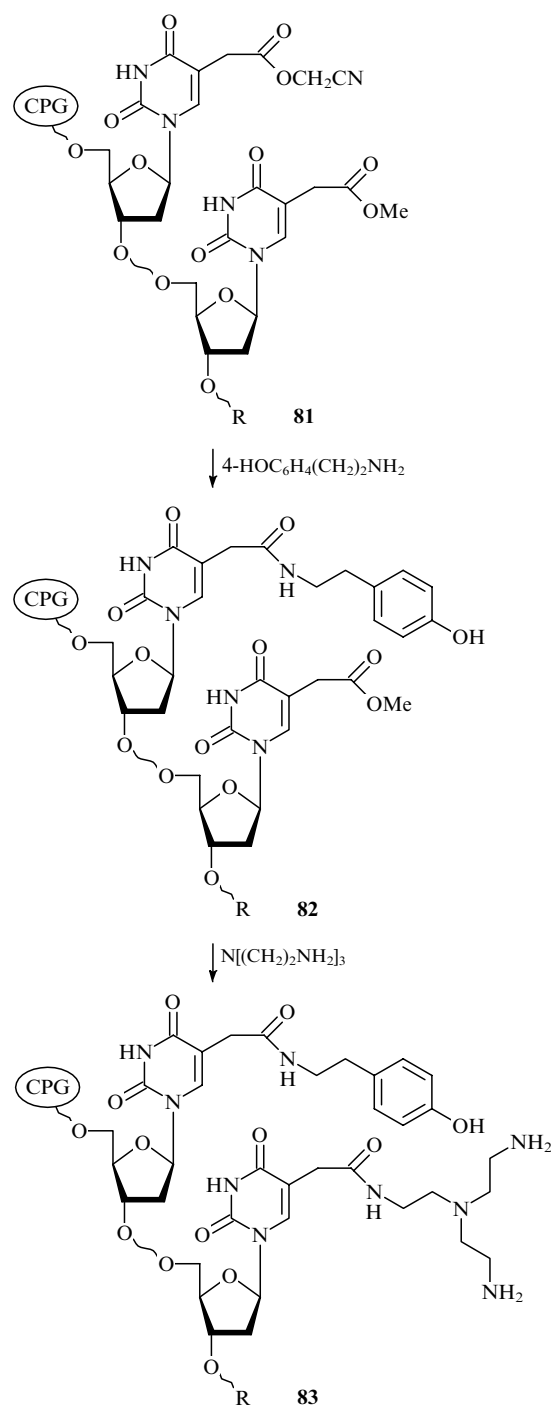


The strategy of synthesis of oligomers with a cyanomethylated carboxy group within the chain is similar to that described in study.³² The presence of a modified unit was confirmed by enzymatic hydrolysis with nuclease P1 and alkaline phosphatase. Aminolysis of the resulting oligonucleotides showed that the cyanomethyl ester is more reactive than the methyl ester and the use of this particular type of oligonucleotides allows the reduction of the reaction time to 1 h, whereas the concentration of the amino component can be decreased to 0.6–1.0 mol litre⁻¹. However, the reaction with tyramine was over only in five days, which can be attributed to poor solubility of this compound in organic solvents and low pK_a of its amino group. It was found that the addition of catalytic amounts of triazole to the reaction mixture significantly increases the rate of aminolysis.

In the synthesis of oligonucleotide conjugates with two different amino components, advantage was taken of the difference in the reactivities of methyl and cyanomethyl esters.³⁴ To this end, the phosphoramidite derivatives **71** and **78** were employed in the synthesis of oligonucleotides **81** containing both 5-methoxycarbonyl and 5-cyanomethoxycarbonylmethyluridine residues.

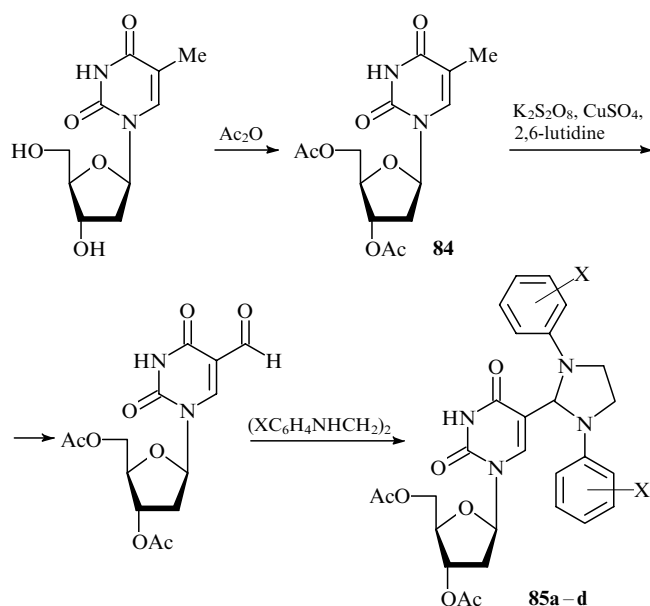
The incorporation of two different functional groups was carried out in the following way. First, the oligonucleotide **81** immobilised on a solid phase was treated with tyramine in the presence of triazole (20 °C, 3 days); in this case, tyramine reacted selectively with the cyanomethyl ester. After washing of the polymer, tris(2-aminoethyl)amine (50% ethanolic solution) was added to the oligonucleotide **82** and complete aminolysis resulted in the derivative **83**. The presence of two different amide groups was confirmed by enzymatic hydrolysis of the isolated oligonucleotide under the action of snake venom phosphodiesterase, alkaline phosphatase and nuclease P1.

The methods for the synthesis of oligonucleotides containing an aldehyde group in the heterocyclic base usually entail mild oxidation of the methyl group of thymine. Thus the synthesis of modified oligomers containing 5-formyl-2'-deoxyuridine residues has been described.^{11,35} The key step in this synthesis was the



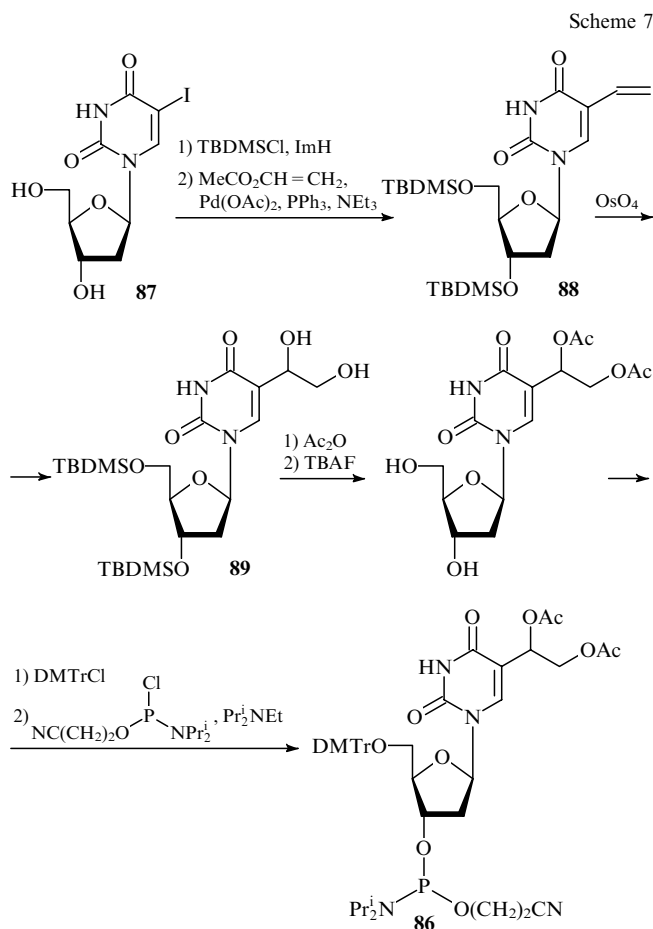
R is a fragment of a protected oligonucleotide chain.

oxidation of the methyl group of protected thymidine **84** to the formyl group under the action of potassium persulfate in the presence of copper sulfate and 2,6-lutidine (yield 52%). It was recommended to use the 1,3-diphenylimidazolidine protective group, which is stable under alkaline conditions and is removed by treatment with an acid, for protection of the aldehyde group.^{36,37} By introducing various electron-withdrawing substituents into the benzene rings of *N,N'*-bis(phenyl)ethylenediamine, one can vary the pK of the amino groups and thus control the ease of cleavage of the protective group under the action of acids.



X = H (**a**), 4-F (**b**), 4-Cl (**c**), 3-Cl (**d**).

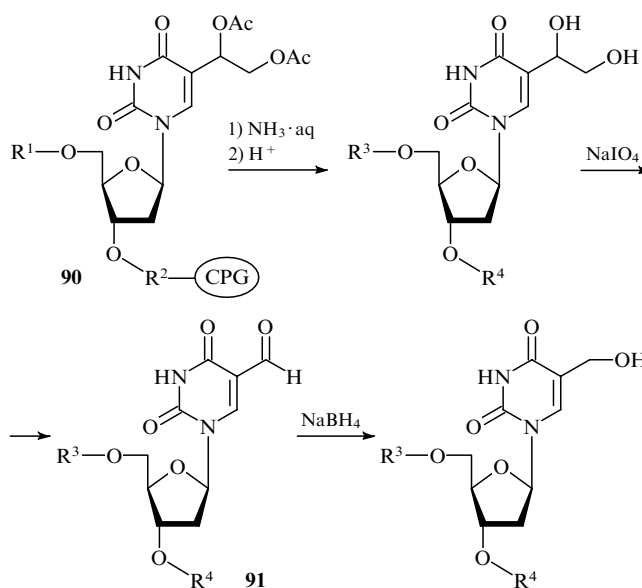
The stabilities of modified nucleosides **85a–d** in acidic media have been investigated. It was shown that the diphenylimidazolidine protective groups do not withstand conditions of the cleavage of the 5'-dimethoxytrityl protective group (3% trichloroacetic acid in dichloromethane, 25 °C). A decrease in the concentration of trichloroacetic acid to 1% helps avoid the deprotection of the introduced carbonyl group in compound **85d**, which has been chosen for the synthesis of the phosphoramidite derivative and subsequent oligonucleotide synthesis. Bis(3-chlorophenyl)-imidazolidine protection was removed in the final step using



80% aqueous acetic acid. The presence of an aldehyde group in modified oligonucleotides was confirmed by enzymatic hydrolysis with a mixture of snake venom phosphodiesterase and alkaline phosphatase. An alternative approach to the synthesis of oligonucleotides containing 5-formyl-2'-deoxyuridine residues has been described.³⁸ In this case, the phosphoramidite derivative of the precursor compound **86** was introduced into the automated nucleotide synthesis. The carbonyl group was generated by post-synthetic treatment of the oligonucleotide fragment containing a *vic*-diol group, with sodium periodate.

5-Iodo-2'-deoxyuridine (**87**), which was further converted into the vinyl derivative **88** by reaction with vinyl acetate in the presence of catalytic amounts of palladium acetate and triphenylphosphine (Scheme 7), has been used as a starting compound for the synthesis of the phosphoramidite **86**.³⁸ The vinyl fragment was oxidised with osmium tetroxide in the presence of *N*-methylmorpholine *N*-oxide and the *vic*-diol group in position 5 of compound **89** was protected by acetyl groups. Phosphoramidite **86** was introduced into the automated oligonucleotide synthesis.

The resulting modified oligomers **90** were treated with concentrated aqueous ammonia to remove acetyl protective groups and to achieve detachment from the solid phase and then the *vic*-diol group was oxidised with sodium periodate (50 equiv. of NaIO₄, 1 min, 0 °C). Compound **91** was reduced with sodium borohydride, which served as an indirect evidence for the internal position of the carbonyl group in the oligonucleotide.

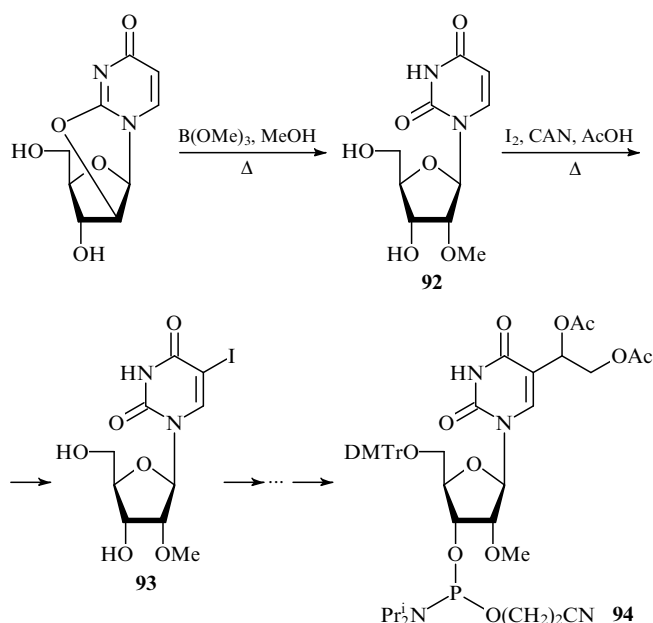


R¹ and R² are fragments of a protected oligonucleotide chain;
R³ and R⁴ are fragments of a deprotected oligonucleotide chain.

The effect of the aldehyde group incorporated into a heterocyclic base on the thermal stabilities of duplexes formed from the oligomer **91** and its complementary natural oligonucleotide, has been studied.³⁸ It was shown that the presence of a formyl group decreases the melting temperatures of the heterogeneous 12- and 6-membered duplexes by 4.1 °C and 5.8 °C, respectively, in comparison with the non-modified analogues.

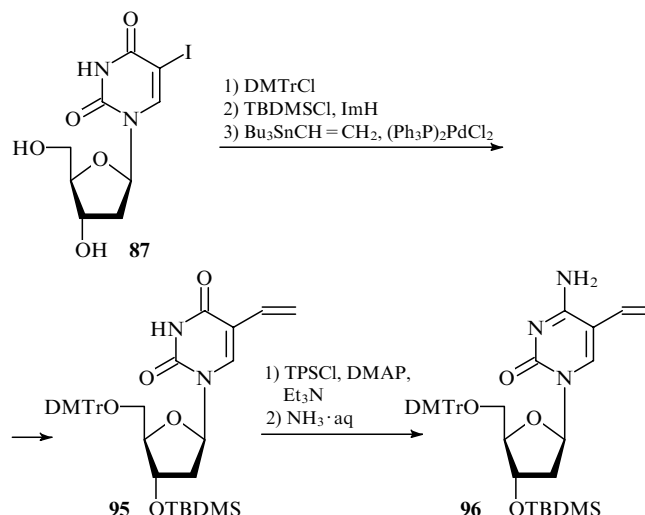
The phosphoramidite derivative **86** was also used in the synthesis of an oligonucleotide sequence containing a recognition site for the transcription factor NFκB.³⁹ It is known⁴⁰ that 5-formyluridine binds covalently to the ε-amino group of lysine. Compound **86** was synthesised according to a scheme similar to that described in³⁸ except that the vinyl fragment was introduced into the derivative **87** using tributylvinyltin in the presence of catalytic amounts of the Pd(MeCN)₂Cl₂ complex instead of vinyl acetate, which made it possible to increase the yield of compound **88** from 68% to 80%.³⁹

Oligomers containing 5-formyl-2'-*O*-methyluridine residues were synthesised in order to investigate the covalent binding of modified oligonucleotides to the transcription factor NF κ b.³⁹ Commercially available *O*²,2'-anhydrouridine was used as a starting compound in this synthesis; the anhydro ring was opened with trimethylborate. Iodination of the resulting derivative **92** afforded modified nucleoside **93**, which was further converted into the phosphoramidite derivative **94**.



After termination of the automated oligonucleotide synthesis and complete deprotection of the functional groups, the *vic*-diol group was oxidised with sodium periodate. It was shown³⁹ that the introduction of a formyl group did not virtually affect the binding of the modified oligomer to the transcription factor.

The above-described approach was also used in the synthesis of oligonucleotides containing 5-formyl-2'-deoxycytidine.⁴¹ The vinyl residue was introduced into the C(5) position of the heterocyclic base **87** by treatment of the protected nucleoside with a mixture of tributylvinyltin and bis(triphenylphosphine)dichloropalladium, which made it possible to markedly reduce the reaction time (from 16 to 1.5 h) and to increase the yield of the target product **95** to 80%. The modified 2'-deoxycytidine **96** was prepared from the protected uridine **95** by activation of the



TPSCl = 2,4,6- $\text{Pr}_3\text{C}_6\text{H}_2\text{SO}_2\text{Cl}$.

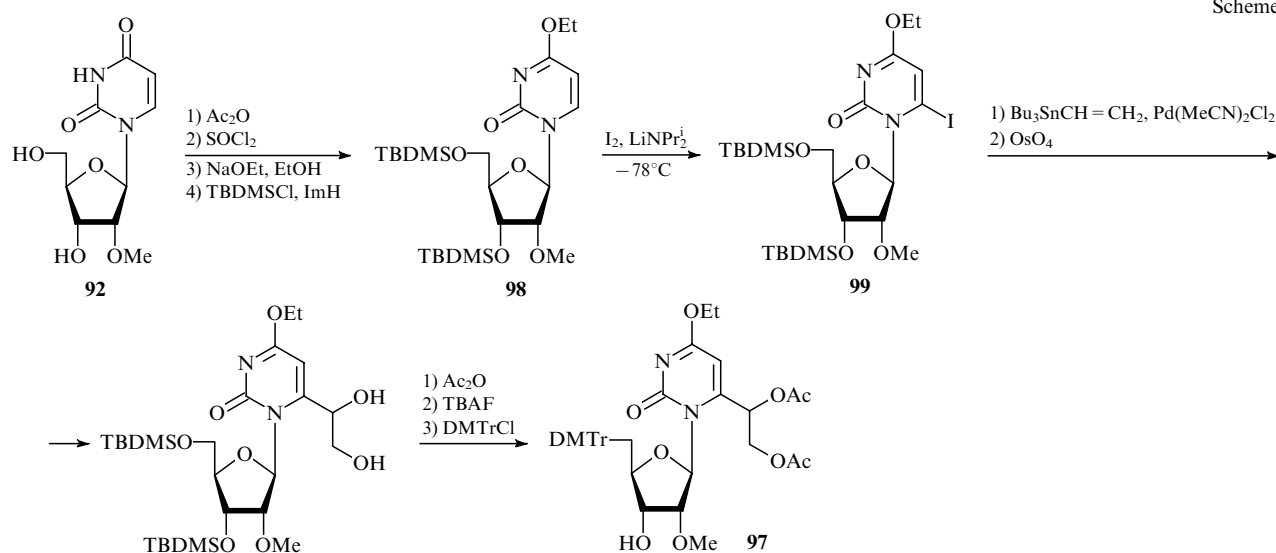
4-oxo group with 2,4,6-triisopropylbenzenesulfonyl chloride and subsequent interaction of the intermediate compound with ammonia. In compound **96**, the vinyl group was oxidised, the exocyclic amino group and the hydroxy groups of the *vic*-diol formed were simultaneously protected and the 3'-hydroxy group was selectively deprotected. The nucleoside formed was used for the preparation of the corresponding phosphoramidite derivative incorporated into the oligonucleotide chain.

After deprotection of the oligonucleotides and oxidative cleavage of the *vic*-diol group with sodium periodate, some physicochemical properties of the synthetic oligomers, *e.g.*, pK_a of the 5-formyl-2'-deoxycytidine residue and the melting temperatures of the DNA duplexes formed by the modified oligonucleotides and the complementary NA matrices, were established. It was shown⁴¹ that the introduction of the carbonyl function had virtually no effect on the thermal stability of the modified duplex.

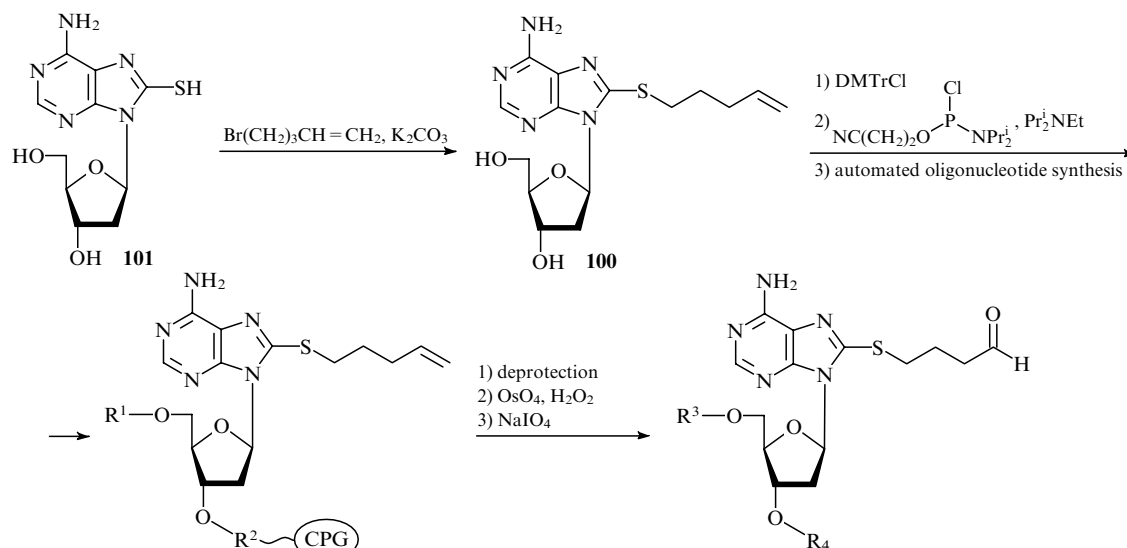
Oligomers containing 6-formyl-2'-*O*-methylcytidine fragments were synthesised in order to investigate the DNA-binding domain of the protooncogen *c-myc*.⁴² Since 6-(1,2-diacetoxyethyl)-2'-deoxyuridine is unstable even at room temperature,³⁸ its protected analogue, *viz.*, 1-6-(1,2-diacetoxyethyl)-[4-ethoxy-2-oxo-1,2-dihydropyrimidin-1-yl]-2'-*O*-methyl-5'-*O*-dimethoxytrityl- β -D-ribofuranoside (**97**), was used as a precursor of 6-formyl-2'-*O*-methylcytidine.⁴²

2'-*O*-Methyluridine (**92**), in which the acylation of the hydroxy groups of the carbohydrate fragment was followed by the activation of the 4-oxo group with thionyl chloride (Scheme 8), was used

Scheme 8



Scheme 9



R^1 and R^2 are fragments of a protected oligonucleotide chain; R^3 and R^4 are fragments of a deprotected oligonucleotide chain.

as a starting compound in the synthesis of nucleoside **97**. Subsequent treatment of the protected 2'-*O*-methyluridine product with sodium ethoxide in ethanol and *tert*-butyldimethylsilyl chloride yielded the derivative **98**. Treatment of nucleoside **98** with iodine in the presence of lithium diisopropylamide at -78°C afforded the corresponding protected 6-iodouridine **99**. The introduction of a vinyl fragment into the derivative **99** and its subsequent oxidation with osmium tetroxide in the presence of *N*-methylmorpholine *N*-oxide was carried out as described previously.³⁸

After acetylation of hydroxy groups, removal of *tert*-butyldimethylsilyl protection and introduction of dimethoxytrityl protective groups, compound **97** was used for the preparation of the corresponding phosphoramidite derivative which was incorporated into the oligonucleotide chain by the automated synthesis. Standard postsynthetic treatments and oxidation with sodium periodate afforded target oligomers containing 6-formyl-2'-*O*-methylcytidine.

It was shown⁴² that the introduction of one modified fragment decreased the melting temperature of a 23-membered DNA duplex in comparison with its natural analogue by 6°C .

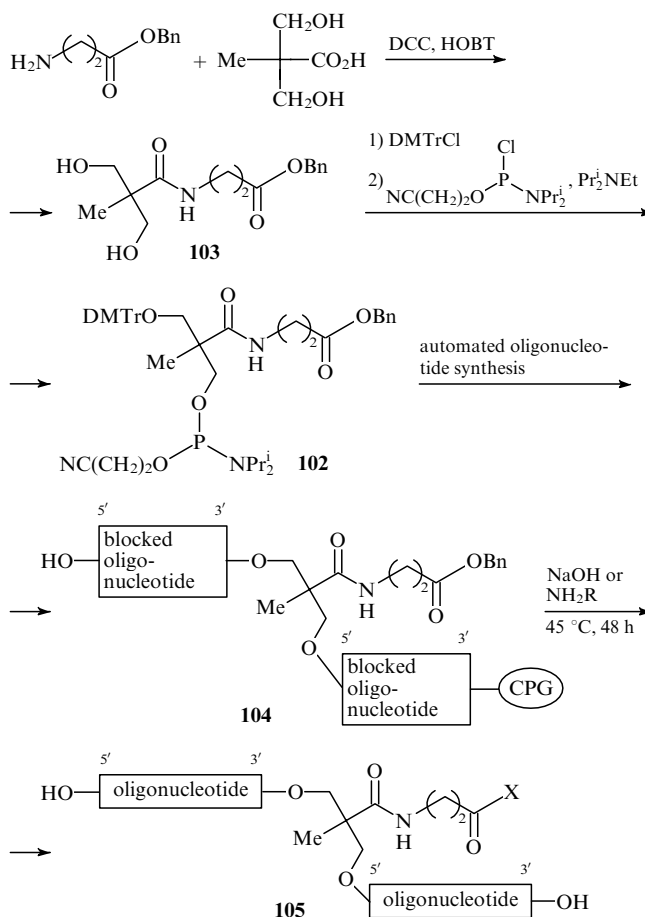
An original approach to the synthesis of oligonucleotides containing an aldehyde group in position 8 of deoxyadenosine has been described.⁴³ This approach involves the introduction of the phosphoramidite derivative of compound **100** containing a pent-4-enylthio group and prepared starting from thiol **101**, into an automated synthesis (Scheme 9).⁴⁴ The oxidation of the double bond of the pent-4-enyl residue was carried out after termination of the synthesis of the oligonucleotide with osmium tetroxide in the presence of hydrogen peroxide and *N*-methylmorpholine *N*-oxide in the dark at 25°C . These conditions excluded the destruction of the modified oligomer and the unwanted oxidation of sulfur.

The *vic*-diol group was converted into the aldehyde group by oxidation with sodium periodate (100 equiv.); the presence of this group was confirmed by reactions of the modified oligonucleotide with aminoxy compounds and ^1H NMR spectroscopic data.

Conjugates of modified oligonucleotides with fluorescent labels have been prepared.⁴⁵ It was shown that the introduction of one heterocyclic base with an aldehyde group localised in a C(3) linker decreases the melting temperature of an 11-mer duplex by 14°C .

2. Oligonucleotides containing a carboxy or aldehyde group in a non-nucleotide fragment

Endo *et al.*⁴⁶ have prepared a non-nucleoside phosphoramidite **102** containing a protected carboxy group which can be incorporated into the chain or be attached to the 5'-end of the oligonucleotide. The key step in the synthesis of compound **102** is condensation of benzyl 4-aminobutyrate with 2,2-bis(hydroxymethyl)propionic acid in the presence of DCC and HOBT resulting in compound **103**. Phosphoramidite **102**, which was further used for the synthesis of model oligonucleotides **104** containing an

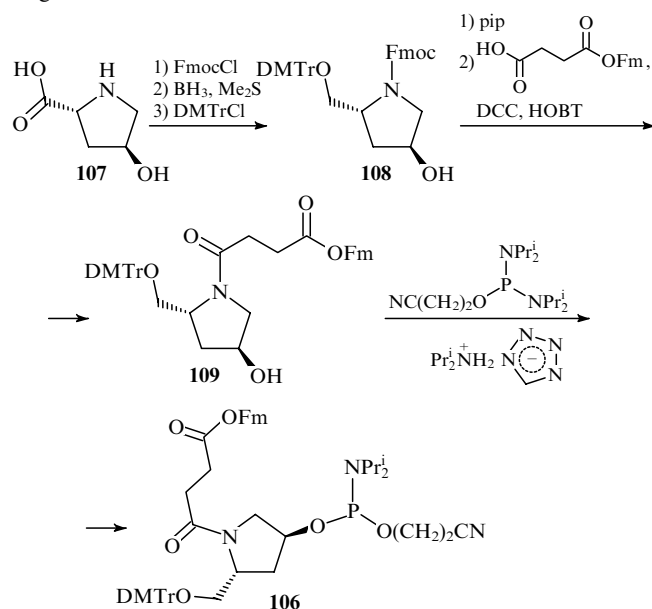


$\text{X} = \text{OH}$ or NHR .

internal protected carboxy group, was obtained by protection of one primary hydroxy group of the diol **103** with an equimolar amount of dimethoxytrityl chloride and subsequent phosphitylation of the tritylation product. Conjugates of modified oligomers **104** with various amines and diamines were synthesised using the solid-phase method. It was shown⁴⁶ that treatment of the oligonucleotide **104** immobilised on a polymeric support with a solution of alkyl amine in an organic solvent results in the quantitative formation of the conjugate **105** ($X = \text{NHR}$).

An alternative procedure for the introduction of a protected carboxy group into the oligonucleotide was proposed by Hebert *et al.*⁴⁷ who synthesised model dinucleoside phosphates from the phosphoramidite derivative **106**.

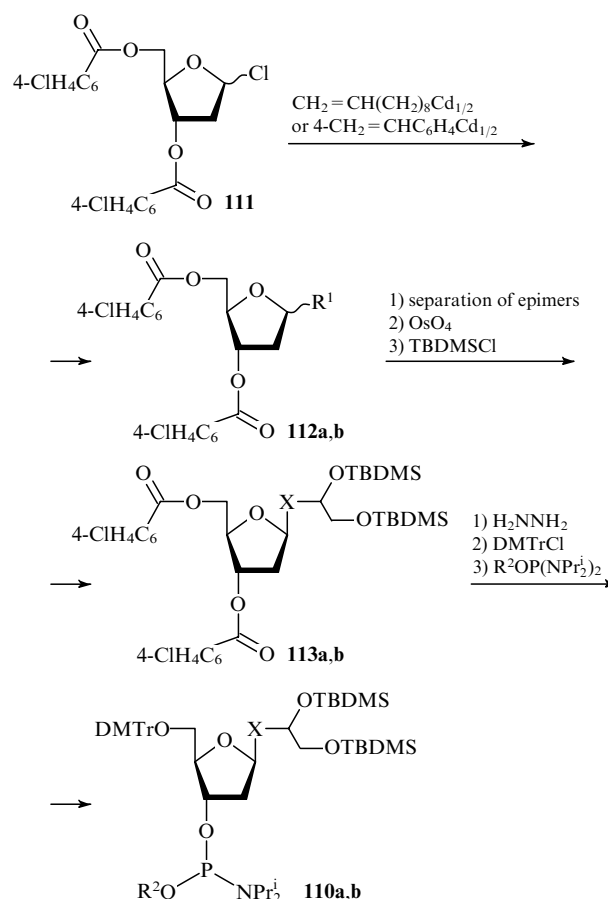
The amino and carboxy groups in 4-hydroxy-L-proline (**107**) were protected, which has been used as a starting compound in the synthesis of phosphoramidite **106**; deprotection of the amino group in the resulting compound **108** with piperidine and subsequent acylation with fluorenylmethyl hydrogen succinate in the presence of DCC and HOBT led to the amide **109**. The derivative **109** was then phosphitylated with the formation of the target phosphoramidite **106** which was employed in the oligonucleotide synthesis. The yield for the step of attachment of the modified fragment was 97%.



Fm is fluorenylmethyl; pip is piperidine.

The use of other acylating reagents for the treatment of compound **108** with a deprotected amino group has made it possible⁴⁷ to prepare dinucleoside phosphates containing various functional groups.

The introduction of an aldehyde group into the oligonucleotide chain was carried out by a group of Belgian investigators^{48,49} who used non-nucleoside phosphoramidites **110a,b** containing a *vic*-diol fragment for automated synthesis. The phosphoramidite derivative **110a** was prepared from commercially available deoxyribofuranosyl chloride **111**. The introduction of the dec-9-enyl fragment was carried out under the action of the corresponding organocadmium compound⁵⁰ with subsequent separation of the epimers **112a** ($R:S = 65:35$). Despite the fairly high yield of the *R*-epimer, further modification was performed on the *S*-epimer, since its configuration corresponded to the β -configuration of the anomeric centre of natural nucleosides. As a consequence, modified oligonucleotides synthesised with the use of the *S*-epimer can form stable duplexes with mRNA. The *S*-epimer **112a** was oxidised with osmium tetroxide in the presence of *N*-methylmorpholine *N*-oxide; the hydroxy groups in the resulting *vic*-diol derivative were protected as *tert*-butyldimethylsilyl ethers eventually resulting in the derivative **113a**.



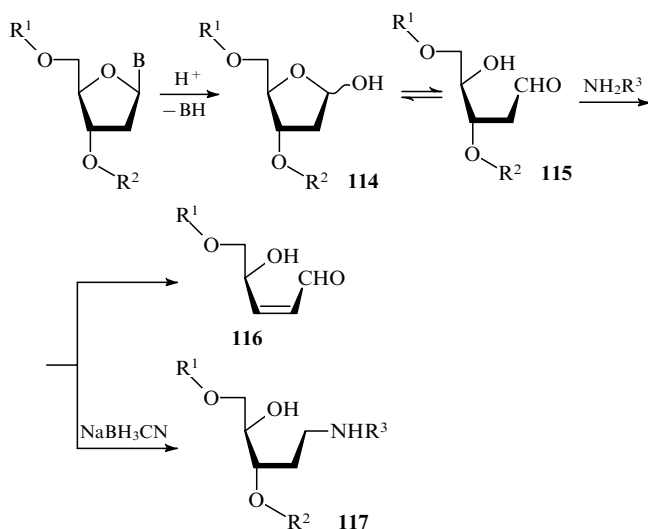
$R^1 = (\text{CH}_2)_8\text{CH}=\text{CH}_2$ (**112a**), $\text{C}_6\text{H}_4\text{CH}=\text{CH}_2$ -4 (**112b**);
 $R^2 = (\text{CH}_2)_2\text{CN}$ (**110a**), Me (**110b**);
 $X = (\text{CH}_2)_8$ (**110a**, **113a**), 4-C₆H₄ (**110b**, **113b**).

Compound **113b** was prepared in a similar way. In this compound, the protected *vic*-diol group is located in the *para*-position of the benzene ring, which was used as an analogue of the heterocyclic base of the nucleoside. Removal of *p*-chlorobenzoyl protection and selective incorporation of dimethoxytrityl protective groups with subsequent phosphitylation of compounds **113a,b** gave the phosphoramidite derivatives **110a,b**, which were introduced into the automated oligonucleotide synthesis.

After deprotection of the modified oligonucleotides, the *vic*-diol groups were oxidised with sodium periodate. The carbonyl-containing oligonucleotides were used^{48,49} for the synthesis of conjugates with biotin and fluorescent labels.

3. Oligonucleotides containing an aldehyde group in the apurine site

The formation of the apurine (AP) site is a simpler and, therefore, more popular procedure for the introduction of the aldehyde group into the oligonucleotide chain. Elimination of the purine base from the oligonucleotide occurs under the action of strong acids (HCl, HCOOH). In the oligomeric chain, the apurine fragment exists as three tautomers, *viz.*, α - and β -anomeric forms of deoxyribofuranose **114** (1:1) and the aldehyde-containing structure **115** (~1%).^{51,52} Depending on the nature and concentration of the amine, its addition to the AP-containing oligonucleotide leads to either the scission of the chain due to β -elimination of 3'-phosphate and the formation of the derivative **116**,^{51,53-55} or the addition of the corresponding amine and the formation of the Schiff base which is reduced to the conjugate **117** upon treatment with sodium cyanoborohydride (pH 5.0).^{51,52,56,57}

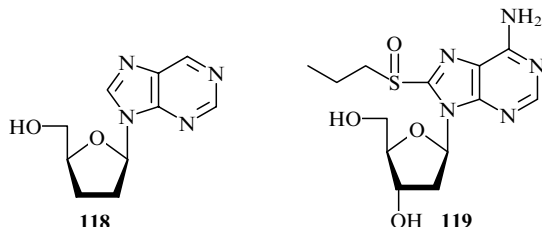


B is purine heterocyclic base;

R¹ and R² are fragments of an oligonucleotide chain.

The rate of acid hydrolysis of the *N*-glycosidic bond, which depends on pH, plays a crucial role in the formation of the apurine site. It is known⁵⁸ that among other natural nucleosides, the highest apurinisation rate ($7.3 \times 10^{-2} \text{ min}^{-1}$) is manifested by 2'-deoxyadenosine. The half-transformation time upon treatment of 2'-deoxyadenosine with 30 mM HCl at 37 °C is 9.5 min. Most frequently, apurinisation of an oligonucleotide is effected by treatment with 80% formic acid (20 °C, 30 min) or 0.2 M hydrochloric acid (37 °C, 90 min).⁵⁶

To avoid drastic acid conditions for the formation of the apurine site, it was proposed⁵¹ to use the artificial adenosine analogue, dideoxynebularin (**118**).



The apurinisation rate constant of this unit within the oligonucleotide chain upon treatment with 30 mM HCl (37 °C, 13 min) is $23.7 \times 10^{-2} \text{ min}^{-1}$, the half-transformation time is 2.9 min. However, the absence of a 3'-hydroxy group in the structure of the monomeric fragment **118** makes impossible its use for the formation of the intrachain AP site.

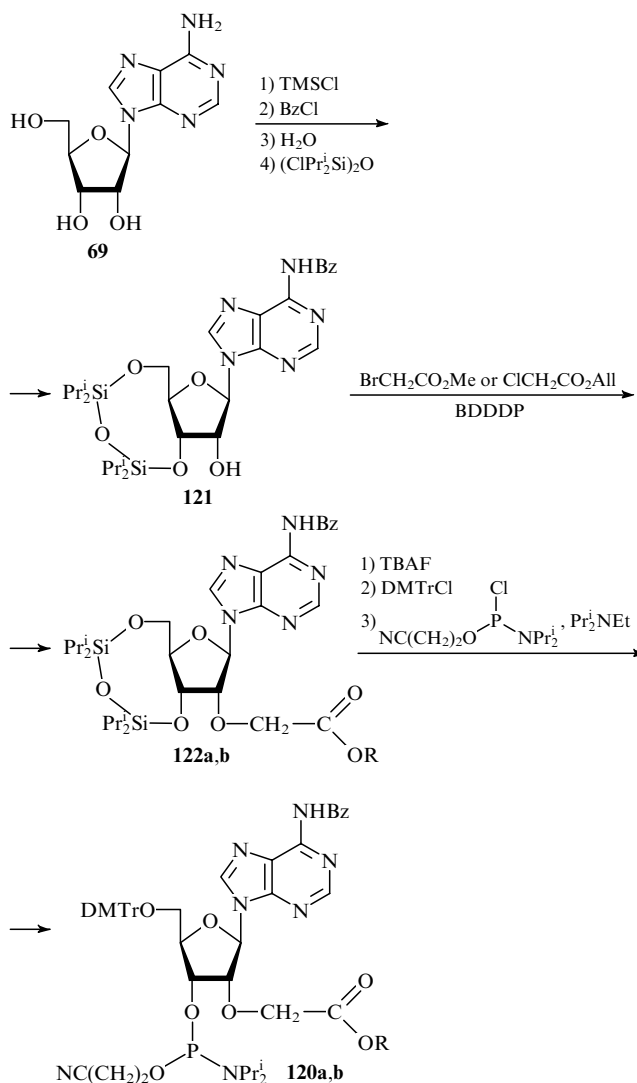
Synthesis of oligonucleotides containing 8-propylsulfinyl-2'-deoxyadenosine residues **119** obtained by the oxidation of the corresponding sulfide⁴⁴ has been described.⁵⁷ Apurinisation of this unit was carried out at pH 3 (65 °C), which was followed by the preparation of modified oligonucleotide conjugates with fluorescent labels.

4. Oligonucleotides containing a carboxy or aldehyde group in the 2'-position of the carbohydrate fragment

In the majority of cases, modification of the 2'-position does not result in any significant destabilisation of the DNA duplex. It should be noted, however, that the synthesis of oligonucleotides containing a reactive group in the carbohydrate residue is the most tedious procedure, which requires the selection of an orthogonal system of protective groups.

Obviously, the 2'-carboxy group should be blocked in the course of the automated synthesis. The methyl ester commonly used for this purpose is removed with sodium hydroxide in H₂O or methanol.

Modified oligonucleotides containing 2'-*O*-carboxymethyl groups protected with methyl or allyl esters have been synthesised.⁵⁹ The latter can selectively be removed by treatment with a Pd(0) complex in the presence of morpholine which facilitates further transformations of the carboxymethyl group on solid supports in organic media. Modified phosphoramidite derivatives **120a,b** were synthesised starting from adenosine (**69**). The key step in this synthesis was the alkylation of the 2'-position of the carbohydrate residue of protected adenosine **121** with methyl bromoacetate or with allyl chloroacetate in the presence of a strong organic base, *e.g.*, *tert*-butylimino-2-diethylamino-1,3-dimethylperhydro-1,3,2-diazaphosphorine (BDDDP).⁶⁰ The use of alkali metal hydrides as a base^{61, 62} has several disadvantages, *e.g.*, formation of side products, fairly low yields ($\leq 18\%$), *etc.*, and significantly restricts the selection of protective groups. Alkylation in the presence of BDDDP leads to the formation of the target compounds **122a,b** in 35%–40% yields. Deprotection of 3'- and 5'-hydroxy groups, selective introduction of dimethoxytrityl protection and further phosphitylation of nucleosides **122a,b** yielded the phosphoramidite derivatives **120a,b**, which were further incorporated into the oligonucleotide chain in the course of the automated synthesis.

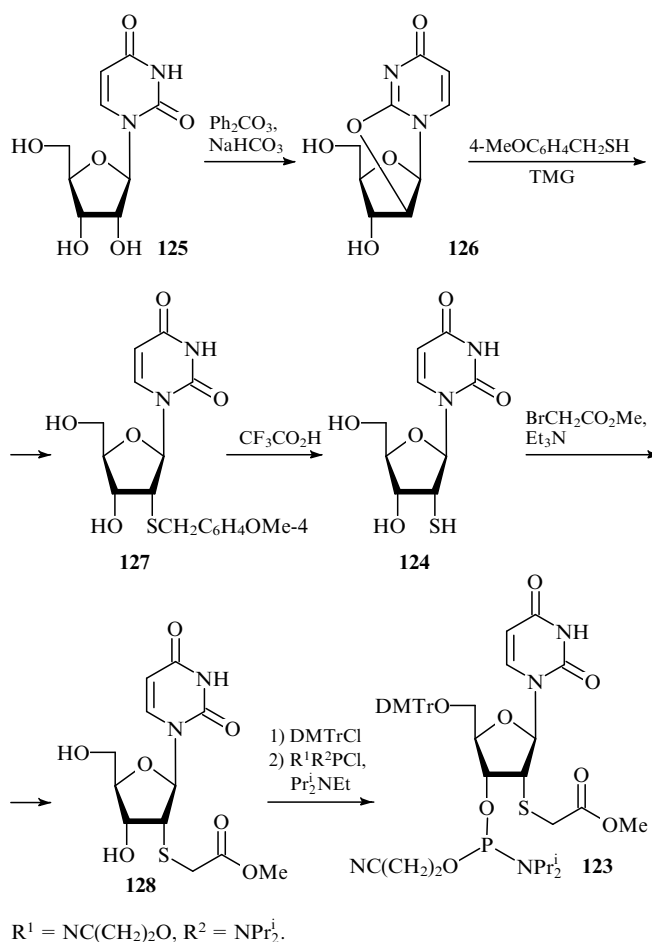


R = Me (a), All (b).

On completion of the synthesis, methyl ester is saponified with 2 M sodium hydroxide (20 °C, 30 min), while allyl ester is selectively removed by treatment with tetrakis(triphenylphosphine)-palladium in the presence of morpholine. The reactivity of the incorporated 2'-*O*-carboxy group was confirmed by reaction with

ethylenediamine in aqueous solution in the presence of water-soluble carbodiimide.

An original approach to the preparation of oligonucleotides containing a 2'-carboxymethylthio group has been developed.⁶³ The phosphoramidite derivative of 2'-methoxycarbonylmethylthio-2'-deoxyuridine **123** obtained from 2'-mercapto-2'-deoxyuridine (**124**) was introduced into the automated oligonucleotide synthesis.



The synthesis of 2'-mercapto-2'-deoxyuridine (**124**) from uridine **125** was carried out *via* the cyclic nucleoside **126** using

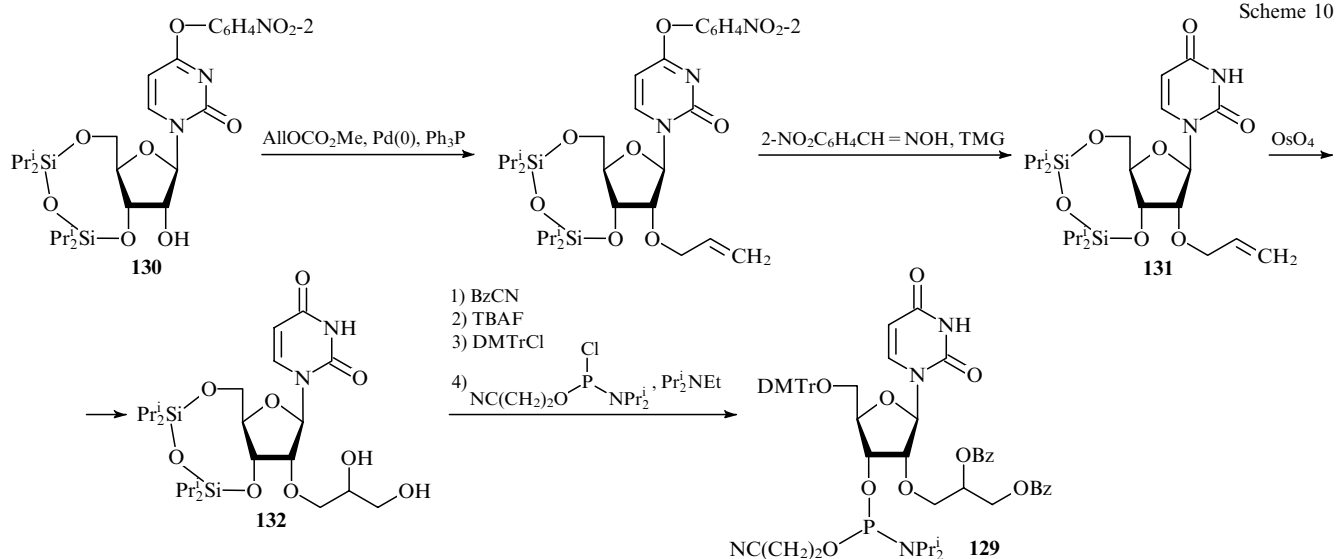
the opening of the anhydro ring with 4-methoxytoluenethiol in the presence of tetramethylguanidine with subsequent treatment of the derivative **127** with trifluoroacetic acid. The alkylation of compound **124** was carried out using methyl bromoacetate without any preliminary protection of the heterocyclic base and the carbohydrate residue. The yield of 2'-methoxycarbonylmethylthio-2'-deoxyuridine (**128**) was 73%; the reaction was accompanied by the formation of trace amounts of the side product, *viz.*, the N^3 -alkylated nucleoside.⁶³

The yield of the model dinucleoside phosphate dU^*pT (dU^* is a modified deoxyuridine fragment) during the introduction of the modified fragment **123** was 60%–70%. This fact is attributed to the steric hindrances due to the presence of a bulky substituent in the 2'-position. The solid-phase method was used in the synthesis of conjugates of the model compound dU^*pT with aliphatic amines (yield 50%).

Syntheses of 15-mer 2'-modified oligonucleotides with heterogeneous composition have been carried out; the presence of the modified unit was confirmed by enzymatic hydrolysis with a mixture of snake venom phosphodiesterase and alkaline phosphatase.

The synthesis of oligonucleotides containing an aldehyde group in the 2'-position of the carbohydrate residue has been developed.^{59, 64} In this synthesis, the phosphoramidite derivative **129** containing a protected *vic*-diol fragment was used as a modified unit. The key steps in the synthesis of compound **129** include alkylation of the 2'-position of the protected uridine **130** with allyl methyl carbonate in the presence of $\text{Pd}(0)$ and triphenylphosphine and subsequent oxidation of compound **131** with osmium tetroxide in the presence of *N*-methylmorpholine *N*-oxide to give the derivative **132**. These authors have selected the conditions where the oxidation of 2'-*O*-allylic ether occurred selectively, without the involvement of the double bond of the heterocyclic base. The hydroxy groups of the *vic*-diol fragment of the modified uridine **132** were protected as benzoates (Scheme 10).

The phosphoramidite derivative **129** was used in the synthesis of modified oligonucleotides. The benzoyl protective groups of the 2'-*vic*-diol fragment were removed by standard postsynthetic treatments; the aldehyde function was generated by treatment with sodium periodate. Model conjugates of modified oligonucleotides with 2,4-dinitrophenylhydrazine, methyl ester of methionine⁶⁴ and some compounds containing aminoxy, hydrazino, hydrazido or 1,2-aminothio groups have been prepared.⁶⁵



V. Conclusion

At present, the preparation of oligonucleotide conjugates with various molecules holds great promise for directed changes in physicochemical and substrate properties of nucleic acid fragments, which is a prerequisite for their application in molecular biological and clinical studies. Synthesis of conjugates wherein the reactive group of the oligonucleotide reacts selectively with the ligand, whereas other functional groups of the reacting molecules remain unaffected, seems to be an optimum procedure for the synthesis of conjugates. Such reactions include interaction of carboxy or aldehyde groups of modified oligonucleotides with amino compounds.

The formation of conjugates with amide bonds requires the activation of the carboxy group. The choice of an activating reagent depends, in particular, on the composition of the reaction medium. In aqueous solutions, water-soluble carbodiimide is most commonly used, while the syntheses performed in organic media utilise preferably condensation reagents based on phosphonium or uronium salts. Each of these variants has disadvantages of its own. In the former case, heterocyclic fragments of nucleic acids react with carbodiimide involving the polarised double bond C=N. In the latter case, conjugation in organic media often poses the problem of solubility of the reacting molecules. For this reason, very often the ligand molecule is added to an oligonucleotide immobilised on an insoluble polymeric support. Further treatment of the conjugate with ammonia or alkali aimed at the cleavage of the bond between the oligonucleotide and the polymer and deprotection of functional groups may lead to the destruction of the non-nucleotide fragment of the hybrid molecule.

In the case of oligonucleotides containing an aldehyde group, additional activation of the electrophilic group is unnecessary and the reaction can be carried out in water-organic media, which helps overcome the problem of solubility of the interacting molecules. The possibility of using hydrazines, hydrazides, hydroxylamines and compounds containing 1,2-aminothiol groups along with amines for the synthesis of conjugates is an indisputable advantage of oligonucleotides containing aldehyde groups. Therefore, the use of modified oligonucleotides with aldehyde groups is synthetically more preferable as can be judged from the increasing number of publications on this subject.

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